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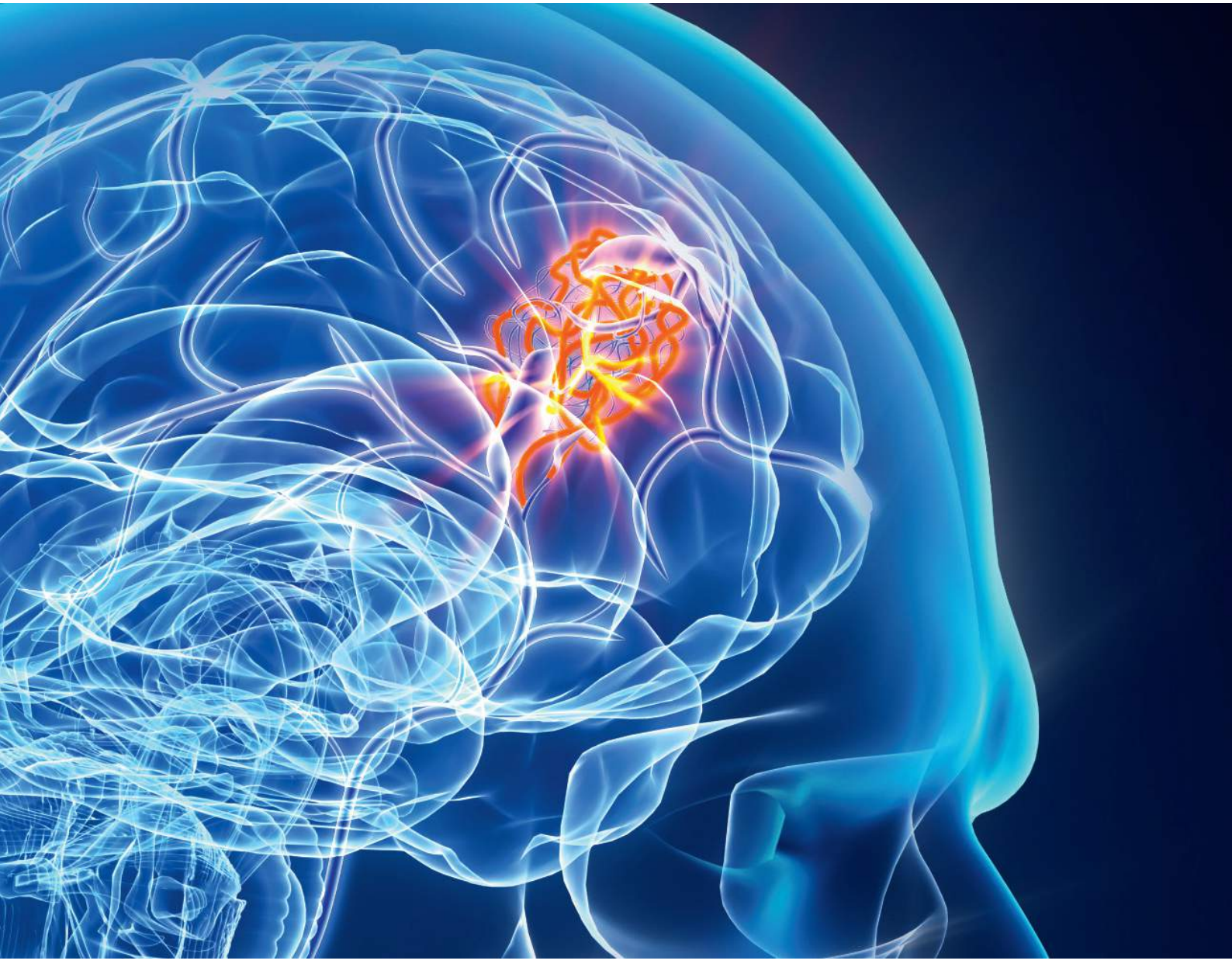
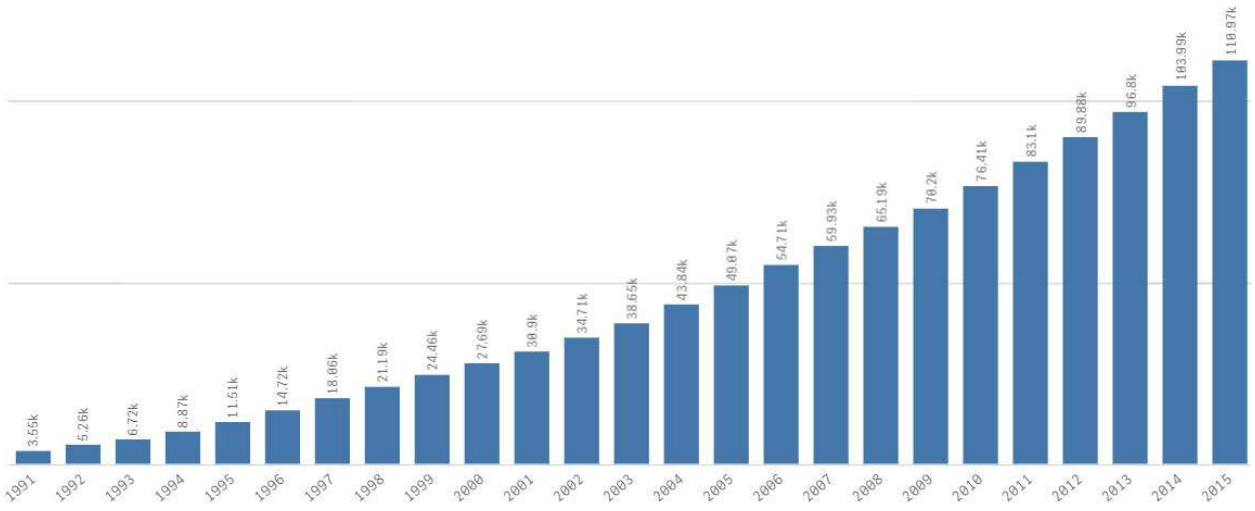


Vascular Malformation Bibliography
2006 - 2016

VASCULAR MALFORMATIONS

Includes Gamma Knife-focused abstracts posted to PubMed during 2006 to 2016.



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Anatomical Location

Neurosurgery.2013;Epub 2013/07/23

Radiosurgery for Primary Motor and Sensory Cortex Arteriovenous Malformations: Outcomes and the Effect of Eloquent Location

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BACKGROUND: Eloquent intracranial arteriovenous malformations (AVMs) located in the primary motor or somatosensory cortex (PMSC) carry a high risk of microsurgical morbidity. OBJECTIVE: To evaluate the outcomes of radiosurgery on PMSC AVMs and compare them to radiosurgery outcomes in a matched cohort of non-eloquent, lobar AVMs. METHODS: Between 1989 and 2009, 134 patients with PMSC AVMs underwent Gamma Knife radiosurgery with median radiographic and clinical follow-up of 64 and 80 months, respectively. Seizure (40.3%) and hemorrhage (28.4%) were the most common presenting symptoms. Pre-radiosurgery embolization was performed in 33.6% of AVMs. Median AVM volume was 4.1 cc (0.1-22.6 cc) and prescription dose was 20 Gy (7-30 Gy). Cox regression analysis was performed to identify factors associated with obliteration. RESULTS: The overall obliteration rate, including MRI and angiography, following radiosurgery was 63%. Obliteration was achieved in 80% of AVMs with volume less than 3 cc compared to 55% for AVMs greater than 3 cc. No prior embolization (P=0.002) and a single draining vein (P=0.001) were independent predictors of obliteration on multivariate analysis. The annual post-radiosurgery hemorrhage risk was 2.5%. Radiosurgery-related morbidity was temporary and permanent in 14% and 6% of patients, respectively. In comparing PMSC AVMs with matched non-eloquent, lobar AVMs, the obliteration rates and clinical outcomes following radiosurgery were not statistically different. CONCLUSION: For patients harboring PMSC AVMs, radiosurgery offers a reasonable chance of obliteration with a relatively low complication rate. Eloquent location does not appear to confer the same negative prognostic value for radiosurgery that it does for microsurgery.

Neurosurgery.2011;Epub 2011/12/22

Stereotactic Radiosurgery for Arteriovenous Malformations Located in Deep Critical Regions

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BACKGROUND: Radiosurgery is widely used to treat deep eloquent arteriovenous malformations (AVMs). OBJECTIVE: To evaluate how anatomical location, AVM size and treatment parameters define outcome. METHODS: Retrospective analysis of 356 thalamic/basal ganglia and 160 brainstem AVMs treated with gamma knife radiosurgery. RESULTS: Median volume was 2cm (range 0.02-50) for supratentorial and 0.5cm (0.01-40) for brainstem AVMs; the marginal treatment doses were 17.5-25Gy. After single treatment, obliteration was achieved in 65% of the brainstem, in 69% of the supratentorial, and 40% of the peritectal AVMs. Obliteration of lesions <4cm was better in the brainstem (70%) and in the supratentorium (80%), but not in the peritectal region (40%). Complications were rare (6-15%) and mild (</=MRS2). Rebleed rate increased with size, but was not higher than before treatment. AVMs
>4cm in the brainstem were treated with unacceptable morbidity and low cure rate. Obliteration of large supratentorial AVMs was 65-47% with more complications >/=MRS3. Repeat radiosurgical treatment led to obliteration in 66% of the cases with minor morbidity. CONCLUSION: Deep eloquent AVMs <4cm can be treated safely and effectively with radiosurgery. Obliteration of peritectal AVMs is significantly lower after a single treatment. However, morbidity is low and repeat treatment leads to good obliteration. Radiosurgical treatment >4cm in the brainstem is not recommended. Supratentorial deep AVMs >8cm can be treated with radiosurgery with higher risk and lower obliteration rate.
However, these lesions are difficult to treat with other treatment modalities and a 50% success rate makes radiosurgery a good alternative even in this challenging group.

Acta Neurochirurgica.2009;151(12):1575-82. Epub 2009/05/06

Gamma knife radiosurgery for arteriovenous malformations of basal ganglia, thalamus and brainstem--a retrospective study comparing the results with that for AVMs at other intracranial locations

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OBJECTIVE: The objective of this retrospective study was to study the outcome in patients with basal ganglia, thalamus and brainstem (central/deep) arteriovenous malformations (AVMs) treated with gamma knife radiosurgery (GKS) and to compare the results with that for AVMs at other intracranial locations. METHODS AND RESULTS: The results of 53 patients with central AVMs and 255 patients with AVMs at other locations treated with GKS at our center between April 1997 and March 2005 with minimum follow-up of 1 year were analyzed. CENTRAL AVMS: Forty of these 53 AVMs were Spetzler- Martin grade III, 11 were grade IV, and 2 were grade V. The mean AVM volume was 4.3 cm(3) (range 0.1-36.6 cm(3)). The mean marginal dose given was 23.3 Gy (range 16-25 Gy). The mean follow-up was 28 months (range 12-96 months). Check angiograms were advised at 2 years after GKS and yearly thereafter in the presence of residual AVM till 4 years. Presence of a residual AVM on an angiogram at 4 years after radiosurgery was considered as radiosurgical failure. Complete obliteration of the AVM was documented in 14 (74%) of the 19 patients with complete angiographic follow-up. Significantly lower obliteration rates (37% vs. 100%) were seen in larger AVMs (>3 cm(3)) and AVMs of higher (IV and V) Spetzler-Martin grades (28% vs. 100%). The 3- and 4-year actuarial rates of nidus obliteration were 68% and 74%, respectively. Eight patients (15%) developed radiation edema with a statistically significantly higher incidence in patients with AVM volume >3 cm(3) and in patients with Spetzler-Martin grade IV and V AVMs. Five patients (9.4%) had hemorrhage in the period of latency. COMPARISON OF RESULTS WITH AVMS AT OTHER LOCATIONS: Patients with central AVMs presented at a younger age (mean age 22.7 years vs. 29 years), with a very high proportion (81% vs. 63%) presenting with hemorrhage. Significantly higher incidence of radiation edema (15% vs. 5%) and lower obliteration rates (74% vs. 93%) were seen in patients with central AVMs. CONCLUSIONS: GKS is an effective modality of treatment for central AVMs, though relatively lower obliteration rates and higher complication rates are seen compared to AVMs at other locations.

Neurology India.2009;57(5):617-21. Epub 2009/11/26

Gamma knife radiosurgery for arteriovenous malformations located in eloquent regions of the brain

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BACKGROUND: Stereotactic radiosurgery is an effective treatment strategy for selected group of patients with cerebral arteriovenous malformations (AVMs). AIM: The aim of this study was to evaluate the obliteration rates, complications, and patient outcomes after Gamma knife radiosurgery for cerebral arteriovenous malformations (AVMs) located in eloquent regions of the brain with an emphasis on neurological morbidity. MATERIALS AND METHODS: Between 2000 and December 2005, 37 patients with AVMs in eloquent locations (sensory, motor, speech, visual cortex, basal ganglia, and brain stem) underwent stereotactic radiosurgery. We retrospectively reviewed the clinical data of these patients to asses the outcomes. Of the 37 patients, only two patients had prior embolization. Three underwent prospective staged volume radiosurgery. Two patients needed redo-radiosurgery for residual AVM. Mean target volume was 9.1 cc. Three lesions had nidus volume more than 20 cc. Average marginal dose was 18.75 Gy. The median duration of follow-up was 23 months (range, 6-60 months). 15 patients had follow-up of more than 36 months. RESULTS: A total of 15 patients had follow-up of more than 36 months, thus available for evaluation of angiographic obliteration rates. Complete angiographic obliteration was documented in seven patients (46.7%). Four patients experienced hemorrhage during the latency period. One patient who had subsequent hemorrhage on follow-up developed worsening of neurological deficit. One patient developed significant sensory symptoms which resolved after steroids. No additional clinical deterioration related to treatment was noted in rest of the patients.
CONCLUSIONS: AVMs located in eloquent and in deep locations can be treated safely with stereotactic radiosurgery with acceptable obliteration rates and minimal morbidity.

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Deep Arteriovenous Malformations in the Basal Ganglia, Thalamus, and Insula: Multimodality Management, Patient Selection, and Results

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Objective: To describe a single institution's experience treating arteriovenous malformations (AVMs) of the basal ganglia, thalamus, and insula in a multimodal fasion. Methods: We conducted a retrospective review of all deep AVMs treated at our institution between 1997-2011 with attention to patient selection, treatment strategies, and radiographic and functional outcomes. Results: 97 patients underwent initial treatment at our institution. 64% presented with hemorrhage. 29% were located in the basal ganglia, 41% in the thalamus, and 30% in the insula. 80% were Spetzler-Martin grade III-IV. Initial treatment was microsurgical resection in 42%, stereotactic radiosurgery (SRS) in 45%, and observation in 12%. Radiographic cure was achieved in 54% after initial surgical or SRS treatment (71% and 23%, respectively) and in 63% after subsequent treatments, with good functional outcomes in 78% (median follow-up 2.2 years). Multivariate logistic regression analysis revealed treatment group and age as factors associated with radiographic cure, while Spetzler-Martin score and time to follow-up were significantly associated with improved/ unchanged functional status at time of last follow-up. Post-treatment hemorrhage occurred in 11% (7% of surgical and 18% of SRS patients). Conclusions: Modern treatment of deep AVMs includes a multidisciplinary approach utilizing microsurgery, SRS, embolization, and observation. Supplementary grading adds meaningfully to traditional Spetzler-Martin grading to guide patient selection. Surgical resection is more likely to result in obliteration compared to SRS, and is associated with satisfactory results in highly selected patients.

Journal of Neurosurgery.2012;116(1):33-43. Epub 2011/11/15

Stereotactic radiosurgery for arteriovenous malformations, Part 4: management of basal ganglia and thalamus arteriovenous malformations

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Object The authors conducted a study to define the long-term outcomes and risks of stereotactic radiosurgery (SRS) for arteriovenous malformations (AVMs) of the basal ganglia and thalamus. Methods Between 1987 and 2006, the authors performed Gamma Knife surgery in 996 patients with brain AVMs; 56 patients had AVMs of the basal ganglia and 77 had AVMs of the thalamus. In this series, 113 (85%) of 133 patients had a prior hemorrhage. The median target volume was 2.7 cm(3) (range 0.1-20.7 cm(3)) and the median margin dose was 20 Gy (range 15-25 Gy). Results Obliteration of the AVM eventually was documented on MR imaging in 78 patients and on angiography in 63 patients in a median follow-up period of 61 months (range 2-265 months). The actuarial rates documenting total obliteration after radiosurgery were 57%, 70%, 72%, and 72% at 3, 4, 5, and 10 years, respectively. Factors associated with a higher rate of AVM obliteration included AVMs located in the basal ganglia, a smaller target volume, a smaller maximum diameter, and a higher margin dose. Fifteen (11%) of 133 patients suffered a hemorrhage during the latency period and 7 patients died. The rate of post-SRS AVM hemorrhage was 4.5%, 6.2%, 9.0%, 11.2%, and 15.4% at 1, 2, 3, 5, and 10 years, respectively. The overall annual hemorrhage rate was 4.7%. When 5 patients with 7 hemorrhages occurring earlier than 6 months after SRS were removed from this analysis, the annual hemorrhage rate decreased to 2.7%. Larger volume AVMs had a higher risk of hemorrhage after SRS. Permanent neurological deficits due to adverse radiation

effects (AREs) developed in 6 patients (4.5%), and in 1 patient a delayed cyst developed 56 months after SRS. No patient died of AREs. Factors associated with a higher risk of symptomatic AREs were larger target volume, larger maximum diameter, lower margin dose, and a higher Pollock- Flickinger score. Conclusions Stereotactic radiosurgery is a gradually effective and relatively safe management option for deep-seated AVMs in the basal ganglia and thalamus. Although hemorrhage after obliteration did not occur in the present series, patients remain at risk during the latency interval between SRS and obliteration. The best candidates for SRS are patients with smaller volume AVMs located in the basal ganglia.

Neurosurgery.2010;67(2):398-403. Epub 2010/07/21

Long-term outcomes of stereotactic radiosurgery for arteriovenous malformations in the thalamus

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BACKGROUND: Arteriovenous malformations (AVMs) in the thalamus carry a high risk of hemorrhage. Although stereotactic radiosurgery (SRS) is widely accepted because of the high surgical morbidity and mortality of these lesions, precise long-term outcomes are largely unknown. OBJECTIVE: To review our experience with SRS for thalamic AVMs based on the latest follow-up data. METHODS: Forty-eight patients with thalamic AVMs were treated by SRS using the Leksell Gamma Knife and were followed. Long-term outcomes including the obliteration rate, hemorrhage after treatment, and adverse effects were retrospectively analyzed. RESULTS: The annual hemorrhage rate before SRS was 14%. The mean follow-up period after SRS was 66 months (range 6-198 months). The actuarial obliteration rate confirmed by angiography was 82% at 5 years after treatment, and the annual hemorrhage rate after SRS was 0.36%. Factors associated with higher obliteration rates were previous hemorrhage (P = .004) and treatment using new planning software (P = .001). Persistent worsening of neurological symptoms was observed in 17% and more frequently seen in patients who were treated using older planning software (P = .04) and a higher margin dose (P = .02). The morbidity rate for patients who received treatment planned using new software with a margin dose not more than 20 Gy was 12%. CONCLUSION: SRS for thalamic AVMs achieved a high obliteration rate and effectively decreased the risk of hemorrhage, with less morbidity compared with other modalities. Longer follow-up to evaluate the risk of delayed complications and the effort to minimize the morbidity is necessary.

Brainstem

Journal of Neurosurgery.2012;116(1):44-53. Epub 2011/11/15

Stereotactic radiosurgery for arteriovenous malformations, Part 5: management of brainstem arteriovenous malformations

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Object In this paper, the authors' goal was to define the long-term outcomes and risks of stereotactic radiosurgery (SRS) for arteriovenous malformations (AVMs) of the medulla, pons, and midbrain.

Methods: Between 1987 and 2006, the authors performed Gamma Knife surgery in 996 patients with brain AVMs; 67 patients had AVMs in the brainstem. In this series, 51 patients (76%) had a prior hemorrhage. The median target volume was 1.4 cm(3) (range 0.1-13.4 cm(3)). The median margin dose was 20 Gy (range 14-25.6 Gy).

Results: Obliteration of the AVMs was eventually documented in 35 patients at a median follow-up of 73 months (range 6-269 months). The actuarial rates of documentation of total obliteration were 41%, 70%, 70%, and 76% at 3, 4, 5, and 10 years, respectively. Higher rates of AVM obliteration were associated only with a higher margin dose. Four patients (6%) suffered a hemorrhage during the latency period, and 2 patients died. The rate of AVM hemorrhage after SRS was 3.0%, 3.0%, and 5.8% at 1, 5, and 10 years, respectively. The overall annual hemorrhage rate was 1.9%. Permanent neurological deficits due to adverse radiation effects (AREs) developed in 7 patients (10%) after SRS, and a delayed cyst developed in 2 patients (3%). One patient died at an outside institution with symptoms of AREs and unrecognized hydrocephalus. Higher 12-Gy volumes and higher Spetzler-Martin grades were associated with a higher risk of symptomatic AREs. Ten of 22 patients who had ocular dysfunction before SRS had improvement, 9 were unchanged, and 3 were worse due to AREs. Eight of 14 patients who had hemiparesis before SRS improved, 5 were unchanged, and 1 was worse.

Conclusions: Although hemorrhage after obliteration did not occur in this series, patients remained at risk during the latency interval until obliteration occurred. Thirty-eight percent of the patients who had neurological deficits due to prior hemorrhage improved. Higher dose delivery in association with conformal and highly selective SRS is required for safe and effective radiosurgery.

World Neurosurg.2011;76(1-2):87-95; discussion 57-8. Epub 2011/08/16

Gamma knife surgery for brainstem arteriovenous malformations

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OBJECTIVE: To evaluate the long-term imaging and clinical outcomes of patients with brainstem arteriovenous malformations (AVMs) treated with Gamma Knife surgery (GKS). METHODS: The study included 85 patients with brainstem AVMs undergoing GKS during the period 1989-2007. The locations of the nidi were the midbrain in 42 patients, pons in 31 patients, and medulla oblongata in 12 patients. The volume of the nidi ranged from 0.1-8.9 mL (median 1.4 mL, mean 1.9 mL), and the prescription dose ranged from 5-32 Gy (median 20 Gy, mean 19.9 Gy). After the initial Gamma procedure, 18 patients had repeat GKS for AVM residuals that were still patent. Two patients had a third GKS 7 years and 16 years after a failed repeat GKS. Clinical follow-up ranged from 24-252 months with a mean of 100 months (median 102 months) after the initial GKS. RESULTS: GKS yielded a total angiographic obliteration in 50 (58.8%) patients and subtotal obliteration in 4 (4.7%) patients. In 22 (25.9%) patients, the AVMs remained patent. In 9 patients (10.6%), no flow voids were observed on magnetic resonance imaging (MRI), but angiographic confirmation was unavailable. A small nidus volume and a high prescription dose were significantly associated with increased AVM obliteration rate. Radiation-induced changes developed in 34 patients (40%); 24 were asymptomatic, 1 patient had only headache, and 9 patients developed neurologic deficits. One patient developed a large cyst 6 years after GKS. CONCLUSIONS: Given the poor surgical outcome of brainstem AVMs, the results of 59% nidus obliteration and 6% permanent neurologic deficits make GKS a reasonable management of these difficult lesions.

Neurosurgery.2011;69(1):45-51; discussion 51-2. Epub 2011/03/04

Outcomes of radiosurgery for brainstem arteriovenous malformations

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BACKGROUND: Arteriovenous malformations (AVMs) in the brainstem yield a high risk of hemorrhage. Although stereotactic radiosurgery (SRS) is accepted, because of high surgical morbidity and mortality, outcomes are still unclear. OBJECTIVE: We previously reported the early results of SRS for brainstem AVMs. Here, we obtained data from a longer follow-up for a larger number of patients and present precise outcomes based on the latest follow-up data. METHODS: Forty-four patients with brainstem AVMs were treated by SRS. Outcomes such as the rates of obliteration, hemorrhage after treatment, and adverse effects were retrospectively analyzed. RESULTS: The annual hemorrhage rate before SRS was 17.5%. The mean follow-up period after SRS was 71 months (range, 2-168 months). The actuarial obliteration rate confirmed by angiography was 52% at 5 years. Factors associated with higher obliteration rate were previous hemorrhage (P = .048) and higher margin dose (P = .048). For patients treated with a margin dose of >/= 18 Gy, the obliteration rate was 71% at 5 years. Persistent worsening of neurological symptoms was observed in 5%. The annual hemorrhage rate after SRS was 2.4%. Four patients died of rebleeding, and disease-specific survival rate was 86% at 10 years after treatment. CONCLUSION: Nidus obliteration must be achieved for brainstem AVMs because they possibly cause lethal hemorrhage even after SRS. Treatment with a high margin dose is desirable to obtain favorable outcomes for these lesions. Additional treatment should be considered for an incompletely obliterated nidus.

Cerebellar

World Neurosurg.2014;Epub 2014/02/18

Radiosurgery for Cerebellar Arteriovenous Malformations: Does Infratentorial Location Affect Outcome?

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Object: The cerebellum is an uncommon location for arteriovenous malformations (AVM) with unique angioarchitecture compared to the cerebrum. We evaluate the outcomes of radiosurgery in a cohort of cerebellar AVMs and assess the effect of infratentorial location by comparing them to a matched cohort of supratentorial AVMs.

Methods: From a prospective AVM radiosurgery database of 1400 patients, we identified 60 cerebellar AVM patients with at least 2 years of radiologic follow-up or obliteration. The median volume and prescription dose were 2.3 cc and 22 Gy, respectively. The median radiologic follow-up was 39 months. The cerebellar AVM patients were matched (3:1) to a cohort of supratentorial, lobar AVM patients based on AVM size and patient age. Univariate and multivariate Cox proportional hazards regression analyses were used to identify factors associated with obliteration and favorable outcome.

Results: Cerebellar and supratentorial AVMs were similar in baseline characteristics except for an increased incidence of ruptured lesions in the cerebellar AVM cohort (P<0.001). Obliteration was achieved in 72% of cerebellar AVMs. Younger age (P=0.019), no pre-radiosurgery embolization (P<0.001), and decreased volume (P=0.034) were independent predictors of obliteration. The annual risk of post-radiosurgery hemorrhage in cerebellar AVMs was 1.3%. The rates of symptomatic and permanent RIC were 7% and 3%, respectively. Compared to the matched supratentorial AVM cohort, there was no difference in the rates of obliteration, post-radiosurgery hemorrhage, or symptomatic RIC.

Conclusion: Radiosurgery is an effective treatment modality for cerebellar AVMs with relatively limited adverse events. Infratentorial location did not affect radiosurgery outcomes.

Sylvian Fissure

J Neurosurg.2014;1-8. Epub 2014/06/14

Stereotactic radiosurgery for sylvian fissure arteriovenous malformations with emphasis on hemorrhage risks and seizure outcomes

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Object: Sylvian fissure arteriovenous malformations (AVMs) present substantial management challenges because of the critical adjacent blood vessels and functional brain. The authors investigated the outcomes, especially hemorrhage and seizure activity, after stereotactic radiosurgery (SRS) of AVMs within or adjacent to the sylvian fissure. Methods: This retrospective single-institution analysis examined the authors' experiences with Gamma Knife surgery for AVMs of the sylvian fissure in cases treated from 1987 through 2009. During this time, 87 patients underwent SRS for AVMs in the region of the sylvian fissure. Before undergoing SRS, 40 (46%) of these patients had experienced hemorrhage and 36 (41%) had had seizures. The median target volume of the AVM was 3.85 cm3 (range 0.1-17.7 cm3), and the median marginal dose of radiation was 20 Gy (range 13-25 Gy). Results: Over a median follow-up period of 64 months (range 3-275 months), AVM obliteration was confirmed by MRI or angiography for 43 patients. The actuarial rates of confirmation of total obliteration were 35% at 3 years, 60% at 4 and 5 years, and 76% at 10 years. Of the 36 patients who had experienced seizures before SRS, 19 (53%) achieved outcomes of Engel class I after treatment. The rate of seizure improvement was 29% at 3 years, 36% at 5 years, 50% at 10 years, and 60% at 15 years. No seizures developed after SRS in patients who had been seizure free before treatment. The actuarial rate of AVM hemorrhage after SRS was 5% at 1, 5, and 10 years. This rate equated to an annual hemorrhage rate during the latency interval of 1%; no hemorrhages occurred after confirmed obliteration. No permanent neurological deficits developed as an adverse effect of radiation; however, delayed cyst formation occurred in 3 patients. Conclusions: Stereotactic radiosurgery was an effective treatment for AVMs within the region of the sylvian fissure, particularly for smaller-volume AVMs. After SRS, a low rate of hemorrhage and improved seizure control were also evident.

Vein of Galen

J Neurosurg.2014;120(1):120-5. Epub 2013/07/23

Definitive treatment of vein of Galen aneurysmal malformation with stereotactic radiosurgery

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Vein of Galen aneurysmal malformations (VGAMs) are uncommon congenital malformations arising from fistulous communication with the median vein of the prosencephalon, a primitive precursor of midline cerebral venous structures. Angiographic embolization is the primary modality for treatment given historically poor microsurgical outcomes. Only a few reports of treatment by Gamma Knife radiosurgery (GKRS) exist in the literature, and the results are variable. The authors present 2 cases of VGAM in which GKRS provided definitive treatment with good outcome: one case involving antenatal presentation of a high-output, mural-type VGAM with complex clinical course refractory to multiple embolic procedures, and the other a choroidal-type VGAM presenting with hemorrhage in an adult and without a feasible embolic approach. With discussion of these cases and review of the literature, the authors advocate inclusion of GKRS as a therapeutic option for treatment of these complex lesions.

Ventricular

J Neurosurg.2014;1-8. Epub 2014/06/01

Gamma Knife surgery for arteriovenous malformations within or adjacent to the ventricles

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Object: The outcomes of stereotactic radiosurgery for arteriovenous malformations (AVMs) within or adjacent to the ventricular system are largely unknown. This study assessed the long-term outcomes and hemorrhage risks for patients with AVMs within this region who underwent Gamma Knife surgery (GKS) at the University of Pittsburgh.

Methods: The authors retrospectively identified 188 patients with ventricular-region AVMs who underwent a single-stage GKS procedure during a 22-year interval. The median patient age was 32 years (range 3-80 years), the median target volume was 4.6 cm3 (range 0.1-22 cm3), and the median marginal dose was 20 Gy (range 13-27 Gy).

Results: Arteriovenous malformation obliteration was confirmed by MRI or angiography in 89 patients during a median follow-up of 65 months (range 2-265 months). The actuarial rates of total obliteration were 32% at 3 years, 55% at 4 years, 60% at 5 years, and 64% at 10 years. Higher rates of AVM obliteration were obtained in the 26 patients with intraventricular AVMs. Twenty-five patients (13%) sustained a hemorrhage during the initial latency interval after GKS, indicating an annual hemorrhage rate of 3.4% prior to AVM obliteration. No patient experienced a hemorrhage after AVM obliteration was confirmed by imaging. Permanent neurological deficits due to adverse radiation effects developed in 7 patients (4%).

Conclusions: Although patients in this study demonstrated an elevated hemorrhage risk that remained until complete obliteration, GKS still proved to be a generally safe and effective treatment for patients with these high-risk intraventricular and periventriclar AVMs.

Posterior Fossa

Neurol Med Chir (Tokyo).2014;Epub 2014/01/15

Long-Term Outcomes of Gamma Knife Surgery for Posterior Fossa Arteriovenous Malformations

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The long-term outcomes of gamma knife surgery (GKS) in patients with posterior fossa arteriovenous malformations (AVMs) were retrospectively analyzed in 82 patients followed up for more than 5 years to evaluate the efficacy and safety. The median AVM volume at GKS was 0.95 cm3. The prescribed dose to the AVM margin was median 18 Gy with 1-18 isocenters. The actual complete AVM obliteration rate was 58.5% at 3 years and 78.0% at 5 years. The significant factors for higher complete obliteration rate were younger patient age and smaller maximum/minimum nidus diameter ratio. Two patients experienced hemorrhage caused by residual AVM rupture at 4 and 49 months. Twenty patients developed peri-nidal edema as an adverse radiation-induced reaction at median 13 months. One patient developed radiationinduced necrosis at 6.8 years. Neurological complication was observed in 12 patients and 6 patients remained with neurological dysfunction permanently. Larger nidus volume and location adjacent to an eloquent area significantly increased the risk of neurological complication. Pittsburgh radiosurgery-based AVM grading scale was significantly correlated with

the outcome of neurological symptoms after GKS. GKS achieved acceptable and complete obliteration rate for posterior fossa AVM with relatively low risk of morbidity on neuroimaging and neurological symptoms for the long-term period after treatment. We recommend conformable and selective treatment planning to achieve both obliteration of the AVM nidus and preservation of neurological function.

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Resolution of hemifacial spasm after successful treatment of posterior fossa arteriovenous malformation by gamma knife radiosurgery

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Post Geniculate Visual Pathway

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Stereotactic radiosurgery for arteriovenous malformations of the postgeniculate visual pathway

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Object: A visual field deficit resulting from the management of an arteriovenous malformation (AVM) significantly impacts a patient's quality of life. The present study was designed to investigate the clinical and radiological outcomes of stereotactic radiosurgery (SRS) performed for AVMs involving the postgeniculate visual pathway.

Methods: In this retrospective single-institution analysis, the authors reviewed their experience with Gamma Knife surgery for postgeniculate visual pathway AVMs performed during the period between 1987 and 2009.

Results: During the study interval, 171 patients underwent SRS for AVMs in this region. Forty-one patients (24%) had a visual deficit prior to SRS. The median target volume was 6.0 cm3 (range 0.4-22 cm3), and 19 Gy (range 14-25 Gy) was the median margin dose. Obliteration of the AVM was confirmed in 80 patients after a single SRS procedure at a median follow-up of 74 months (range 5-297 months). The actuarial rate of total obliteration was 67% at 4 years. Arteriovenous malformations with a volume < 5 cm3 had obliteration rates of 60% at 3 years and 79% at 4 years. The delivered margin dose proved significant given that 82% of patients receiving >/= 22 Gy had complete obliteration. The AVM was completely obliterated in an additional 18 patients after they underwent repeat SRS. At a median of 25 months (range 11-107 months) after SRS, 9 patients developed new or worsened visual field deficits. One patient developed a complete homonymous hemianopia, and 8 patients developed quadrantanopias. The actuarial risk of sustaining a new visual deficit was 3% at 3 years, 5% at 5 years, and 8% at 10 years. Fifteen patients had hemorrhage during the latency period, resulting in death in 9 of the patients. The annual hemorrhage rate during the latency interval was 2%, and no hemorrhages occurred after confirmed obliteration.

Conclusions: Despite an overall treatment mortality of 5%, related to latency interval hemorrhage, SRS was associated with only a 5.6% risk of new visual deficit and a final obliteration rate close to 80% in patients with AVMs of the postgeniculate visual pathway.

Cyst Formation

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Authors' reply to "Pathogenesis of radiosurgery-induced cyst formation in patients with arteriovenous malformation".

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Comment on

Pathological characteristics of cyst formation following gamma knife surgery for arteriovenous malformation. [Acta Neurochir (Wien). 2015]

Pathogenesis of radiosurgery-induced cyst formation in patients with cerebral arteriovenous malformations. [Acta Neurochir (Wien). 2015]

Acta Neurochir (Wien).2015; Epub 2015/03/10
Pathogenesis of radiosurgery-induced cyst formation in patients with cerebral arteriovenous malformations
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Acta Neurochir (Wien).2015; 157(2):293-8. Epub 2014/12/17
Pathological characteristics of cyst formation following gamma knife surgery for arteriovenous malformation
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BACKGROUND: The pathological characteristics of cyst development after gamma knife surgery (GKS) for arteriovenous malformation (AVM) were analysed. METHOD: Sixteen male and 12 female patients aged 17-67 years (mean 31.3 years) were retrospectively identified among 868 patients who underwent GKS for AVM at our hospital. The pathological characteristics of the reddish nodular lesion and chronic encapsulated expanding haematoma associated with cyst following GKS for AVM were examined. RESULTS: Cyst was associated with chronic encapsulated expanding haematoma in 13, and with nodular lesion in 12 patients. The nidus volume at GKS was 0.1-36 ml (median 6.0 ml), and the prescription dose at the nidus margin was 18-25 Gy (median 20 Gy). Cyst formation was detected from 1.1 to 16 years (mean 7.3 years) after GKS. Seven of the 12 patients with nodular lesion underwent surgery. Ten of the 13 patients with expanding haematoma underwent surgical removal of expanding haematoma. Histological examination was possible in 17 cases. Dilated capillary vessels with wall damage such as hyalinisation and fibrinoid necrosis, marked protein exudation and haemorrhage were the most common findings. Brain parenchyma was observed among the dilated vessels in some cases. Structureless necrotic tissue was not evident. CONCLUSIONS: The present study suggests that enhanced nodular lesion on magnetic resonance imaging and chronic encapsulated expanding haematoma associated with cyst may have common aetiopathology caused by late radiation effects, mainly consisting of dilated capillary vessels with wall damage. Massive protein exudation from such damaged capillary vessels is important in cyst development.

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Mechanisms of cyst formation after radiosurgery for intracranial arteriovenous malformations
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Elderly

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Radiosurgery for Cerebral Arteriovenous Malformations in Elderly Patients: Effect of Advanced Age on Outcomes After Intervention.
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OBJECTIVE: Cerebral arteriovenous malformations (AVM) are infrequently diagnosed and treated in elderly patients (age, >60 years). We hypothesize that, in contrast to AVM surgical outcomes, radiosurgery outcomes are not adversely affected by increased age. The goals of this case-control study are to analyze the radiosurgery outcomes for elderly patients with AVMs and determine the effect of elderly age on AVM radiosurgery outcomes.
METHODS: We evaluated a prospective database of patients with AVMs treated with radiosurgery from 1989 to 2013. Elderly patients with AVM (age, ≥ 60 years) with radiologic follow-up of ≥ 2 years or nidus obliteration were selected for analysis, and matched, in a 1:1 fashion and blinded to outcome, to adult nonelderly patients with AVM (age, <60 years). Statistical analyses were performed to determine actuarial obliteration rates and evaluate the relationship between elderly age and AVM radiosurgery outcomes.

RESULTS: The matching processes yielded 66 patients in each of the elderly and nonelderly AVM cohorts. In the elderly AVM cohort, the actuarial AVM obliteration rates at 3, 5, and 10 years were 37%, 65%, and 77%, respectively; the rates of radiologically evident, symptomatic, and permanent radiation-induced changes were 36%, 11%, and 0%, respectively; the annual hemorrhage risk after radiosurgery was 1.1%, and the AVM-related mortality rate was 1.5%. Elderly age was not significantly associated with AVM obliteration, radiation-induced changes, or hemorrhage after radiosurgery. CONCLUSIONS:
Advanced age does not appear to confer appreciably worse AVM radiosurgery outcomes, unlike its negative effect on AVM surgical outcomes. Thus, when an AVM warrants treatment, radiosurgery may be the preferred treatment for elderly patients.

Epilepsy/ Seizure

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Seizure outcomes after stereotactic radiosurgery for the treatment of cerebral arteriovenous malformations

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OBJECTIVE Patients with cerebral arteriovenous malformations (AVMs) commonly present with seizure. Seizure outcomes in patients treated with stereotactic radiosurgery (SRS) are poorly defined. A case series of patients with cerebral AVMs treated with SRS is presented to evaluate long-term seizure outcome. METHODS A retrospective review of the medical record was performed, identifying 204 consecutive patients with AVMs treated with SRS between January 1991 and June 2012. Clinical and radiographic data were evaluated. Seizure outcome was measured using the Engel Epilepsy Surgery Outcome Scale. Mean duration of follow-up was 37.1 months (SD 38.3 months) with a minimum follow-up period of 1 month. RESULTS Of the 204 patients with cerebral AVMs treated with SRS, 78 patients (38.2%) presented with seizures and 49 of those patients were treated with antiepileptic drugs (AEDs). Following SRS, 63 (80.8%) of the 78 patients who had had seizures prior to SRS were seizure-free at a mean follow-up time of 37.2 months (SD 41.3 months). Of the 49 patients who had been treated with AEDs, 17 were still taking AEDs at last follow-up. Of the 126 patients who did not present with seizures prior to treatment with SRS, only 5 patients (4.0%) had seizures in the post-SRS period. There was no significant correlation between post-SRS seizure status and patient demographic features, comorbidities, AVM characteristics, history of operative intervention, pre- or posttreatment hemorrhage, or radiographic degree of AVM resolution. CONCLUSIONS Stereotactic radiosurgery for treatment of cerebral AVMs is effective at providing long-term control of seizures. A substantial number of patients who were treated with SRS were not only seizure free at their last follow-up, but had been successfully weaned from antiepileptic medications.

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Cerebral Arteriovenous Malformations and Epilepsy, Part 2: Predictors of Seizure Outcomes Following Radiosurgery.

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OBJECTIVE: Seizure outcomes after arteriovenous malformation (AVM) management with radiosurgery are incompletely understood. In this case-control study, we aim to determine the incidences and define the predictors of seizure improvement and de novo seizures in patients with AVM with and without seizures at presentation, respectively.
METHODS: We evaluated our institutional AVM radiosurgery database to determine the factors that were associated with favorable seizure outcome (seizure improvement or lack of de novo seizures). In patients with seizures at presentation, seizure improvement was defined as decreased seizure frequency or complete seizure remission. In patients without seizures at presentation, de novo seizures were defined as new-onset seizures

after radiosurgery. Logistic regression analyses were performed to identify predictors of favorable seizure outcome.
RESULTS: In 229 patients with seizures at presentation, the rates of seizure improvement and seizure remission were 57% and 20%, respectively. Prior AVM hemorrhage (P = 0.015), longer follow-up (P < 0.0001), and lack of hemorrhage after radiosurgery (P = 0.048) were independent predictors of seizure improvement in the multivariate analysis. In 778 patients without seizures at presentation, the overall rate of de novo seizures was 1.7%. Prior AVM hemorrhage (P = 0.001) and higher Spetzler-Martin grade (P = 0.018) were independent predictors of the absence of de novo seizures in the multivariate analysis. AVM obliteration was not significantly associated with seizure outcomes after radiosurgery.
CONCLUSIONS: Radiosurgery provides reasonable rates of seizure improvement for patients with AVM who present with seizures. For patients with AVM without seizures at presentation, the risk of de novo seizures after radiosurgery is very low, obviating the need for prophylactic antiepileptic drug therapy. Further investigation of epilepsy in patients with AVM undergoing stereotactic radiosurgery should be considered with validated outcome measures and prospective study design.

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Radiosurgery for temporal lobe arteriovenous malformations: effect of temporal location on seizure outcomes
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OBJECT: The temporal lobe is particularly susceptible to epileptogenesis. However, the routine use of anticonvulsant therapy is not implemented in temporal lobe AVM patients without seizures at presentation. The goals of this case-control study were to determine the radiosurgical outcomes for temporal lobe AVMs and to define the effect of temporal lobe location on postradiosurgery AVM seizure outcomes. METHODS: From a database of approximately 1400 patients, the authors generated a case cohort from patients with temporal lobe AVMs with at least 2 years follow-up or obliteration. A control cohort with similar baseline AVM characteristics was generated, blinded to outcome, from patients with non-temporal, cortical AVMs. They evaluated the rates and predictors of seizure freedom or decreased seizure frequency in patients with seizures or de novo seizures in those without seizures. RESULTS: A total of 175 temporal lobe AVMs were identified based on the inclusion criteria. Seizure was the presenting symptom in 38% of patients. The median AVM volume was 3.3 cm3, and the Spetzler-Martin grade was III or higher in 39% of cases. The median radiosurgical prescription dose was 22 Gy. At a median clinical follow-up of 73 months, the rates of seizure control and de novo seizures were 62% and 2%, respectively. Prior embolization (p = 0.023) and lower radiosurgical dose (p = 0.027) were significant predictors of seizure control. Neither temporal lobe location (p = 0.187) nor obliteration (p = 0.522) affected seizure outcomes. The cumulative obliteration rate was 63%, which was significantly higher in patients without seizures at presentation (p = 0.046). The rates of symptomatic and permanent radiation-induced changes were 3% and 1%, respectively. The annual risk of postradiosurgery hemorrhage was 1.3%. CONCLUSIONS: Radiosurgery is an effective treatment for temporal lobe AVMs. Furthermore, radiosurgery is protective against seizure progression in patients with temporal lobe AVM-associated seizures. Temporal lobe location does not affect radiosurgery-induced seizure control. The low risk of new-onset seizures in patients with temporal or extratemporal AVMs does not seem to warrant prophylactic use of anticonvulsants.

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Cerebral Arteriovenous Malformations and Epilepsy, Part 1: Predictors of Seizure Presentation
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OBJECTIVE: Seizures are relatively common in patients harboring cerebral arteriovenous malformations (AVM). Since the pathogenesis of AVM-associated epilepsy is not well-defined, we aim to determine the factors associated with seizure presentation in AVM patients. METHODS: We evaluated our institutional AVM radiosurgery database, from 1989 to 2013, to select patients in whom pertinent clinical information at presentation and adequate clinical and radiologic follow-up was available. Baseline patient demographics and AVM angioarchitectural features were compared between patients with and without seizure presentation. In addition to standard descriptive statistics, logistic regression analyses were performed to identify predictors of seizure presentation. RESULTS: Of the 1,007 AVM patients included for analysis, 229 patients presented with seizures (22.7%). The incidence of seizure presentation was significantly higher in cortical than non-cortical AVMs (33.1% versus 6.6%, P<0.0001). Amongst the cortical locations, occipital AVMs had the lowest rate of seizure presentation (21.5%, P=0.0012), whereas the rates of seizure presentation in frontal (37.3%), temporal (37.7%), and parietal (34.0%) AVMs were similar. The lack of prior AVM hemorrhage (P<0.0001), larger nidus diameter (P<0.0001), and cortical location (P<0.0001) were independent predictors of seizure presentation in the multivariate analysis. The strongest independent predictors of seizure presentation were lack of prior AVM hemorrhage (OR 16.8) and cortical location (OR 4.2). CONCLUSIONS: Large, unruptured, cortical nidi are most prone to seizure presentation in patients referred for radiosurgery. Further investigations of the molecular biology, neuronal and glial physiology, and natural history of AVM-associated epilepsy appear warranted.

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Seizure and anticonvulsant outcomes following stereotactic radiosurgery for intracranial arteriovenous malformations

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OBJECT: Epilepsy associated with arteriovenous malformations (AVMs) has an unclear course after stereotactic radiosurgery (SRS). Neither the risks of persistent seizures nor the requirement for postoperative antiepileptic drugs (AEDs) are well defined. METHODS: The authors performed a retrospective review of all patients with AVMs who underwent SRS at the University of Virginia Health System from 1989 to 2012. Seizure status was categorized according to a modified Engel classification. The effects of demographic, AVM-related, and SRS treatment factors on seizure outcomes were evaluated with logistic regression analysis. Changes in AED status were evaluated using McNemar's test. RESULTS: Of the AVM patients with pre- or post-SRS seizures, 73 with pre-SRS epilepsy had evaluable data for subsequent analysis. The median patient age was 37 years (range 5-69 years), and the median follow-up period was 65.6 months (range 12-221 months). Sixty-five patients (89%) achieved seizure remission (Engel Class IA or IB outcome). Patients presenting with simple partial or secondarily generalized seizures were more likely to achieve Engel Class I outcome (p = 0.045). Twenty-one (33%) of 63 patients tapered off of pre-SRS AEDs. The incidence of freedom from AED therapy increased significantly after SRS (p < 0.001, McNemar's test). Of the Engel Class IA patients who continued AED therapy, 54% had patent AVM nidi, whereas only 19% continued AED therapy with complete AVM obliteration (p = 0.05). CONCLUSIONS: Stereotactic radiosurgery is an effective treatment for long-term AVM-related epilepsy. Seizure-free patients on continued AED therapy were more likely to have residual AVM nidi. Simple partial or secondarily generalized seizure type were associated with better seizure outcomes following SRS.

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Radiosurgery for unruptured cerebral arteriovenous malformations: Long-term seizure outcome

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OBJECTIVE: To date, seizures in relation to arteriovenous malformations (AVM) have been a secondary target of most studies. The insufficient evaluation, in conjunction with the lack of consistent seizure outcome assessment, has made it been difficult to draw conclusions about seizure outcome after radiosurgery for AVM. This study aimed to determine the effect of radiosurgery on seizure outcome depending on AVM obliteration and on the development of new seizure in patients with AVM. METHODS: Between 1997 and 2006, 161 consecutive patients underwent radiosurgery for unruptured AVM and were retrospectively assessed with a mean follow-up of 89.8 months by their medical records, updated clinical information, and, when necessary,

direct patient contact. Seizure outcome was assessed using the Engel seizure frequency scoring system. RESULTS: Of the 86 patients with a history of seizure before radiosurgery, 76.7% (66/86) were seizure-free and 58.1% (50/86) were medication-free at the last follow-up visit. Of the patients who achieved AVM obliteration, 96.7% (58/60) were seizure-free while 30.8% (8/26) of those patients who did not achieve AVM obliteration were seizure-free ($p = 0.001$). The proportion of patients who were medication-free was 81.7% (49/60) of the patients with obliteration and 3.8% (1/26) of patients without obliteration ($p < 0.001$). Of the 75 patients with no history of seizure before radiosurgery, 10 had provoked seizures due to the direct and indirect radiosurgical influences after radiosurgery. CONCLUSIONS: Although radiosurgery tends to cause seizures temporarily, the radiosurgery may improve seizure outcomes in patients with AVM-related seizures, especially in patients with AVM obliteration.

Embolization

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Gamma Knife surgical treatment for partially embolized cerebral arteriovenous malformations

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OBJECTIVE: A combination of embolization and radiosurgery is used as a common strategy for the treatment of large and complex cerebral arteriovenous malformations (AVMs). This study presents the experiences of partially embolized cerebral AVMs followed by Gamma Knife surgery (GKS) and assesses predictive factors for AVM obliteration and hemorrhage. METHODS: The interventional neuroradiology database that was reviewed included 404 patients who underwent AVM embolization. Using this database, the authors retrospectively analyzed all partially embolized AVM cases followed by GKS for a residual nidus. Except for cases of complete AVM obliteration, the authors excluded all patients with radiological follow-up of less than 2 years. Logistic regression analysis was used to analyze the predictive factors related to AVM obliteration and hemorrhage following GKS. Kaplan-Meier analysis was used to evaluate the obliteration with a cutoff AVM nidus volume of 3 cm(3) and 10 cm(3). RESULTS: One hundred sixty-two patients qualified for the study. The median patient age was 26 years and 48.8% were female. Hemorrhage presented as the most common symptom (48.1%). The median preembolization volume of an AVM was 14.3 cm(3). The median volume and margin dose for GKS were 10.92 cm(3) and 16.0 Gy, respectively. The median radiological and clinical follow-up intervals were 47 and 79 months, respectively. The annual hemorrhage rate was 1.71% and total obliteration rate was 56.8%. Noneloquent area ($p = 0.004$), superficial location ($p < 0.001$), decreased volume ($p < 0.001$), lower Spetzler-Martin grade ($p < 0.001$), lower Virginia Radiosurgery AVM Scale (RAS; $p < 0.001$), lower Pollock-Flickinger score ($p < 0.001$), lower modified Pollock-Flickinger score ($p < 0.001$), increased maximum dose ($p < 0.001$), and increased margin dose ($p < 0.001$) were found to be statistically significant in predicting the probability of AVM obliteration in the univariate analysis. In the multivariate analysis, only volume ($p = 0.016$) was found to be an independent prognostic factor for AVM obliteration. The log-rank (Mantel-Cox) test of the Kaplan-Meier analysis (chi-square = 54.402, $p < 0.001$) showed a significantly decreased obliteration rate of different cutoff AVM volume groups of less than 3 cm(3), 3-10 cm(3), and more than 10 cm(3). No independent prognostic factor was found for AVM hemorrhage in multivariate analysis. CONCLUSIONS: Partially embolized AVMs are amenable to successful treatment with GKS. The volume of the nidus significantly influences the outcome of radiosurgical treatment. The Virginia RAS and Pollock-Flickinger score were found to be reliable scoring systems for selection of patient candidates and prediction of partially embolized AVM closure and complications for GKS.

Neurosurgery. 2015 Sep;77(3):406-17; discussion 417.

Effect of Prior Embolization on Cerebral Arteriovenous Malformation Radiosurgery Outcomes: A Case-Control Study.

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BACKGROUND: Embolization before stereotactic radiosurgery (SRS) for cerebral arteriovenous malformations (AVM) has been shown to negatively affect obliteration rates, but its impact on the risks of radiosurgery-induced complications and latency period hemorrhage is poorly defined.
OBJECTIVE: To determine, in a case-control study, the effect of prior embolization on AVM SRS outcomes.
METHODS: We evaluated a database of AVM patients who underwent SRS. Propensity score analysis was used to match the case (embolized nidi) and control (nonembolized nidi) cohorts. AVM angioarchitectural complexity was defined as the sum of the number of major feeding arteries and draining veins to the nidus. Multivariate Cox proportional hazards regression analyses were performed on the overall study population to determine independent predictors of obliteration and radiation-induced changes.
RESULTS: The matching process yielded 242 patients in each cohort. The actuarial obliteration rates were significantly lower in the embolized (31%, 49% at 5, 10 years, respectively) compared with the nonembolized (48%, 64% at 5, 10 years, respectively) cohort (P = .003). In the multivariate analysis for obliteration, lower angioarchitectural complexity (P < .001) and radiologically evident radiation-induced changes (P = .016) were independent predictors, but embolization was not significant (P = .744). In the multivariate analysis for radiologic radiation-induced changes, lack of prior embolization (P = .009) and fewer draining veins (P = .011) were independent predictors.
CONCLUSION: The effect of prior embolization on AVM obliteration after SRS may be significantly confounded by nidus angioarchitectural complexity. Additionally, embolization could reduce the risk of radiation-induced changes. Thus, combined embolization and SRS may be warranted for appropriately selected nidi.

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Combined treatment of brain avms by onyx embolization and gamma knife radiosurgery decreased hemorrhage risk despite low obliteration rate
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AIM: The effectiveness and risk of cerebral arteriovenous malformations (AVMs) treatment with Onyx embolization combined with Gamma Knife surgery (GKS) were rarely reported. In the present study, we analyzed the radiographic and clinical outcomes of combined Onyx embolization and GKS for cerebral AVMs. MATERIAL AND METHODS: A total of 86 patients' clinical outcomes were fully collected. Modalities and complications of the procedure were analyzed as well as the clinical and anatomic outcomes. Risk factors associated with hemorrhage were determined by multivariate analysis. RESULTS: The mean duration of radiological and clinical follow-up was 42 months (12.3-82.5 months) and 57.6 months (12.3-108.9 months), respectively. The total annual hemorrhage rate was 1.66% with 2.26% for ruptured AVMs and 1.08% for unruptured AVMs. The annual mortality rate was 0.4%. The total obliteration rate was 28.2% at follow-up. Clinical deterioration occurred in 4 patients (4.7%). Volume larger than 22 ml, diameter prior GKS larger than 3.5 cm and margin dose less than 16 Gy significantly increased the hemorrhage risk. CONCLUSION: The post-treatment hemorrhage could be predictable based on AVM's characteristics and treatment approaches. The annual hemorrhage rate was low for both ruptured and unruptured AVMs after combined treatment; however, the total obliteration rate was low. Long-term follow-up and larger population are needed for evaluating the clinical effect for this combined treatment.

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Fistula components of brain arteriovenous malformations: Angioarchitecture analysis and embolization prior to gamma-knife surgery
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BACKGROUND: Gamma-knife surgery (GKS) is ineffective for high-flow arteriovenous fistula (AVF). The purpose of this study was to present the angioarchitecture of the AVF of brain arteriovenous malformation (BAVM) and report our experience of endovascular embolization of AVF component prior to GKS. METHODS: In the past 10 years, a total of 523 BAVMs had been treated primarily by GKS. Among these, 10 patients with AVF components were identified and referred for embolization prior to GKS. Those patients underwent GKS within 4 weeks after

embolization. We analyzed retrospectively the angioarchitecture of the AVFs of BAVMs, selection of embolic materials for embolization, and treatment outcomes. RESULTS: The location of the AVFs was anterior (n = 7) or middle (n = 3) cerebral artery. Central and peripheral types of AVFs were found in seven and three patients, respectively. Nine AVFs were totally occluded by a single session of endovascular embolization, while one failed to be embolized because it was inaccessible to a microcatheter. Detachable coils (n = 6) or combination of liquid adhesives (n = 3) were selected to embolize the AVF. No significant periprocedural neurological complication was found. BAVMs were obliterated totally by subsequent GKS in six patients and partial occlusion was achieved in one, while three still awaited the effect of GKS. Mean imaging and clinical follow-up periods were 35 and 48 months, respectively. CONCLUSION: Early detection of the central type of AVF of BAVM prior to GKS may be difficult because of its overlapping with feeder, nidus, and/or venous drains or it being overlooked. Peripheral-type AVFs were usually evident prior to GKS, particularly those with proximal dilated venous drains. Endovascular embolization is an effective modality for managing these AVFs, which may be treated by GKS ineffectively.

Journal of Neurosurgery.2011;115(2):364-70. Epub 2011/04/19

Effect of liquid embolic agents on Gamma Knife surgery dosimetry for arteriovenous malformations. Clinical article

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OBJECT: The effectiveness of Gamma Knife stereotactic surgery to obliterate brain arteriovenous malformations (AVMs) may be diminished by the preoperative adjunctive use of endovascular liquid embolic agents. The purpose of the present investigation was to determine if commercially available liquid embolic agents reduce the radiation dose to the target because of attenuation of the (60)Co beam. METHODS: The apparent linear attenuation coefficients for 120- to 140-keV radiographs in embolized regions were retrieved from CT scans for several patients with AVMs who had undergone embolization procedures with liquid embolic agents to reduce nidal volumes. Based on these coefficients and a virtual model of Gamma Knife surgery (GKS) with basic ray tracing, the authors obtained the path lengths and densities of the embolized regions. The attenuation of (60)Co beams was then calculated for various sizes and positions of embolized AVM regions and for the number of beams used for treatment. Published experiments for several high-atomic-number materials were used to estimate the effective (60)Co beam attenuation coefficients for the N-butyl cyanoacrylate (NBCA, suspended in ethiodized oil) and ethylene vinyl alcohol copolymer (EVOH, with suspended micronized tantalum powder, Onyx) used in the AVM embolizations. Dose reductions during GKS were calculated for a theoretical model based on the CT-documented apparent linear attenuation coefficients and for the (60)Co energy attenuation coefficient. Dose measurements were obtained in a phantom study with EVOH for comparison with the estimates generated from the two attenuation coefficients. RESULTS: Based on CT (keV) apparent attenuation coefficients, the authors' theoretical model predicted that the cumulative effect of either of the embolic agents decreased the number of kilovoltage photons in an embolized nidus by -8% to -15% because of the increased atomic number and density of NBCA and Onyx. However, in using the effective attenuation coefficient for the (60)Co energies as is used in GKS, the authors' theoretical model yielded only a 0.2% dose reduction per beam and a < 0.01%-0.2% dose reduction in total. These theoretical results were validated by measurements in a head phantom containing Onyx. CONCLUSIONS: Dose reduction due to attenuation of the (60)Co beam by the AVM embolization material was negligible for both NBCA and EVOH because of the high-energy (60)Co beam.

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Retrospective analysis of unstaged and staged Gamma Knife surgery with and without preceding embolization for the treatment of arteriovenous malformations

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OBJECT: The authors conducted a retrospective study to examine data on rates of obliteration of arteriovenous malformations (AVMs) with use of various combinations of treatment modalities based on Gamma Knife surgery (GKS). The authors believe that this study is the first to report on patients treated with embolization followed by staged GKS. METHODS: The authors identified 150 patients who underwent GKS for treatment of AVMs between 1994 and 2004. In a retrospective study, 4 independent groups emerged based on the various

combinations of treatment: 92 patients who underwent unstaged GKS, 28 patients who underwent embolization followed by unstaged GKS, 23 patients who underwent staged GKS, and 7 patients who underwent embolization followed by staged GKS. A minimum of 3 years of follow-up after the last GKS treatment was required for inclusion in the retrospective analysis. Angiograms, MR images, or CT scans at follow-up were required for calculating rates of obliteration of AVMs. RESULTS: Fifty-seven of 150 patients (38%) supplied angiograms, and overall obliteration was confirmed in 43 of these 57 patients (75.4%). An additional 37 patients had follow-up MR images or CT scans. The overall obliteration rate, including patients with follow-up angiograms and patients with follow-up MR images or CT scans, was 68 of 94 (72.3%). Patients who underwent unstaged GKS had a follow-up rate of 58.7% (54 of 92) and an obliteration rate of 75.9% (41 of 54). Patients who underwent embolization followed by unstaged GKS had a follow-up rate of 53.5% (15 of 28) and an obliteration rate of 60.0% (9 of 15). Patients who underwent staged GKS had a follow-up rate of 82.6% (19 of 23) and an obliteration rate of 73.7% (14 of 19). Patients who underwent embolization followed by staged GKS had a follow-up rate of 85.7% (6 of 7) and an obliteration rate of 66.7% (4 of 6). CONCLUSIONS: Gamma Knife surgery is an effective means of treating AVMs. Embolization prior to GKS may reduce AVM obliteration rates. Staged GKS is a promising method for obtaining high obliteration rates when treating larger AVMs in eloquent locations.

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Embolization of residual fistula following stereotactic radiosurgery in cerebral arteriovenous malformations
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Treatment of brain arteriovenous malformations (BAVMs) often requires a multitechnique approach. We present 2 cases of BAVM, in which initial stereotactic radiosurgery (SRS) was successful in obliterating a significant volume of the nidus. At follow-up angiography, residual fistulas were identified and selectively embolized; this procedure cured the lesions. Many series describe initial embolization to reduce the nidal volume followed by SRS to the remnant. The described cases highlight the value of primary radiosurgery followed by selective fistula embolization.

Hemorrage

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Delayed hemorrhage from the tissue of an occluded arteriovenous malformation after stereotactic radiosurgery: report of 3 cases
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Stereotactic radiosurgery is widely used to treat cerebral arteriovenous malformations (AVMs), with the goal of complete angiographic obliteration. A number of case series have challenged the assumption that absence of residual AVM on follow-up angiograms is consistent with elimination of the risk of hemorrhage. The authors describe 3 cases in which patients who had angiographic evidence of AVM occlusion presented with late hemorrhage in the area of their prior lesions. They compare the radiographic, angiographic, and histological features of these patients with those previously described in the literature. Delayed hemorrhage from the tissue of occluded AVMs has been reported as early as 4 and as late as 11 years after initial stereotactic radiosurgery. In all cases for which data are available, hemorrhage occurred in the area of persistent imaging findings despite negative findings on conventional angiography. The hemorrhagic lesions that were resected demonstrated a number of distinct histological findings. While rare, delayed hemorrhage from the tissue of occluded AVMs may occur from a number of distinct, angiographically occult postirradiation changes. The hemorrhages in the authors' 3 cases were symptomatic and localized. The correlation of histological and imaging findings in delayed hemorrhage from occluded AVMs is an area requiring further investigation.

Cerebrovasc Dis.2015; 39(1):53-62. Epub 2014/12/31
Effect of prior hemorrhage on intracranial arteriovenous malformation radiosurgery outcomes

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BACKGROUND: Intracerebral hemorrhage is simultaneously the most frequent and most debilitating manifestation of intracranial arteriovenous malformations (AVM), but its impact on success and complications of radiosurgery has not been rigorously assessed. In this case-control study, we define the effect of prior hemorrhage on AVM radiosurgery outcomes. METHODS: From a prospective, institutional database of 1,400 AVM patients treated with Gamma Knife radiosurgery, unruptured and ruptured AVMs were matched in a 1:1 fashion, blinded to outcome, based on patient demographics, prior embolization (26.6% of each cohort), AVM size (mean volume of unruptured AVMs 3.7 cm(3) versus ruptured AVMs 3.5 cm(3), p = 0.195), Spetzler-Martin grade (Grade I 17.0%, Grade II 37.8%, Grade III 34.8%, Grade IV 10.4% for each cohort), and radiosurgical treatment parameters (mean prescription dose for unruptured AVMs 20.9 Gy versus ruptured AVMs 21.0 Gy, p = 0.837). There were 270 patients in each cohort. Matched statistical analyses were used to compare the baseline characteristics, obliteration rates, post-radiosurgery latency period hemorrhage risks, and incidences of radiation-induced changes (RIC) between the two cohorts. RESULTS: The actuarial obliteration rates of the two cohorts were similar (unruptured AVMs: 38, 58, and 76% at 3, 5, 10 years, respectively; ruptured AVMs: 40, 60, and 73% at 3, 5, 10 years, respectively; p = 0.592). However, for embolized AVMs, complete obliteration was more likely to be achieved in unruptured lesions (unruptured AVMs: 25, 32, and 54% at 3, 5, 10 years, respectively; ruptured AVMs: 18, 27, and 42% at 3, 5, 10 years, respectively; p = 0.038). Prior AVM rupture resulted in a higher annual risk of post-radiosurgery latency period hemorrhage (ruptured AVMs 2.3% versus unruptured AVMs 1.1%, p = 0.025) but a lower rate of cumulative and symptomatic RIC (cumulative RIC: ruptured AVMs 30.4% versus unruptured AVMs 48.9%, p < 0.0001; symptomatic RIC: ruptured AVMs 7.0% versus unruptured AVMs 12.2%, p = 0.041, respectively). The rates of permanent RIC were similar between the unruptured (2.2%) and ruptured (1.9%) AVM cohorts (p = 0.761). The mean time interval to onset of RIC (unruptured AVMs 13.3 months versus ruptured AVMs 12.1 months, p = 0.783), and the mean duration of RIC (unruptured AVMs 22.0 months versus ruptured AVMs 21.7 months, p = 0.599) were not significantly different between the two cohorts. CONCLUSIONS: Prior AVM rupture significantly alters the risk of latency period hemorrhage and RIC following radiosurgery. These effects should be taken into consideration with the multidisciplinary management of AVM patients. Radiosurgery does not significantly alter the natural history of the hemorrhage risks of unruptured and ruptured AVMs unless obliteration is achieved.

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Hemorrhage during pregnancy in the latency interval after stereotactic radiosurgery for arteriovenous malformations

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Object: The presentation for patients with arteriovenous malformations (AVMs) is often intracranial hemorrhage; for women, this frequently occurs during the prime childbearing years. Although previous studies have addressed the risk for AVM hemorrhage during pregnancy, such studies have not assessed the risk for hemorrhage among women who become pregnant during the latency interval between stereotactic radiosurgery (SRS) and documented obliteration of the lesion. The authors sought to evaluate the risk for hemorrhage in patients who become pregnant during the latency interval after SRS.

Methods: This single-institution retrospective analysis reviewed the authors' experience with Gamma Knife SRS during 1987-2012. During this time, 253 women of childbearing age (median age 30 years, range 15-40 years) underwent SRS for intracranial AVM. The median target volume was 3.9 cm(3) (range 0.1-27.1 cm(3)), and the median marginal dose was 20 Gy (range 14-38 Gy). For all patients, the date of AVM obliteration was recorded and the latency interval was calculated. Information about subsequent pregnancies and/or bleeding events during the latency interval was retrieved from the medical records and supplemented by telephone contact.

Results: AVM obliteration was confirmed by MRI or angiography at a median follow-up time of 39.3 months (range 10-174 months). There were 828.7 patient-years of follow-up within the latency interval between SRS and the date of confirmed AVM obliteration. Among nonpregnant women, 20 hemorrhages occurred before AVM obliteration, yielding an annual hemorrhage rate of 2.5% for nonpregnant women during the latency interval. Among women who became pregnant during the latency interval, 2 hemorrhages occurred over the course of 18 pregnancies, yielding an annual hemorrhage rate of 11.1% for women who become pregnant

during the latency interval. For the 2 pregnant patients who experienced hemorrhage, the bleeding occurred during the first trimester of pregnancy.
Conclusions: The authors present the first series of data for women with intracranial AVMs who became pregnant during the latency interval after SRS. Hemorrhage during the latency interval occurred at an annual rate of 2.5% for nonpregnant women and 11.1% for pregnant women. The data suggest that pregnancy might be a risk factor for AVM hemorrhage during the interval between SRS and AVM obliteration. However, this suggestion is not statistically significant because only 18 patients in the study population became pregnant during the latency interval. To mitigate any increased risk for hemorrhage, patients should consider deferring pregnancy until treatment conclusion and AVM obliteration.

J Neurointerv Surg.2011;Epub 2011/10/13
Supernova hemorrhage: obliterative hemorrhage of brain arteriovenous malformations following gamma knife radiosurgery
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Hemorrhage represents the most feared complication of cerebral arteriovenous malformations (AVMs) in both untreated patients and those treated with gamma knife radiosurgery. Radiosurgery does not immediately lead to obliteration of the malformation, which often does not occur until years following treatment. Post-obliteration hemorrhage is rare, occurring months to years after radiosurgery, and has been associated with residual or recurrent AVM despite prior apparent nidus elimination. Three cases are reported of delayed intracranial hemorrhage in patients with cerebral AVMs treated with radiosurgery in which no residual AVM was found on catheter angiography at the time of delayed post- treatment hemorrhage. That the pathophysiology of these hemorrhages involves progressive venous outflow occlusion is speculated and the possible mechanistic link to subsequent vascular rupture is discussed.

Stroke.2011;42(6):1691-6. Epub 2011/04/23
Hemorrhage risk of cerebral arteriovenous malformations before and during the latency period after GAMMA knife radiosurgery
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BACKGROUND AND PURPOSE: To evaluate the hemorrhage rates of cerebral arteriovenous malformations (AVM) and the risk factors of hemorrhage before and after Gamma Knife radiosurgery (GKS). METHODS: The annual hemorrhage rate was calculated as the number of hemorrhages divided by the patient-years at risk. Characteristics of patients and AVM related to hemorrhagic or nonhemorrhagic presentation were evaluated by logistic regression. Risk factors predicting AVM hemorrhage during the period from the diagnosis to GKS of AVM and during the latency period after radiosurgery were evaluated using Cox regression hazards model. RESULTS: The annual hemorrhage rate before GKS was 2.0% assuming patients were at risk for hemorrhage since their birth. The hemorrhage rate calculated between the diagnosis and GKS of AVM was 6.6% and reduced to 2.5% after GKS until obliteration of the AVM. Although small and deep nidi and those with deep and single draining veins tended to present themselves with hemorrhage, only nidi with single draining veins and those ruptured before were more likely to bleed once the AVM had been diagnosed. These factors no longer predisposed the nidus to a rupture after radiosurgery and the only predicting factor for hemorrhage was a low radiosurgical prescription dose to the margin of nidus. CONCLUSIONS: The AVM hemorrhage rate seems to reduce after GKS. After radiosurgery, none of the patients or nidus-related risk factors remained relevant to the occurrence of hemorrhage. The nidus treated with a high radiosurgical dose is less likely to bleed.

Cen Eur Neurosurg.2010;71(2):92-5. Epub 2010/05/14
Haemorrhage from a radiosurgically treated arteriovenous malformation after its angiographically proven obliteration: a case report
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Small lower-grade Spetzler-Martin arteriovenous malformations (AVMs) are mainly treated by microsurgical resection or stereotactic radiosurgery. The choice of treatment largely depends on the referring centre's preference and the patient's decision. We present here a patient with an AVM repeatedly treated at our Leksell Gamma Knife unit with radiographically confirmed obliteration of the AVM which subsequently began bleeding. This case demonstrates the possibility of late complications in radiosurgically treated AVMs even after their demonstrable obliteration. Meticulous histological examination was performed, proving patency of the AVM nidus. The risk of haemorrhagic complications of radiosurgically removed AVMs despite angiographic proof of their obliteration is, in our view, a cogent argument for preferring surgical resection if the AVM is accessible and for prolonged follow-up after radiosurgical treatment of an AVM.

Journal of Neurosurgery.2009;110(5):1003-9. Epub 2009/02/10

Outcome after hemorrhage following Gamma Knife surgery for cerebral arteriovenous malformations

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OBJECT: Although the effects of Gamma Knife surgery (GKS) on the risk of hemorrhage are poorly understood, a certain subset of patients does suffer bleeding after GKS. This study was undertaken to analyze the outcome of patients sustaining hemorrhage after GKS; it is the most feared complication of radiosurgical management of cerebral arteriovenous malformations (AVMs). METHODS: Between May 1997 and June 2006, 494 cerebral AVMs in 489 patients were treated using a Leksell Gamma Knife Model B, and follow-up evaluations were conducted until June 2007 at the All India Institute of Medical Sciences in New Delhi. Fourteen patients who sustained a hemorrhage after GKS formed the study group. In most of these patients conservative management was chosen. RESULTS: The mortality rate was 0% and there was a 7% risk of sustaining a severe deficit following rebleeding after GKS. None of the patients sustained rebleeding after complete obliteration. Patients with Spetzler-Martin Grade III or less had increased chances of hemorrhage after GKS ($p < 0.002$). The presence of deep venous drainage, aneurysm, venous hypertension, or periventricular location on angiography was common in patients with hemorrhage after GKS. CONCLUSIONS: The risk of hemorrhage that remains following GKS for cerebral AVMs is highest in the 1st year after treatment. The present study showed a relatively good outcome even in cases with hemorrhage following GKS, with no deaths and minimal morbidity, further substantiating the safety and efficacy of the procedure.

Journal of Neurosurgery.2008;109 Suppl(73-6. Epub 2009/01/10

Optimal timing for Gamma Knife surgery after hemorrhage from brain arteriovenous malformations

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OBJECT: Optimal timing of Gamma Knife surgery (GKS) after hemorrhage from brain arteriovenous malformations (AVMs) is unclear and of concern to neurosurgeons because GKS is usually performed after absorption of the hematoma. The authors investigated whether waiting for hematoma absorption is beneficial and aimed to clarify the optimal treatment timing. METHODS: The authors retrospectively studied 211 patients with AVMs who presented with hemorrhage and underwent GKS as the initial treatment. Patients were categorized into 3 groups according to the interval between the time of first hemorrhage and GKS, as follows: Group 1, 0-3 months (70 patients); Group 2, 3-6 months (62 patients); and Group 3, > 6 months (79 patients). The obliteration rates, number of hemorrhages before and after GKS, and complication rates were compared between these 3 groups. The authors also analyzed a subgroup of 127 patients who presented with intracerebral hemorrhage (ICH) to identify the influence of ICH on outcome. RESULTS: After a median follow-up of 6.3 years, the rates of obliteration, hemorrhage after treatment, and complication were not significantly different between the 3 groups even though the patients with a longer interval before GKS (Group 3) had more AVMs in eloquent areas and neurological deficits. However, the numbers of patients with preoperative hemorrhage in the interval before GKS was significantly higher in Group 3 (1, 3, and 20 patients in Group 1, 2, and 3, respectively). These results were similar in the analyses of 127 patients presenting with ICH. CONCLUSIONS: No benefit was detected in waiting for hematoma absorption until GKS after hemorrhage from AVM. Because of higher hemorrhagic risk until GKS > 6 months after hemorrhage, the authors recommend GKS within 6 months after hemorrhage.

Clinical Neurology and Neurosurgery.2008;110(8):804-9. Epub 2008/06/25

Does hemorrhagic presentation in cerebral arteriovenous malformations affect obliteration rate after gamma knife radiosurgery?

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OBJECTIVES: Radiosurgery has been widely adopted for the treatment of cerebral AVMs. However radiosurgical treatment of patients with hemorrhagic presentation is fraught with risk of rebleed during latency period. The present study intends to analyze the obliteration rate, time to obliteration and chances of rebleed in patients with hemorrhagic versus non-hemorrhagic clinical presentation in cerebral arteriovenous malformations (AVMs) treated with gamma knife radiosurgery (GKS). PATIENTS AND METHODS: Of all the patients with cerebral AVMs treated from May 1997 to June 2006, 157 patients with neuroimaging follow up with digital subtraction angiography harboring 160 AVM nidii formed the study group. The mean age of presentation was 28 years (range, 6-58 years); mean nidus volume being 3.64 cm3 (range, 0.011-36.6 cm3). The mean follow up period was 70 months (range, 13- 121 months). All the patients were treated predominantly by primary GKS with use of adjunctive pre- GKS embolization in selected patients. RESULTS: A total of 103 (64%) patients presented with hemorrhage. There was no difference in the obliteration rate (69% versus 67%, p=0.672), mean latency period to obliteration (30 months versus 32 months, p=0.1989) and chances of hemorrhage (4.8% versus 3.5%, p=0.690) in patients with hemorrhagic as compared to non-hemorrhagic presentation. CONCLUSION: Prior hemorrhage does not affect the outcome after GKS in terms of obliteration rate, latency to obliteration as well as chances of hemorrhage during latency period. Gamma knife appears equally efficacious irrespective of the mode of clinical presentation in the management of cerebral AVMs; a concomitant use of pre-GKS embolization/surgery may be needed in patients with hemorrhagic presentation in selected cases, however.

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Subtotal obliteration of cerebral arteriovenous malformations after gamma knife surgery

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OBJECT: Subtotal obliteration of cerebral arteriovenous malformations (AVMs) after Gamma Knife surgery (GKS) implies a complete angiographic disappearance of the AVM nidus but persistence of an early filling draining vein, indicating that residual shunting is still present; hence, per definition there is still a patent AVM and the risk of bleeding is not eliminated. The aim of this study was to determine the risk of hemorrhage for patients with subtotal obliteration of AVMs. METHODS: After GKS for cerebral AVMs, follow-up angiography demonstrated a subtotally obliterated lesion in 159 patients. Of these, in 16 patients a subtotally obliterated AVM developed after a second GKS was performed for the partially obliterated lesion. The mean age of these patients was 35.2 years at the time of the diagnosis of subtotally obliterated AVMs. The lesion volumes at the time of initial GKS treatment ranged from 0.1 to 11.5 cm3 (mean 2.5 cm3). The mean peripheral dose used in the 175 GKS treatments was 22.5 Gy (median 23 Gy, range 15-31 Gy). To achieve total obliteration of the AVM, 23 patients underwent a new GKS targeting the proximal end of the early filling vein. The mean peripheral dose given in these cases was 23 Gy (median 24, range 18-25 Gy). The incidence of subtotally obliterated AVMs was 7.6% from a total of 2093 AVMs treated and in which follow-up imaging was available. The diagnosis of subtotally obliterated AVMs was made a mean of 29.4 months (range 4-178 months) after GKS. The number of patient-years at risk (from the time of the diagnosis of subtotally obliterated AVMs until either the confirmation of a total obliteration of the lesion on angiography or the time of the latest follow-up angiographic study that still visualized the early filling vein) was a mean of 3.9 years, ranging from 0.5 to 13.5 years, and a total of 601 patient-years. There was no case of bleeding after the diagnosis of subtotally obliterated AVMs. Of 90 patients who did not undergo further treatment and in whom follow- up angiography studies were available, the same early filling veins still filled in 24 (26.7%), and the subtotally obliterated AVMs were subsequently obliterated in 66 patients (73.3%). In 19 patients who underwent repeated GKS for subtotally obliterated AVMs and in whom follow-up angiography studies were available, the AVMs were obliterated in 15 (78.9%) and remained patent in four (21.1%). CONCLUSIONS: The fact that none of the patients with subtotally obliterated AVMs suffered a

rupture is not compatible with the assumption of an unchanged risk of hemorrhage for these lesions, and implies that the protection from rebleeding in patients with subtotal obliteration is significant. Subtotal obliteration does not necessarily seem to be a stage of an ongoing obliteration. At least in some cases it represents an end point of this process, with no subsequent obliteration occurring. This observation requires further confirmation by open-ended follow-up imaging.

Neurosurgery.2007;60(3):453-8; discussion 458-9. Epub 2007/03/01

Radiosurgery to reduce the risk of first hemorrhage from brain arteriovenous malformations

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OBJECTIVE: It remains unclear whether or not and to what extent stereotactic radiosurgery can reduce the risk of first intracranial hemorrhage from brain arteriovenous malformations. METHODS: We performed a retrospective observational investigation of 500 patients with arteriovenous malformations who were treated with gamma knife radiosurgery. The risk of first hemorrhage was analyzed using the Cox proportional-hazards model with age at radiosurgery and angiographic obliteration included as time-dependent covariates. Three periods were defined: from birth to radiosurgery (before radiosurgery); from radiosurgery to angiographic obliteration (latency period); and from angiographic obliteration to end of the follow-up period (after obliteration). RESULTS: Hemorrhage was documented before radiosurgery in 318 patients (median observation period, 30.0 yr), during the latency period in 11 patients (median observation period, 2.2 yr), and after obliteration in two patients (median observation period, 5.5 yr). Compared with the period before radiosurgery, the risk of hemorrhage decreased by 86% after obliteration (hazard ratio, 0.14; 95% confidence interval, 0.03-0.55; P = 0.005), whereas the reduction observed during the latency period was not statistically significant (hazard ratio, 0.56; 95% confidence interval, 0.31-1.04; P = 0.07). Irrespective of obliteration, the risk of hemorrhage decreased by 62% after radiosurgery (hazard ratio, 0.38; 95% confidence interval, 0.22-0.67; P = 0.001). Similar results were observed when the 33 patients who had undergone previous therapy were excluded from the analysis. CONCLUSION: Stereotactic radiosurgery significantly reduces the risk of first hemorrhage from brain arteriovenous malformations. The extent of the decrease might be greater if angiography indicates the evidence of obliteration.

Imaging

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Late morphological changes after radiosurgery of brain arteriovenous malformations: an MRI study

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BACKGROUND: Radiosurgery by Gamma Knife (GK) is an effective treatment for brain arteriovenous malformations (AVM). The aim of the present study was to evaluate late, radiation-induced changes detectable by MRI after AVM radiosurgery in patients treated minimally 10 years prior, with AVM obliteration proven by angiography. METHODS: Thirty-five patients with 37 AVMs were included. AVMs were irradiated 16.6 +/- 3.5 years prior with AVM obliteration proven 13 +/- 4 years prior. All patients underwent recent MRI examinations, including application of gadolinium-based contrast. RESULTS: In one case, post-irradiative cystic formation with mass effect and signs of hemorrhage requiring surgery was found. Post-gadolinium

enhancement at the site of obliterated nidi was apparent in 28 of 37 cases (76 %). In all cases except one, the mean volume of enhancement at the time of review was clearly lower than the volume of the originally irradiated AVM (88 +/- 20 %; median 92 %); in one case the extent was 142 % greater than the irradiated AVM. When we compared enhancing and non-enhancing nidi, we found that enhancing nidi were significantly larger than non-enhancing nidi at the time of radiosurgery (4.39 +/- 3.35 cc vs. 0.89 +/- 0.79 cc, p = 0.004). Enhancement was not influenced by total radiation dose, patient age at the time of irradiation, duration since radiosurgery, or the number of irradiations. Wallerian degeneration was found in nine of 37 cases (24 %); in six cases the optical tracts were affected and visual field defects were proven. In five of nine cases (55.6 %) with Wallerian degeneration previous hemorrhage was present. Dual vascular pathology was found in eight of 35 patients (23 %). CONCLUSIONS: GK radiosurgery for AVM is a safe treatment method although delayed complications may occur. Post-gadolinium enhancement of obliterated nidi may indicate an active post-irradiative process.

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The predictive value of magnetic resonance imaging in evaluating intracranial arteriovenous malformation obliteration after stereotactic radiosurgery.

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OBJECT: The current gold standard for diagnosing arteriovenous malformation (AVM) and assessing its obliteration after stereotactic radiosurgery (SRS) is digital subtraction angiography (DSA). Recently, MRI and MR angiography (MRA) have become increasingly popular imaging modalities for the follow-up of patients with an AVM because of their convenient setup and noninvasiveness. In this study, the authors assessed the sensitivity and specificity of MRI/MRA in evaluating AVM nidus obliteration as assessed by DSA.
METHODS: The authors study a consecutive series of 136 patients who underwent SRS between January 2000 and December 2012 and who underwent regular clinical examinations, several MRI studies, and at least 1 post-SRS DSA follow- up evaluation at the University of Virginia. The average follow-up time was 47.3 months (range 10.1-165.2 months). Two blinded observers were enrolled to interpret the results of MRI/MRA compared with those of DSA. The sensitivity, specificity, positive predictive value, and negative predictive value for the obliteration of AVM were reported.
RESULTS: On the basis of DSA, 73 patients (53.7%) achieved final angiographic obliteration in a median of 28.8 months. The sensitivity (the probability of finding obliteration on MRI/MRA among those for whom complete obliteration was shown on DSA) was 84.9% for one observer (Observer 1) and 76.7% for the other (Observer 2). The specificity was 88.9% and 95.2%, respectively. The false-negative interpretations were significantly related to the presence of draining veins, perinidal edema on T2-weighted images, and the interval between the MRI/MRA and DSA studies.
CONCLUSIONS: MRI/MRA predicted AVM obliteration after SRS in most patients and can be used in their follow-up. However, because the specificity of MRI/MRA is not perfect, DSA should still be performed to confirm AVM nidus obliteration after SRS.

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Detection of residual brain arteriovenous malformations after radiosurgery: diagnostic accuracy of contrast-enhanced four-dimensional MR angiography at 3.0 T

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Objectives: To evaluate the diagnostic accuracy of four-dimensional magnetic resonance angiography (4D-MRA) at 3.0 T for detecting residual arteriovenous malformations (AVMs) after gamma- knife radiosurgery

(GKRS).Methods: We assessed 36 angiographically confirmed AVMs in 36 patients who had been treated with GKRS. 4D-MRA was performed after GKRS and the time intervals were 39.4+/-26.0 months [mean+/-standard deviation (SD)]. 4D-MRA was obtained at 3.0 T after contrast injection, with a measured voxel size of 1x1x1 mm and a temporal resolution of 1.1 s (13 patients) or a voxel size of 1x1x2 mm and a temporal resolution of 0.98 s (23 patients). X-ray angiography was performed as the standard reference within 53+/- 47 days (mean+/-SD) after MRA. To determine a residual AVM, the 4D-MRA results were independently reviewed by two readers blinded to the X-ray angiography results. We evaluated diagnostic sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of 4D-MRA for detection of a residual AVM.Results: A residual AVM was identified in 13 patients (13/36, 36%) on X-ray angiography. According to Readers 1 and 2, 4D-MRA had a sensitivity of 79.6% and 64.3%, a specificity of 90.9% and 100%, a PPV of 84.6% and 100% and an NPV of 90% and 81.5%, respectively, and a diagnostic accuracy of 86.1% for Readers 1 and 2, for detecting residual AVMs after GKRS.Conclusion: The diagnostic accuracy of 4D-MRA at 3.0 T seems high, but there is still the possibility of further improving the spatiotemporal resolution of this technique.

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Outcomes of Diffusion Tensor Tractography-Integrated Stereotactic Radiosurgery

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PURPOSE: To analyze the effect of use of tractography of the critical brain white matter fibers created from diffusion tensor magnetic resonance imaging on reduction of morbidity associated with radiosurgery. METHODS AND MATERIALS: Tractography of the pyramidal tract has been integrated since February 2004 if lesions are adjacent to it, the optic radiation since May 2006, and the arcuate fasciculus since October 2007. By visually confirming the precise location of these fibers, the dose to these fiber tracts was optimized. One hundred forty-four consecutive patients with cerebral arteriovenous malformations who underwent radiosurgery with this technique between February 2004 and December 2009 were analyzed. RESULTS: Tractography was prospectively integrated in 71 of 155 treatments for 144 patients. The pyramidal tract was visualized in 45, the optic radiation in 22, and the arcuate fasciculus in 13 (two tracts in 9). During the follow-up period of 3 to 72 months (median, 23 months) after the procedure, 1 patient showed permanent worsening of pre-existing dysesthesia, and another patient exhibited mild transient hemiparesis 12 months later but fully recovered after oral administration of corticosteroid agents. Two patients had transient speech disturbance before starting integration of the arcuate fasciculus tractography, but no patient thereafter. CONCLUSION: Integrating tractography helped prevent morbidity of radiosurgery in patients with brain arteriovenous malformations.

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Three-dimensional rotational angiography in the assessment of the angioarchitecture of brain arteriovenous malformations

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BACKGROUND AND PURPOSE: The angioarchitecture of brain arteriovenous malformations (BAVM) still remains a complex subject of study despite advances in medical imaging techniques. For this reason, the present study aimed to assess whether or not 3D rotational angiography (3DXA) might improve the assessment of BAVM. PATIENTS AND METHODS: Included prospectively were 72 patients who had undergone conventional digital subtraction angiography (DSA) and 3DXA for pretherapeutic assessment of BAVM prior to radiosurgery. Dimensional criteria, arterial-feed patterns, venous drainage, points of weakness and vascular densities (VD) of the nidus and shunt zone were studied. RESULTS: 3DXA detected all arteriovenous shunts by revealing abnormal venous enhancement. Post-processing tools similar to CT and MRI may also be used to make complex 3D reconstructions. In addition, the technique provided significant help for volumetric estimations, extraction of arterial feeders and origins of draining veins, and analysis of the 3D conformation of the nidus. Furthermore, 3DXA detected significantly more points of weakness, such as intranidus aneurysms and venous anomalies ($P<0.005$). In 65% of cases, a gradient of vascular enhancement intensity was found between the arteries and

draining veins surrounding or comprising the nidus. VD, or the percentages of space occupied by the enhanced vascular elements, was evaluated in both the nidus and shunt zone. VD in the shunt zone was highest in untreated patients with no history of bleeding (P<0.005). CONCLUSION: 3DXA offers a useful approach to BAVM exploration and can improve our knowledge of lesional angioarchitecture, necessary for the planning of therapeutic strategies.

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Early draining vein occlusion after gamma knife surgery for arteriovenous malformations

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BACKGROUND: Increased signals on T2-weighted magnetic resonance imaging usually interpreted as radiation-induced changes or brain edema is a common short- to mid-term complication after Gamma Knife surgery (GKS) for intracranial arteriovenous malformations (AVMs), although its nature remains to be clarified. Early draining vein occlusion with resultant brain edema or hemorrhage, although well established in surgical series, was not described in radiosurgical literature until recently. OBJECTIVE: To outline the incidence, clinical manifestations, and outcomes of this unusual complication in our series of 1256 AVM patients treated with GKS. METHODS: From 1989 to 2008, 1400 patients underwent GKS for cerebral AVMs or dural arteriovenous fistulae at the University of Virginia. In 1256 patients, magnetic resonance imaging after GKS was available for analysis of radiation-induced changes and early draining vein occlusion. RESULTS: After GKS, 456 patients (36%) developed radiation-induced changes surrounding the treated nidi. Among these patients, 12 had early thrombosis of the draining vein accompanied by radiation-induced changes. Venous thrombosis occurred 6 to 25 months (median 11.6 months) after GKS. Three patients were asymptomatic on the image findings of venous occlusion and brain edema, 3 experienced headache, 1 had seizure and headache, and neurological deficits developed in 5. Patients with neurological deficits were treated with corticosteroids; 2 of the patients recovered completely, 1 still had slight hemiparesis, 1 had short-term memory deficits, and 1 died of massive intracerebral hemorrhage. CONCLUSION: Although venous structures are considered more radioresistant, endothelial damage accompanied by venous flow stasis might cause early venous thrombosis and premature venous occlusion after radiosurgery for AVMs. In our series, all patients had a favorable outcome except 1 with a fatal hemorrhage.

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Contrast-enhanced magnetic resonance characteristics of arteriovenous malformations after gamma knife radiosurgery: predictors of post-angiographic obliteration hemorrhage

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BACKGROUND: The reported cumulative risk of post-angiographic obliteration (post-AO) hemorrhage from arteriovenous malformations (AVMs) following gamma knife radiosurgery (GKRS) over 10 years is 2.2%. OBJECTIVE: To identify the warning signs of post-AO hemorrhage by analyzing the characteristics of enhancement on contrast-enhanced MRI magnetic resonance imaging (MRI) of AVMs with post-AO hemorrhage. METHODS: We performed a retrospective analysis of 121 patients whose AVMs were angiographically obliterated within 5 years of GKRS without hemorrhage and who received at least 1 contrast-enhanced MRI after GKRS (group 1), and 7 patients who experienced post-AO hemorrhage (group 2). We analyzed the enhancement persistence ratio (the percentage of AVMs with persisting enhancement on contrast-enhanced T1-weighted image after obliteration) and the change in size of the enhanced region over time in each patient. RESULTS: The enhancement persistence ratio showed no significant difference between the 2 groups (89.4% vs 100% for groups 1 and 2, respectively; P=.401). While most cases in group 1 showed a tendency to decrease in size and gradually stabilize following GKRS, there were significantly more cases in group 2 with obvious increment of the enhanced regions within 1 year of angiographic obliteration compared with the previous measurement (4.96% vs 71.4% for groups 1 and 2, respectively; P<.0001). CONCLUSION: Our results suggest that AVMs that show an increase in the size of the enhanced region within 1 year of angiographic obliteration should be followed up with caution for post-AO hemorrhage. Persisting enhancement itself is not positively associated with subsequent hemorrhage.

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Vascular structure and binomial statistics for response modeling in radiosurgery of cerebral arteriovenous malformations

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Radiation treatment of arteriovenous malformations (AVMs) has a slow and progressive vaso-occlusive effect. Some studies suggested the possible role of vascular structure in this process. A detailed biomathematical model has been used, where the morphological, biophysical and hemodynamic characteristics of intracranial AVM vessels are faithfully reproduced. The effect of radiation on plexiform and fistulous AVM nidus vessels was simulated using this theoretical model. The similarities between vascular and electrical networks were used to construct this biomathematical AVM model and provide an accurate rendering of transnidal and intranidal hemodynamics. The response of different vessels to radiation and their obliteration probability as a function of different angiostructures were simulated and total obliteration was defined as the probability of obliteration of all possible vascular pathways. The dose response of the whole AVM is observed to depend on the vascular structure of the intra-nidus AVM. Furthermore, a plexiform AVM appears to be more prone to obliteration compared with an AVM of the same size but having more arteriovenous fistulas. Finally, a binomial model was introduced, which considers the number of crucial vessels and is able to predict the dose response behavior of AVMs with a complex vascular structure.

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Detection of residual brain arteriovenous malformations after radiosurgery: diagnostic accuracy of contrast-enhanced three-dimensional time of flight MR angiography at 3.0 Tesla

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OBJECTIVE: Although three-dimensional time-of-flight magnetic resonance angiography (3D TOF-MRA) is used frequently as a follow-up tool to assess the response of arteriovenous malformations (AVMs) after radiosurgery, the diagnostic accuracy of 3D TOF-MRA is not well known. We evaluated the diagnostic accuracy of contrast-enhanced 3D TOF-MRA at 3.0 Tesla for the detection of residual AVMs. MATERIALS AND METHODS: This study included 32 AVMs from 32 patients who had been treated with radiosurgery (males/females: 21/11; average patient age, 33.1 years). The time interval between radiosurgery and MRA was an average of 35.3 months (range, 12-88 months). Three-dimensional TOF-MRA was obtained at a magnetic field strength of 3.0 Tesla after infusion of contrast media, with a measured voxel size of 0.40 x 0.80 x 1.4 (0.45) mm(3) and a reconstructed voxel size of 0.27 x 0.27 x 0.70 (0.05) mm(3) after zero-filling. X-ray angiography was performed as the reference of standard within six months after MRA (an average of two months). To determine the presence of a residual AVM, the source images of 3D TOF-MRA were independently reviewed, focusing on the presence of abnormally hyperintense fine tangled or tubular structures with continuity as seen on consecutive slices by two observers blinded to the X-ray angiography results. RESULTS: A residual AVM was identified in 10 patients (10 of 32, 31%) on X-ray angiography. The inter-observer agreement for MRA was excellent (kappa= 0.813). For the detection of a residual AVM after radiosurgery as determined by observer 1 and observer 2, the source images of MRA had an overall sensitivity of 100%/90% (10 of 10, 9 of 10), specificity of 68%/68% (15 of 22, 15 of 22), positive predictive value of 59%/56% (10 of 17, 9 of 16), negative predictive value of 100%/94% (15 of 15, 15 of 16) and diagnostic accuracy of 78%/75% (25 of 32, 24 of 32), respectively. CONCLUSION: The sensitivity of contrast-enhanced 3D TOF-MRA at 3.0 Tesla is high but the specificity is not sufficient for the detection of a residual AVM after radiosurgery.

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Time-of-flight magnetic resonance angiography imaging of a residual arteriovenous malformation nidus after Onyx embolization for stereotactic radiosurgery planning. Technical note

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This report demonstrates that time-of-flight (TOF) MR angiography is a useful adjunct for planning stereotactic radiosurgery (SRS) of large arteriovenous malformations (AVMs) after staged embolization with Onyx. Onyx

(ethylene vinyl copolymer), a recently approved liquid embolic agent, has been increasingly used to exclude portions of large AVMs from the parent circulation prior to SRS. Limiting SRS to regions of persistent arteriovenous shunting and excluding regions eliminated by embolization may reduce unnecessary radiation doses to eloquent brain structures. However, SRS dosimetry planning presents unique challenges after Onyx embolization because it creates extensive artifacts on CT scans, and it cannot be delineated from untreated nidus on standard MR sequences. During the radiosurgery procedure, MR images were obtained using a GE Signa 1.5-T unit. Standard axial T2 fast spin echo high- resolution images (TR 3000 msec, TE 108 msec, slice thickness 2.5 mm) were generated for optimal visualization of brain tissue and AVM flow voids. The 3D TOF MR angiography images of the circle of Willis and vertebral arteries were subsequently obtained to visualize AVM regions embolized with Onyx (TR 37 msec, TE 6.9 msec, flip angle 20 degrees). Adjunct TOF MR angiography images demonstrated excellent contrast between nidus embolized with Onyx and regions of persistent arteriovenous shunting within a large AVM prior to SRS. Additional information derived from these sequences resulted in substantial adjustments to the treatment plan and an overall reduction in the treated tissue volume.

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Transcranial Doppler study of cerebral arteriovenous malformations after gamma knife radiosurgery

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The aim of this study was to evaluate the clinical value of the Transcranial Doppler (TCD) in follow-up examinations after gamma knife radiosurgery (GKS) for arteriovenous malformations (AVM). We performed TCD after GKS in 18 patients who had cerebral AVMs to evaluate the hemodynamic effects of the procedure. Ten patients underwent TCD within 12 months after GKS, and eight between 12 and 24 months. The mean blood velocity (Vm) and pulsatility index (PI) were primarily analyzed in the feeding arteries (FAs) and non-FAs. Fifteen healthy volunteers served as control patients. The Vm values in the FAs after GKS ranged from 31 cm/s to 90 cm/s, with PI values ranging from 0.48 to 1.03. The Vm values in the comparable normal arteries ranged from 28 cm/s to 87 cm/s, and the PI values in these arteries ranged from 0.62 to 1.02. The Vm and PI values in every FA in all patients were normal compared to the values in the non-FAs (p=0.67 and 0.38, respectively). Our results suggest that AVM vessels with high Vm and low PI values return to normal as the nidus of the AVM is obliterated after GKS. Although there was a trend toward a reduction of the Vm values after obliteration, this trend was not significant, except when the < 12 month subgroup was compared to the 12-24 month subgroup. In our limited study, TDC proved to be a reliable, safe and non-invasive method to monitor the outcome of GKS for cerebral AVMs.

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Arcuate fasciculus tractography integrated into Gamma Knife surgery

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OBJECT: To prevent speech disturbances after Gamma Knife surgery (GKS), the authors integrated arcuate fasciculus (AF) tractography based on diffusion tensor (DT) MR imaging into treatment planning for GKS. METHODS: Arcuate fasciculus tractography was retrospectively integrated into planning that had been previously performed by neurosurgeons and radiation oncologists. This technique was retrospectively applied to 12 patients with arteriovenous malformations adjacent to the AF. Diffusion tensor images were acquired before the frame was affixed to the patient's head and DT tractography images of the AF were created using the authors' original software. The data from DT tractography and stereotactic 3D imaging studies obtained after frame fixation were transported to a treatment planning workstation for GKS and coregistered so that the delivered doses and incidence of posttreatment aphasia could be assessed. RESULTS: The AF could not be depicted in 2 patients who initially presented with motor aphasia caused by hemorrhaging from arteriovenous malformations. During the median follow-up period of 29 months after GKS, aphasia developed in 2 patients: 30 Gy delivered to the frontal portion of the AF caused conduction aphasia in 1 patient, and 9.6 Gy to the temporal portion led to motor aphasia in the other. Speech dysfunction was not observed after a maximum radiation dose of 10.0-16.8 Gy was delivered to the frontal fibers in 4 patients, and 3.6-5.2 Gy to the temporal fibers in 3. CONCLUSIONS: The authors found that administration of a 10-Gy radiation dose during GKS was

tolerated in the frontal but not the temporal fibers of the AF. The authors recommend confirmation of the dose by integration of AF tractography with GKS, especially in lesions located near the temporal language fibers.

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Definition of the key target volume in radiosurgical management of arteriovenous malformations: a new dynamic concept based on angiographic circulation time

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OBJECT: The cumulative experience worldwide indicates complete radiosurgical obliteration rates of brain arteriovenous malformations (AVMs) ranging from 35 to 90%. The purpose of this study was to propose a strategy to increase the obliteration rate for AVMs through the dynamic definition of the key target volume (KTV). METHODS: A prospective series of patients harboring an AVM was assessed using digital subtraction angiography in which a digital counter was used to measure the several stages of the frame-by-frame circulation time. All the patients were analyzed using dynamic measurement planning to define the KTV, corresponding to the volume of the shunt with the least vascular resistance and the earliest venous drainage. All patients underwent catheter-based angiography, a subgroup was additionally assessed by means of a superselective catheterization, and among these a further subgroup received embolization. The shunts were also categorized according to their angioarchitectural type: fistulous, plexiform, or mixed. The authors applied the radiosurgery-based grading system (RBGS) as well to find a correlation with the obliteration rate. RESULTS: This series includes 44 patients treated by radiosurgery; global angiography was performed for all patients, including dynamic measurement planning. Eighty-four percent of them underwent superselective catheterization, and 50% of the total population underwent embolization. In the embolized arm of the study, the pretreatment volume was up to 120 ml. In patients with a single treatment, the mean volume was 8.5 ml, and the median volume was 6.95 +/- 4.56 ml (mean +/- standard deviation), with a KTV of up to 15 ml. For prospectively staged radiosurgery, the mean KTV was 28 ml. The marginal radiation dose was 18-22 Gy, with a mean of dose 20 Gy. The mean RBGS score was 1.70. The overall obliteration rate was 91%, including the repeated radiosurgery group (4 patients), in which 100% showed complete obliteration. The overall permanent deficit was 2 of 44 patients, 1 in each group. CONCLUSIONS: Dynamic definition of the KTV might increase the obliteration rate, even in complex AVMs, allowing the treatment of smaller volumes off the recruitment vessels (pseudonidus). By using this technique, the authors avoided double-blind treatment, where the neurosurgeon does not know precisely which type of lesion he or she is irradiating and the interventionalist does not know why and what he or she is embolizing.

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Cerebral arteriovenous malformations: comparison of novel magnetic resonance angiographic techniques and conventional catheter angiography

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OBJECTIVE: To investigate the potential of novel magnetic resonance (MR) angiographic techniques for the assessment of cerebral arteriovenous malformations. METHODS: Forty patients who were about to undergo stereotactic radiosurgery were prospectively recruited. Three-dimensional, sliding-slab interleaved ky (SLINKY), time-of-flight acquisition was performed, as was a dynamic MR digital subtraction angiography (DSA) procedure in which single thick slices (6-10 cm) were obtained using a radiofrequency spoiled Fourier-acquired steady-state sequence (1 image/s). Sixty images were acquired, in two or three projections, during passage of a 6- to 10-ml bolus of gadolinium chelate. Subtraction and postprocessing were performed, and images were viewed in an inverted cine mode. SLINKY time-of- flight acquisition was repeated after the administration of gadolinium. Routine stereotactic conventional catheter angiography was performed after MR imaging. All images were assessed (in a blinded randomized manner) for Spetzler-Martin grading and determination of associated vascular pathological features. RESULTS: Forty-one arteriovenous malformations were assessed in 40 patients. Contrast- enhanced (CE) SLINKY MR angiography was the most consistent MR imaging technique, yielding a 95% correlation with the Spetzler-Martin classification defined by conventional catheter angiography; MR DSA exhibited 90% agreement, and SLINKY MR angiography exhibited 81% agreement. CE SLINKY MR angiography provided improved nidus delineation, compared with non-CE SLINKY MR angiography. Dynamic

information from MR DSA significantly improved the observation of early-draining veins and associated aneurysms. CONCLUSION: CE SLINKY MR angiographic assessment of cerebral arteriovenous malformations offers significant advantages, compared with the use of non-CE SLINKY MR angiography, including improved nidus demonstration. MR DSA shows promise as a noninvasive method for dynamic angiography but is presently restricted by limitations in both temporal and spatial resolution.

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Gamma Knife surgery for arteriovenous malformations in the brain: integration of time-resolved contrast-enhanced magnetic resonance angiography into dosimetry planning. Technical note

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OBJECT: The aim of this study was to develop an algorithm for the integration of time-resolved contrast-enhanced magnetic resonance (MR) angiography into dosimetry planning for Gamma Knife surgery (GKS) of arteriovenous malformations (AVMs) in the brain. METHODS: Twelve patients harboring brain AVMs referred for GKS underwent intraarterial digital subtraction (DS) angiography and time-resolved MR angiography while wearing an externally applied cranial stereotactic frame. Time-resolved MR angiography was performed on a 1.5-tesla MR unit (Achieva, Philips Medical Systems) using contrast-enhanced 3D fast field echo sequencing with stochastic central k-space ordering. Postprocessing with interactive data language (Research Systems, Inc.) produced hybrid data sets containing dynamic angiographic information and the MR markers necessary for stereotactic transformation. Image files were sent to the Leksell GammaPlan system (Elekta) for dosimetry planning. RESULTS: Stereotactic transformation of the hybrid data sets containing the time-resolved MR angiography information with automatic detection of the MR markers was possible in all 12 cases. The stereotactic coordinates of vascular structures predefined from time-resolved MR angiography matched with DS angiography data in all cases. In 10 patients dosimetry planning could be performed based on time-resolved MR angiography data. In two patients, time-resolved MR angiography data alone were considered insufficient. The target volumes showed a notable shift of centers between modalities. CONCLUSIONS: Integration of time-resolved MR angiography data into the Leksell GammaPlan system for patients with brain AVMs is feasible. The proposed algorithm seems concise and sufficiently robust for clinical application. The quality of the time-resolved MR angiography sequencing needs further improvement.

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Optic radiation tractography integrated into simulated treatment planning for Gamma Knife surgery

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OBJECT: No definitive method of preventing visual field deficits after stereotactic radiosurgery for lesions near the optic radiation (OR) has been available so far. The authors report the results of integrating OR tractography based on diffusion tensor (DT) magnetic resonance imaging into simulated treatment planning for Gamma Knife surgery (GKS). METHODS: Data from imaging studies performed in 10 patients who underwent GKS for treatment of arteriovenous malformations (AVMs) located adjacent to the OR were used for the simulated treatment planning. Diffusion tensor images performed without the patient's head being secured by a stereotactic frame were used for DT tractography, and the OR was visualized by means of software developed by the authors. Data from stereotactic 3D imaging studies performed after frame fixation were coregistered with the data from DT tractography. The combined images were transferred to a GKS treatment-planning workstation. Delivered doses and distances between the treated lesions and the OR were analyzed and correlated with posttreatment neurological changes. RESULTS: In patients presenting with migraine with visual aura or occipital lobe epilepsy, the OR was located within 11 mm from AVMs. In a patient who developed new quadrantanopia after GKS, the OR had received 32 Gy. A maximum dose to the OR of less than 12 Gy did not cause new visual field deficits. A maximum dose to the OR of 8 Gy or more was significantly related to neurological change ($p < 0.05$), including visual field deficits and development or improvement of migraine. CONCLUSIONS: Integration of OR tractography into GKS represents a promising tool for preventing GKS-induced visual disturbances and headaches. Single-session irradiation at a dose of 8 Gy or more was associated with neurological change.

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A treatment paradigm for high-grade brain arteriovenous malformations: volume-staged radiosurgical downgrading followed by microsurgical resection

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OBJECT The surgical treatment of many large arteriovenous malformations (AVMs) is associated with substantial risks, and many are considered inoperable. Furthermore, AVMs larger than 3 cm in diameter are not usually treated with conventional single-session radiosurgery encompassing the entire AVM volume. Volume-staged stereotactic radiosurgery (VS-SRS) is an option for large AVMs, but it has mixed results. The authors report on a series of patients with high-grade AVMs who underwent multiple VS-SRS sessions with resultant downgrading of the AVMs, followed by resection. METHODS A cohort of patients was retrieved from a single-institution AVM patient registry consisting of prospectively collected data. VS-SRS was performed as a planned intentional treatment. Surgery was considered as salvage therapy in select patients. RESULTS Sixteen AVMs underwent VS-SRS followed by surgery. Four AVMs presented with rupture. The mean patient age was 25.3 years (range 13-54 years). The average initial Spetzler-Martin grade before any treatment was 4, while the average supplemented Spetzler-Martin grade (Spetzler-Martin plus Lawton-Young) was 7.1. The average AVM size in maximum dimension was 5.9 cm (range 3.3-10 cm). All AVMs were supratentorial in location and all except one were in eloquent areas of the brain, with 7 involving primary motor cortex. The mean number of VS-SRS sessions was 2.7 (range 2-5 sessions). The mean interval between first VS-SRS session and resection was 5.7 years. There were 4 hemorrhages that occurred after VS-SRS. The average Spetzler-Martin grade was reduced to 2.5 (downgrade, -1.5) and the average supplemented Spetzler-Martin grade was reduced to 5.6 (downgrade, -1.5). The maximum AVM size was reduced to an average of 3.0 cm (downsize = -2.9 cm). The mean modified Rankin Scale (mRS) scores were 1.2, 2.3, and 2.2 before VS-SRS, before surgery, and at last follow-up, respectively (mean follow-up, 6.9 years). Fifteen AVMs were cured after surgery. Ten patients had good outcomes at last follow-up (7 with mRS Score 0 or 1, and 3 with mRS Score 2). There were 2 deaths (both mRS Score 1 before treatment) and 4 patients with mRS Score 3 outcome (from mRS Scores 0, 1, and 2 [n = 2]). CONCLUSIONS Volume-staged SRS can downgrade AVMs, transforming high-grade AVMs (initially considered inoperable) into operable AVMs with acceptable surgical risks. This treatment paradigm offers an alternative to conservative observation for young patients with unruptured AVMs and long life expectancy, where the risk of hemorrhage is substantial. Difficult AVMs were cured in 15 patients. Surgical morbidity associated with downgraded AVMs is reduced to that of postradiosurgical/preoperative supplemented Spetzler-Martin grades, not their initial AVM grades.

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Application of Single-Stage Stereotactic Radiosurgery for Cerebral Arteriovenous Malformations >10 cm3

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Background and Purpose: Stereotactic radiosurgery (SRS) is a safe and effective treatment for small arteriovenous malformations (AVMs), the use of this modality for the treatment of large AVMs is still controversial, although it has been used in difficult cases. The aim of this study was to evaluate the treatment outcomes of patients who underwent single-stage SRS for large AVMs and to discuss the role of SRS in the treatment of these challenging lesions.

Methods: Between 1998 and 2010, 65 patients with AVMs >10 cm3 underwent single-stage SRS using the Leksell Gamma Knife. Patients who had prospective volume-staged SRS were excluded from this series. Outcomes including the rates of obliteration, hemorrhage after treatment, and adverse events were retrospectively evaluated.

Results: The mean nidus volume was 14.9 cm3 (+/-3.8 cm3), and a mean margin dose of 20 Gy (+/-1.5 Gy) was applied. The mean observation period was 60 months (range, 7-178 months). The nidus obliteration rates after

SRS were 44%, 76%, and 81% at 3, 5, and 6 years, respectively. The annual hemorrhage rate after SRS was 1.94% and permanent adverse events were observed in 2 patients (3%).
Conclusions: For large AVMs <20 cm3, single-stage radiosurgery by applying >16 Gy marginal dose presented favorable obliteration rates with relatively low rate of morbidity. Further accumulation of cases is awaited to fully evaluate the results of single-stage radiosurgery for large AVMs.

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Stereotactic radiosurgery with neoadjuvant embolization of larger arteriovenous malformations: an institutional experience

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Objective: This study investigates the safety and efficacy of a multimodality approach combining staged endovascular embolizations with subsequent SRS for the management of larger AVMs.
Methods: Ninety-five patients with larger AVMs were treated with staged endovascular embolization followed by SRS between 1996 and 2011.
Results: The median volume of AVM in this series was 28 cm(3) and 47 patients (48%) were Spetzler-Martin grade IV or V. Twenty-seven patients initially presented with hemorrhage. Sixty-one patients underwent multiple embolizations while a single SRS session was performed in 64 patients. The median follow-up after SRS session was 32 months (range 9-136 months). Overall procedural complications occurred in 14 patients. There were 13 minor neurologic complications and 1 major complication (due to embolization) while four patients had posttreatment hemorrhage. Thirty-eight patients (40%) were cured radiographically. The postradiosurgery actuarial rate of obliteration was 45% at 5 years, 56% at 7 years, and 63% at 10 years. In multivariate analysis, larger AVM size, deep venous drainage, and the increasing number of embolization/SRS sessions were negative predictors of obliteration. The number of embolizations correlated positively with the number of stereotactic radiosurgeries ($P < 0.005$).
Conclusions: Multimodality endovascular and radiosurgical approach is an efficacious treatment strategy for large AVM.

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A historical analysis of single-stage gamma knife radiosurgical treatment for large arteriovenous malformations: evolution and outcomes

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BACKGROUND: Large arteriovenous malformations (AVMs) remain challenging and difficult to treat, reflected by evolving strategies developed from simple radiosurgical plans, to encompass embolization and, recently, staged volume treatments. To establish a baseline for future practice, we reviewed our clinical experience. METHOD: The outcomes for 492 patients (564 treatments) with AVMs >10 cm(3) treated by single-stage radiosurgery were retrospectively analysed in terms of planning, previous embolization and size. RESULTS: Twenty-eight percent of the patients presented with haemorrhage at a median age of 29 years (range: 2-75). From 1986 to 1993 (157 patients) plans were simplistic, based on angiography using a median of 2 isocentres and a marginal dose of 23 Gy covering 45-70% of the AVM (median volume 15.7 cm(3)). From 1994 to 2000 (225 patients) plans became more sophisticated, a median of 5 isocentres was used, covering 64-95% of the AVM (14.6 cm(3)), with a marginal dose of 21 Gy. Since 2000, MRI has been used with angiography to plan for 182 patients. Median isocentres increased to 7 with similar coverage (62-94%) of the AVM (14.3 cm(3)) and marginal dose of 21 Gy. Twenty-seven percent, 30% and 52% of patients achieved obliteration at 4 years, respectively. The proportion of prior embolization increased from 9% to 44% during the study. Excluding the embolized patients, improvement in planning increased obliteration rates from 28% to 36% and finally 63%. Improving treatment plans did not significantly decrease the rate of persisting radiation-induced side effects (12-16.5%). Complication rate rose with increasing size. One hundred and twenty-three patients underwent a second radiosurgical treatment, with a 64% obliteration rate, and mild and rare complications (6%). CONCLUSIONS: Better visualization of the nidus with multimodality imaging improved obliteration rates

without changing morbidity. Our results support the view that prior embolization can make interpretation of the nidus more difficult, reducing obliteration rate. It will be important to see how results of staged volume radiosurgery compare with this historical material.

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Staged Gamma Knife Radiosurgery for Large Cerebral Arteriovenous Malformations

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Background: We present our experience over a 10-year period of staged radiosurgery for large arteriovenous malformations (AVMs) including patient outcomes and methods. Methods: From July 2000 to December 2010, 80 patients with AVMs were treated with gamma knife radiosurgery (GKS) at our institution; of these patients, 5 were treated for large AVMs with staged GKS (volumes >20 cm(3)). The mean interval between treatments was 10 months (range 7-16). The mean dose for the margin used was 18.0 Gy (range 16-20). The mean volume treated was 37.2 cm(3) (range 22-50). The mean total follow-up was 76.5 months (range 42-120). Results: Two patients had complete obliteration of the AVM nidus. One patient had 95% obliteration (31 months after radiosurgery), one had 90% obliteration (38 months after radiosurgery), and one had less than 50% obliteration at 53 months with a 16-month interval between staged treatments. Conclusions: Staged radiosurgery is an effective and safe method for the treatment of large AVMs. We report achieving higher marginal doses with staging in planned intervals of 6-9 months between staged treatments. It appears that the longer the wait between treatments, the less likely it is that complete obliteration will be achieved.

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Combined endovascular embolization and stereotactic radiosurgery in the treatment of large arteriovenous malformations

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OBJECT: Large cerebral arteriovenous malformations (AVMs) are often not amenable to direct resection or stereotactic radiosurgery (SRS) treatment. An alternative treatment strategy is staged endovascular embolization followed by SRS (Embo/SRS). The object of this study was to examine the experience at Washington University in St. Louis with Embo/SRS for large AVMs and review the results in earlier case series. METHODS: Twenty-one cases involving patients with large AVMs treated with Embo/SRS between 1994 and 2006 were retrospectively evaluated. The AVM size (before and after embolization), procedural complications, radiological outcome, and neurological outcome were examined. Radiological success was defined as AVM obliteration as demonstrated by catheter angiography, CT angiography, or MR angiography. Radiological failure was defined as residual AVM as demonstrated by catheter angiography, CT angiography, or MR angiography performed at least 3 years after SRS. RESULTS: The maximum diameter of all AVMs in this series was > 3 cm (mean 4.2 cm); 12 (57%) were Spetzler-Martin Grade IV or V. Clinical follow-up was available in 20 of 21 cases; radiological follow-up was available in 19 of 21 cases (mean duration of follow-up 3.6 years). Forty-three embolization procedures were performed; 8 embolization-related complications occurred, leading to transient neurological deficits in 5 patients (24%), minor permanent neurological deficits in 3 patients (14%), and major permanent neurological deficits in none (0%). Twenty-one SRS procedures were performed; 1 radiation-induced complication occurred (5%), leading to a permanent minor neurological deficit. Of the 20 patients with clinical follow-up, none experienced cerebral hemorrhage. In the 19 patients with radiological follow-up, AVM obliteration was confirmed by catheter angiography in 13, MR angiography in 2, and CT angiography in 1. Residual nidus was found in 3 patients. In patients with follow-up catheter angiography, the AVM obliteration rate was 81% (13 of 16 cases). CONCLUSIONS: Staged endovascular embolization followed by SRS provides an effective means of treating large AVMs not amenable to standard surgical or SRS treatment. The outcomes and complication rates reported in this series compare favorably to the results of other reported therapeutic strategies for this very challenging patient population.

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Gamma Knife surgery for large cerebral arteriovenous malformations

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OBJECT: Treatment of arteriovenous malformations (AVMs) is problematic due to many factors, including lesion size, lesion location, unacceptable complications, and negative outcomes. To overcome the limitation imposed by a large nidus volume, neurosurgeons have used Gamma Knife surgery (GKS) in a variety of ways, including combined with other treatment modalities, as volume-staged radiosurgery, and as repeat radiosurgery. We performed repeat radiosurgeries in patients who harbored large AVMs (> 30 cm(3)) and analyzed the AVM obliteration rates and complications. METHODS: The authors reviewed the cases of 44 patients at a single institution who underwent GKS between 1992 and 2007 for treatment of an AVM whose nidus was 30 cm(3) or larger. The mean age of the patients was 27 years (range 4.5-62.3 years), and the median duration of follow-up was 109.4 months (range 27-202 months). The mean AVM nidus volume was 48.8 cm(3) (range 30.3-109.5 cm(3)), and the mean radiation dose delivered to the margin of the nidus was 13.9 Gy (range 8.4-17.5 Gy). The authors determined complete AVM nidus obliteration based on findings on both MR images and digital subtraction angiograms. When they did not detect complete obliteration after GKS, they performed 1 or more additional GKSs separated by a minimum interval of 3 years. RESULTS: The overall obliteration rate following repeat GKS was 34.1%, and the estimated obliteration rate at 120 months was 41.8%. Three patients (6.8%) experienced hemorrhages after GKS, and 2 patients (4.5%) developed cysts. One patient (2.3%) experienced a newly developed seizure following GKS, and another patient (2.3%) was found to have radiation necrosis. CONCLUSIONS: Even though complete obliteration of the large AVMs after repeat GKS took a long time, the complication rate was quite acceptable. In addition, the estimated obliteration rate at long-term follow-up was respectable. Repeat GKS should be considered as a primary treatment option for symptomatic large AVMs to overcome the limitation imposed on successful obliteration by the large volume of the nidus.

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Radiosurgical considerations in the treatment of large cerebral arteriovenous malformations

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OBJECTIVE: In order to establish the role of Gamma Knife radiosurgery (GKS) in large intracranial arteriovenous malformations (AVMs), we analyzed clinical characteristics, radiological features, and radiosurgical outcomes. METHODS: Between March 1992 and March 2005, 28 of 33 patients with large AVMs (> 10 cm(3) in nidus-volume) who were treated with GKS underwent single session radiosurgery (RS), and the other 5 patients underwent staged volumetric RS. Retrospectively collected data were available in 23 cases. We analyzed treatment outcomes in each subdivided groups and according to the AVM sizes. We compared the estimated volume, defined as primarily estimated nidus volume using MR images, with real target volume after excluding draining veins and feeding arteries embedded into the nidus. RESULTS: Regarding those patients who underwent single session RS, 44.4% (8/18) had complete obliteration; regarding staged volumetric RS, the obliteration rate was 40% (2/5). The complete obliteration rate was 60% (6/10) in the smaller nidus group (10-15 cm(3) size), and 25% (2/8) in the larger nidus group (over 15 cm(3) size). One case of cerebral edema and two cases (8.7%) of hemorrhage were seen during the latent period. The mean real target volume for 18 single sessions of RS was 17.1 cm(3) (10.1-38.4 cm(3)), in contrast with the mean estimated volume of 20.9 cm(3) (12.0-45.0 cm(3)). CONCLUSION: The radiosurgical treatment outcomes of large AVMs are generally poor. However, we presume that the recent development in planning software and imaging devices aid more accurate measurement of the nidus volume, therefore improving the treatment outcome.

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Staged radiosurgery for extra-large cerebral arteriovenous malformations: method, implementation, and results

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OBJECT: The effectiveness and safety of radiosurgery for small- to medium-sized cerebral arteriovenous malformations (AVMs) have been well established. However, the management for large cerebral AVMs remains a great challenge to neurosurgeons. In the past 5 years the authors performed preplanned staged radiosurgery to treat extra-large cerebral AVMs. METHODS: An extra-large cerebral AVM is defined as one with nidus volume

> 40 ml. The nidus volume of cerebral AVM is measured from the dose plan-that is, as being the volume contained within the best-fit prescription isodose. From January 2003 to December 2007, the authors treated 6 patients with extra-large AVMs by preplanned staged GKS. Staged radiosurgery is implemented by rigid transformation with translation and rotation of coordinates between 2 stages. The average radiation-targeted volume was 60 ml (range 47-72 ml). The presenting symptoms were seizure in 4 patients and a bleeding episode in 2. One patient had undergone a previous craniotomy and evacuation of hematoma. The mean interval between the 2 radiosurgical sessions was 6.9 months (range 4.5-9.1 months). The prescribed marginal dose given to the nidus volume in each stage ranged from 16 to 18.6 Gy. The expected marginal dose of total nidus was 17-19 Gy. Regular follow-up MR imaging was performed every 6 months. The mean follow-up period was 28 months (range 12-54 months). RESULTS: Most of the patients exhibited clinical improvement: relief of headache and reduced frequency of seizure attack. All patients had significant regression of nidus observed on MR imaging follow-up. Two patients had angiogram-confirmed complete obliteration of the nidus 45 and 60 months after the second-stage radiosurgical session. One patient experienced minor bleeding 8 months after the second-stage radiosurgery with mild headache. She had satisfactory recovery without clinical neurological deficit after conservative treatment. CONCLUSIONS: These preliminary results indicate that staged radiosurgery is a practical strategy to treat patients with extra-large cerebral AVMs. It takes longer to obliterate the AVMs. The observed high signal T2 changes after the radiosurgery appeared clinically insignificant in 6 patients followed up for an average of 28 months. Longer follow-up is necessary to confirm its long-term safety.

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Advances in the radiosurgical treatment of large inoperable arteriovenous malformations

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Radiosurgery has proven useful in the treatment of small arteriovenous malformations (AVMs) of the brain. However, the volume of healthy tissue irradiated around large lesions is rather significant, necessitating reduced radiation doses to avoid complications. As a consequence, this can produce poorer obliteration rates. Several strategies have been developed in the past decade to circumvent dose-volume problems with large AVMs, including repeated treatments as well as dose, and volume fractionation schemes. Although success on par with that achieved in lesions smaller than 3 ml remains elusive, improvements over the obliteration rate, the complication rate or both have been reported after conventional single-dose stereotactic radiosurgery (SRS). Radiosurgery with a marginal dose or peripheral dose < 15 Gy rarely obliterates AVMs, yet most lesions diminish in size posttreatment. Higher doses may then be reapplied to any residual nidi after an appropriate follow-up period. Volume fractionation divides AVMs into smaller segments to be treated on separate occasions. Doses > 15 Gy irradiate target volumes of only 5-15 ml, thereby minimizing the radiation delivered to the surrounding brain tissue. Fewer adverse radiological effects with the use of fractionated radiosurgery over standard radiosurgery have been reported. Advances in AVM localization, dose delivery, and dosimetry have revived interest in hypofractionated SRS. Investigators dispensing >or= 7 Gy per fraction minimum doses have achieved occlusion with an acceptable number of complications in 53-70% of patients. The extended latency period between treatment and occlusion, about 5 years for emerging techniques (such as salvage, staged volume, and hypofractionated radiotherapy), exposes the patient to the risk of hemorrhage during that period. Nevertheless, improvements in dose planning and target delineation will continue to improve the prognosis in patients harboring inoperable AVMs.

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Is repeated radiosurgery an alternative to staged radiosurgery for very large brain arteriovenous malformations?

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OBJECT: The results of a novel radiosurgical approach to treat large arteriovenous malformations (AVMs) with repeated radiosurgery are presented and discussed. METHODS: The outcome was studied following repeated Gamma Knife surgery (GKS) for large AVMs, defined as a nidus volume of 9 ml or more. The philosophy was to treat the whole AVM with a low dose of radiation (> or = 10 Gy), and to repeat the treatment if the AVM shrank but was not obliterated. The study included 133 patients with AVMs treated at one of three different

institutions. Clinical information was available for all patients, and complete radiological follow-up was available in 89 patients after the first treatment, and in 19 after the second treatment. RESULTS: The estimated obliteration rate following repeated GKS was 62%. Four patients (3%) developed neurological deficits caused by the radiation, whereas five others (4%) developed cystic changes. The annual incidence of hemorrhage was high (7%), of which 35% occurred within the 1st year after the first treatment. CONCLUSIONS: Repeated radiosurgery seems to be a viable option for some AVMs considered to be too large for conventional radiosurgical treatment. The incidence of posttreatment hemorrhages seems to be a larger clinical problem than radiation-induced complications.

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Anatomic landmarks versus fiducials for volume-staged gamma knife radiosurgery for large arteriovenous malformations
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PURPOSE: The purpose of this investigation was to compare the accuracy of using internal anatomic landmarks instead of surgically implanted fiducials in the image registration process for volume-staged gamma knife (GK) radiosurgery for large arteriovenous malformations. METHODS AND MATERIALS: We studied 9 patients who had undergone 10 staged GK sessions for large arteriovenous malformations. Each patient had fiducials surgically implanted in the outer table of the skull at the first GK treatment. These markers were imaged on orthogonal radiographs, which were scanned into the GK planning system. For the same patients, 8-10 pairs of internal landmarks were retrospectively identified on the three-dimensional time-of-flight magnetic resonance imaging studies that had been obtained for treatment. The coordinate transformation between the stereotactic frame space for subsequent treatment sessions was then determined by point matching, using four surgically embedded fiducials and then using four pairs of internal anatomic landmarks. In both cases, the transformation was ascertained by minimizing the chi-square difference between the actual and the transformed coordinates. Both transformations were then evaluated using the remaining four to six pairs of internal landmarks as the test points. RESULTS: Averaged over all treatment sessions, the root mean square discrepancy between the coordinates of the transformed and actual test points was 1.2 +/- 0.2 mm using internal landmarks and 1.7 +/- 0.4 mm using the surgically implanted fiducials. CONCLUSION: The results of this study have shown that using internal landmarks to determine the coordinate transformation between subsequent magnetic resonance imaging scans for volume-staged GK arteriovenous malformation treatment sessions is as accurate as using surgically implanted fiducials and avoids an invasive procedure.

Pediatric

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Gamma Knife Radiosurgery for Pediatric Arteriovenous Malformations: A Canadian Experience
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BACKGROUND: Gamma Knife (GK) radiosurgery for pediatric arteriovenous malformations (AVM) of the brain presents a non-invasive treatment option. We report our institutional experience with GK for pediatric AVMs. METHODS: We performed a retrospective review of all pediatric patients treated with GK for cerebral AVMs at our institution from November 2003 up to and including September 2014. Patient demographics, AVM characteristics, treatment parameters and AVM responses were recorded. RESULTS: Nineteen patients were treated, with 4 lost to follow-up. The mean age was 14.2 years (range. 7-18 years), with 10 being males (52.6%). The mean AVM diameter and volume were 2.68 cm and 3.10 cm3 respectively. The mean Spetzler-Martin (SM) and Pollock grades of the treated AVMs were 2.4 and 0.99 respectively. The mean follow-up was 62 months. All AVMs treated demonstrated a response on follow-up imaging. Nine of 15 (60.0%) patients displayed obliteration of their AVMs. Nine of 11 patients with a minimum of 3 years follow-up (81.8%) displayed obliteration, with SM and Pollock grades correlating to the chance of obliteration in this group. Two

patients developed post-GK edema requiring short course dexamethasone therapy. No other major complications occurred. No permanent complications occurred. CONCLUSIONS: GK radiosurgery for pediatric AVMs offers a safe and effective treatment option, with low permanent complication rates during early follow-up.

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The long-term outcomes of radiosurgery for arteriovenous malformations in pediatric and adolescent populations.

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OBJECT Although stereotactic radiosurgery (SRS) has been accepted as a therapeutic option for arteriovenous malformations (AVMs) in children and adolescents, substantial data are still lacking regarding the outcomes of SRS for AVMs in this age group, especially long-term complications. This study aimed to clarify the long-term outcomes of SRS for the treatment of AVM in pediatric patients aged ≤ 18 years. METHODS Outcomes of 116 patients who were aged 4-18 years when they underwent SRS between 1990 and 2009 at the study institute were analyzed retrospectively. RESULTS The median follow-up period after SRS was 100 months, with 6 patients followed up for more than 20 years. Actuarial obliteration rates at 3 and 5 years after SRS were 68% and 88%, respectively. Five hemorrhages occurred in 851 patient-years of follow-up. The annual bleeding rate after SRS before obliteration was calculated as 1.3%, which decreased to 0.2% after obliteration. Shorter maximum nidus diameter ($p = 0.02$) and higher margin dose ($p = 0.03$) were associated with a higher obliteration rate. Ten patients experienced adverse events after SRS. Of them, 4 patients presented with delayed complications years after SRS (range 9-20 years after SRS). CONCLUSIONS SRS can reduce the risk of hemorrhage in pediatric and adolescent AVMs, with an acceptable risk of complications in the long term. However, adverse events such as expanding hematoma and radiation necrosis that can occur after substantial follow-up should be taken into account at the time that treatment decisions are made and informed consent is obtained.

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Radiosurgery for unruptured cerebral arteriovenous malformations in pediatric patients

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Background: Unruptured cerebral arteriovenous malformations (AVMs) in pediatric patients (age <18 years) were excluded from A Randomized Trial of Unruptured AVMs (ARUBA). Therefore, the efficacy of radiosurgery for unruptured pediatric AVMs is poorly understood. The goal of this study is to determine the outcomes and define the predictors of obliteration following radiosurgery for unruptured AVMs in pediatric patients.

Methods: We evaluated a prospective database, from 1989 to 2013, of AVM patients treated with radiosurgery at our institution. Patients with age less than 18 years at the time of radiosurgery, unruptured nidi, and at least 2 years of radiologic follow-up or AVM obliteration were selected for analysis. Statistical analyses were performed to determine actuarial obliteration rates and identify factors associated with obliteration.

Results: In the 51 unruptured pediatric AVM patients included for analysis, the median age was 13 years, and the most common presentation was seizure in 53 %. The median nidus volume and radiosurgical margin dose were 3.2 cm3 and 21.5 Gy, respectively. The median radiologic follow-up was 45 months. The actuarial AVM obliteration rates at 3, 5, and 10 years were 29 %, 54 %, and 72 %, respectively. In the multivariate Cox proportional hazards regression analysis, higher margin dose ($P = 0.002$), fewer draining veins ($P = 0.038$), and lower Virginia Radiosurgery AVM Scale ($P = 0.003$) were independent predictors of obliteration. Obliteration rates were significantly higher with a margin dose of at least 22 Gy ($P = 0.003$) and for nidi with 2 or fewer draining veins ($P = 0.001$). The incidences of radiologically evident, symptomatic, and permanent radiation-induced changes were 55 %, 16 %, and 2 %, respectively. The annual post-radiosurgery hemorrhage rate was 1.3 %, and the incidence of post-radiosurgery cyst formation was 2 %.

Conclusion: Radiosurgery affords a favorable risk to benefit profile for unruptured pediatric AVMs. Pediatric patients with unruptured AVMs merit further study to define an optimal management approach.

Childs Nerv Syst.2014;30(9):1485-92. Epub 2014/06/29

Gamma Knife radiosurgery for arteriovenous malformations in pediatric patients

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Objective: The authors present the results of Gamma Knife stereotactic radiosurgery performed in a series of children with arteriovenous malformations (AVMs).

Methods: Between June 2005 and January 2014, 75 patients 18 years old or younger received Gamma Knife radiosurgery for AVMs. Of these, 58 patients were eligible for further analysis. The median age of the population was 12 years; 41 % presented with hemorrhage, 34 % with neurological insult, and 24 % patients were diagnosed incidentally. The median AVM volume was 3.5 cm(3). The median radiosurgery-based AVM score (RSBAVMS) was 0.86. The median follow-up period was 32 months.

Results: Single session Gamma Knife radiosurgery resulted in complete AVM obliteration in 40 (68.9 %) patients. There were 35 (60.3 %) excellent outcome (complete obliteration with no new deficits) in this series. During the follow-up period, nine (15.51 %) patients experienced new deficits and three (5.1 %) patients experienced intracranial hemorrhage. The annual rate of developing new deficits and hemorrhage was calculated as 5.45 and 1.8 %, respectively. Volume, gender, RSBAVMS, and nidus type factor were factors associated with excellent outcome.

Conclusions: Radiosurgery was successful in majority of patients with minimal morbidity. Gamma Knife radiosurgery for AVMs can be a safe and successful method in pediatric patients.

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Stereotactic radiosurgery at a low marginal dose for the treatment of pediatric arteriovenous malformations: obliteration, complications, and functional outcomes

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Object: Stereotactic radiosurgery (SRS) is an established treatment modality for brain arteriovenous malformations (AVMs) in children, but the optimal treatment parameters and associated treatment-related complications are not fully understood. The authors present their single-institution experience of using SRS, at a relatively low marginal dose, to treat AVMs in children for nearly 20 years; they report angiographic outcomes, posttreatment hemorrhage rates, adverse treatment-related events, and functional outcomes.

Methods: The authors conducted a retrospective review of 2 cohorts of children (18 years of age or younger) with AVMs treated from 1991 to 1998 and from 2000 to 2010.

Results: A total of 80 patients with follow-up data after SRS were identified. Mean age at SRS was 12.7 years, and 56% of patients had hemorrhage at the time of presentation. Median target volume was 3.1 cm3 (range 0.09-62.3 cm3), and median prescription marginal dose used was 17.5 Gy (range 12-20 Gy). Angiograms acquired 3 years after treatment were available for 47% of patients; AVM obliteration was achieved in 52% of patients who received a dose of 18-20 Gy and in 16% who received less than 18 Gy. At 5 years after SRS, the cumulative incidence of hemorrhage was 25% (95% CI 16%-37%). No permanent neurological deficits occurred in patients who did not experience posttreatment hemorrhage. Overall, good functional outcomes (modified Rankin Scale Scores 0-2) were observed for 78% of patients; for 66% of patients, functional status improved or remained the same as before treatment.

Conclusions: A low marginal dose minimizes SRS-related neurological deficits but leads to low rates of obliteration and high rates of hemorrhage. To maximize AVM obliteration and minimize posttreatment hemorrhage, the authors recommend a prescription marginal dose of 18 Gy or more. In addition, SRS-related symptoms such as headache and seizures should be considered when discussing risks and benefits of SRS for treating AVMs in children.

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Fatal glioblastoma after Gamma Knife radiosurgery for arteriovenous malformation in a child

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We describe a fatal case of glioblastoma multiforme that was induced by Gamma Knife radiosurgery (GKS; Elekta AB, Stockholm, Sweden) for an arteriovenous malformation (AVM). A 4-year-old girl presented with repeated convulsions. Imaging studies revealed an AVM located in the right thalamus. One year after initial symptoms, GKS was performed to obliterate the nidus. The maximum and marginal radiation doses were 32 and 16Gy, respectively. Seventy months after GKS, the patient represented with severe headache. MRI showed a poorly demarcated tumor with heterogeneous gadolinium enhancement in the right thalamus and adjacent to the white matter of the temporal lobe. After a generalised convulsion, the patient deteriorated into a deep coma. CT scans showed severe brain swelling with intratumoral hemorrhage. An emergency craniotomy was performed, and the hematoma was removed. During this surgery, a tumor mass, which was found adjacent to the hematoma, was resected. Microscopic examination revealed glioblastoma multiforme. Despite intensive treatment, the patient died 1month after surgery. A GKS-induced secondary tumor is a rare but serious complication. It is important to be aware of the adverse effects of GKS, including secondary neoplasms, before its clinical application, especially in young patients.

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Angiographic features help predict outcome after stereotactic radiosurgery for the treatment of pediatric arteriovenous malformations
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PURPOSE: Arteriovenous malformations (AVMs) are a frequent cause of hemorrhagic stroke in children. Stereotactic radiosurgery (SRS) is an established treatment for these lesions, particularly those that are surgically inaccessible. Because only complete AVM obliteration is believed to protect against the future risk of hemorrhage, identifying lesion characteristics that predict response to therapy is an important objective. The goal of this study is to evaluate the influence of angiographic features of AVMs on the rate of obliteration following treatment with SRS. METHODS: This is a retrospective cohort study of pediatric patients (age </=18 years) treated with Gamma Knife SRS for cerebral AVMs between 2000 and 2012. Detailed angiographic data at the time of initial angiographic evaluation were prospectively recorded by experienced neurointerventional radiologists. The primary outcome was the rate of obliteration on a 3-year follow-up angiogram. RESULTS: We identified 42 pediatric patients treated with SRS for cerebral AVMs. Twenty-seven patients completed 3-year angiographic follow-ups. Complete obliteration was seen in 30 %, partial response in 67 %, and no response in 4 %. Higher SRS dose was associated with complete obliteration. Larger AVM diameter, presence of multiple draining veins, and presence of multiple draining veins reaching a sinus were associated with partial response. In this small cohort, diffuse AVM borders, presence of aneurysm, and pre-SRS embolization were not associated with obliteration. CONCLUSIONS: Our study identifies AVMs in the pediatric population with a nidus diameter of <2.5 cm and a solitary draining vein as the most likely to undergo complete obliteration after SRS treatment.

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Stereotactic radiosurgery for arteriovenous malformations, Part 2: management of pediatric patients
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Object The authors conducted a study to define the long-term outcomes and risks of stereotactic radiosurgery (SRS) for pediatric arteriovenous malformations (AVMs). Methods Between 1987 and 2006, the authors performed Gamma Knife surgery in 996 patients with brain AVMs; 135 patients were younger than 18 years of age. The median maximum diameter and target volumes were 2.0 cm (range 0.6-5.2 cm) and 2.5 cm(3) (range 0.1-17.5 cm(3)), respectively. The median margin dose was 20 Gy (range 15-25 Gy). Results The actuarial rates of total obliteration documented by angiography or MR imaging at 71.3 months (range 6-264 months) were 45%, 64%, 67%, and 72% at 3, 4, 5, and 10 years, respectively. The median time to complete angiographically documented obliteration was 48.9 months. Of 81 patients with 4 or more years of follow-up, 57 patients (70%)

had total obliteration documented by angiography. Factors associated with a higher rate of documented AVM obliteration were smaller AVM target volume, smaller maximum diameter, and larger margin dose. In 8 patients (6%) a hemorrhage occurred during the latency interval, and 1 patient died. The rates of AVM hemorrhage after SRS were 0%, 1.6%, 2.4%, 5.5%, and 10.0% at 1, 2, 3, 5, and 10 years, respectively. The overall annual hemorrhage rate was 1.8%. Larger volume AVMs were associated with a significantly higher risk of hemorrhage after SRS. Permanent neurological deficits due to adverse radiation effects developed in 2 patients (1.5%) after SRS, and in 1 patient (0.7%) delayed cyst formation occurred. Conclusions Stereotactic radiosurgery is a gradually effective and relatively safe management option for pediatric patients in whom surgery is considered to pose excessive risks. Although hemorrhage after AVM obliteration did not occur in the present series, patients remain at risk during the latency interval until obliteration is complete. The best candidates for SRS are pediatric patients with smaller volume AVMs located in critical brain regions.

Childs Nervous System.2011;27(7):1109-19. Epub 2011/02/03

Clinico-radiological outcomes following gamma knife radiosurgery for pediatric arteriovenous malformations

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PURPOSE: The aim of this study was to evaluate clinico-radiological outcomes following gamma knife radiosurgery (GKS) for pediatric arteriovenous malformations (AVMs). METHODS: The present series included 39 children (3-17 years of age) who underwent GKS for cerebral AVMs between January 2002 and February 2008. Twenty-five patients presented with hemorrhages. The median AVM volume was
1.5 cm(3), and the median marginal dose was 20 Gy. All patients continued to have follow-up for more than 24 months with serial magnetic resonance images (MRIs)/angiograms. Current school performance has been evaluated using a telephone survey answered by the patients' parents. RESULTS: Follow-up angiograms, available in 34 patients, confirmed complete obliteration in 16 patients. Serial MRIs indicated obliteration of the nidus in one of five patients without angiography. The diffuse nidus structure and low marginal dose were significantly associated with incomplete obliteration. Twelve patients underwent a second GKS, and subsequent angiographies, available in six patients, demonstrated complete obliteration in two of them. Complications included new-onset seizures (n = 1), apraxia (n = 1), and temporal horn entrapment requiring a shunt operation (n = 1). School performance declined in 14 out of 32 patients. Both the AVM volume and modified AVM score were found to be reliable predictors of school performance. CONCLUSIONS: The results of the present study substantiate the diffuse and other atypical features of pediatric AVMs as major determinants of treatment failure following GKS. Considering the apparent declination of school performance, future prospective studies would be required to investigate the possible late-effects of GKS on neuropsychological function.

J Neurosurg Pediatr.2010;6(5):426-34. Epub 2010/11/03

Gamma Knife surgery for arteriovenous malformations in children

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OBJECT: The aim of this study was to evaluate the long-term imaging and clinical outcomes of intracranial arteriovenous malformations (AVMs) in children treated with Gamma Knife surgery (GKS). METHODS: Between 1989 and 2007, 200 patients with AVMs who were 18 years of age or younger were treated at the University of Virginia Health System. Excluding 14 patients who had not reached 2-year follow-up, 186 patients comprised this study. Hemorrhage was the most common presenting symptom leading to the diagnosis of AVMs (71.5%). The mean nidus volume was 3.2 cm(3) at the time of GKS, and a mean prescription dose of 21.9 Gy was used. RESULTS: After initial GKS, 49.5% of patients achieved total angiographic obliteration. Forty-one patients whose AVM nidi remained patent underwent additional GKS. The obliteration rate increased to 58.6% after a second or multiple GKS. Subtotal obliteration was achieved in 9 patients (4.8%). Forty-nine patients (26.3%) still had a patent residual nidus. In 19 patients (10.2%), obliteration was confirmed on MR imaging only. Ten patients had 17 hemorrhages during the follow-up period. The hemorrhage rate was 5.4% within 2 years after GKS and 0.8% between 2 and 5 years. Six patients developed neurological deficits along with the radiation- induced changes. Two patients developed asymptomatic meningiomas 10 and 12 years after GKS. After a mean clinical follow-up of 98 months, less than 4% of patients had difficulty attending school or developing a career. CONCLUSIONS: Gamma Knife surgery offers a reasonable chance of obliteration of an AVM in pediatric patients. The incidence

of symptomatic radiation-induced changes is relatively low; however, long-term clinical and imaging follow-up is required to identify delayed cyst formation and secondary tumors.

Neurosurgery Clinics of North America.2010;21(3):457-61. Epub 2010/06/22

Stereotactic radiosurgery for pediatric arteriovenous malformations

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Children with intracranial arteriovenous malformations (AVM) have a high cumulative risk of hemorrhage and therefore effective treatment of AVMs in the pediatric population is imperative. Treatment options include microsurgical resection, endovascular embolization, staged or single fraction radiosurgery, or some combination of these treatments, with the ultimate goal of eliminating the risk of hemorrhage. In this article the authors review the current data on the use of radiosurgery for the treatment of childhood AVMs. Factors associated with successful AVM radiosurgery in this population are examined, and comparisons with outcomes in adult patients are reviewed.

Journal of Neurosurgery.2007;107(6 Suppl):479-84. Epub 2007/12/25

Gamma Knife surgery for intracranial arteriovenous malformations in children: a retrospective study in 103 patients

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OBJECT: This retrospective study was designed to study the outcome in children with intracranial arteriovenous malformations (AVMs) treated with Gamma Knife surgery (GKS). METHODS: One hundred and forty-two children were treated with GKS at the authors' institution between April 1997 and March 2006; of these, 103 patients with a mean follow-up of 26.4 months (range 6-96 months) were included. The mean age at presentation was 13.9 years (range 3-18 years). Eighty-six (83%) patients presented with hemorrhage. In 57 children the AVMs were Spetzler-Martin Grade I or II, and in 46 the AVMs were Grades III, IV, or V. The mean volume of the AVMs was 2.4 ml (range 0.04-23.3 ml). The mean marginal dose administered was 24.4 Gy (range 15-27 Gy). Follow-up angiography was advised at 2 years after GKS and yearly thereafter. In patients with residual AVMs, follow-up angiography was advised yearly until 4 years after GKS. If residual AVM was present, even on a follow-up angiogram obtained 4 years postsurgery, the GKS was considered a failure. RESULTS: Complete obliteration of the AVM was documented in 34 (87%) of the 39 patients with complete angiographic follow-up. The 3- and 4-year actuarial rates of nidus obliteration were 66 and 86% respectively. Three patients (2.9%) experienced bleeding during the latency period, and symptomatic radiation-induced edema was noted in four patients (3.8%). A significantly higher incidence of radiation edema was noted in patients with AVM volumes greater than 3 ml and in patients with Spetzler-Martin Grade IV and V AVMs. CONCLUSIONS: Gamma Knife radiosurgery is an effective modality for the treatment of intracranial AVMs in children, yielding high obliteration rates and low complication rates.

Prognostic Factors/Models

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Stereotactic radiosurgery for Spetzler-Martin Grade III arteriovenous malformations: an international multicenter study

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OBJECTIVE Because of the angioarchitectural diversity of Spetzler-Martin (SM) Grade III arteriovenous malformations (AVMs), the management of these lesions is incompletely defined. The aims of this multicenter, retrospective cohort study were to evaluate the outcomes after stereotactic radiosurgery (SRS) for SM Grade III AVMs and to determine the factors predicting these outcomes. METHODS The authors analyzed and pooled data from patients with SM Grade III AVMs treated with SRS at 8 institutions participating in the International Gamma Knife Research Foundation. Patients with these AVMs and a minimum follow-up length of 12 months were included in the study cohort. An optimal outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes (RICs). Data were analyzed by univariate and multivariate regression analyses. RESULTS The SM Grade III AVM cohort comprised 891 patients with a mean age of 34 years at the time of SRS. The mean nidus volume, radiosurgical margin dose, and follow-up length were 4.5 cm3, 20 Gy, and 89 months, respectively. The actuarial obliteration rates at 5 and 10 years were 63% and 78%, respectively. The annual postradiosurgery hemorrhage rate was 1.2%. Symptomatic and permanent RICs were observed in 11% and 4% of the patients, respectively. Optimal outcome was achieved in 56% of the patients and was significantly more frequent in cases of unruptured AVMs (OR 2.3, $p < 0.001$). The lack of a previous hemorrhage ($p = 0.037$), absence of previous AVM embolization ($p = 0.002$), smaller nidus volume ($p = 0.014$), absence of AVM-associated arterial aneurysms ($p = 0.023$), and higher margin dose ($p < 0.001$) were statistically significant independent predictors of optimal outcome in a multivariate analysis. CONCLUSIONS Stereotactic radiosurgery provided better outcomes for patients with small, unruptured SM Grade III AVMs than for large or ruptured SM Grade III nidi. A prospective trial or registry that facilitates a comparison of SRS with conservative AVM management might further clarify the authors' observations for these often high-risk AVMs.

Stroke.2016;47(5):1247-52.Epub 2016/04/14
Risk Reduction of Cerebral Stroke After Stereotactic Radiosurgery for Small Unruptured Brain Arteriovenous Malformations
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BACKGROUND AND PURPOSE: A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA) indicated the superiority of medical management in reducing the risks for strokes and other neurological deficits over observation alone. The aim of our study was to verify the rationale for stereotactic radiosurgery (SRS) for small unruptured arteriovenous malformation. METHODS: A retrospective review was performed for 292 patients with unruptured arteriovenous malformations referred for SRS. The risks for cerebral hemorrhages were statistically compared before and after SRS. RESULTS: Of the 292 patients in whom arteriovenous malformation was found unruptured at initial diagnosis, 17 sustained hemorrhages in the period between the diagnosis and the initial therapeutic intervention (annual bleeding rate, 2.1%; 95% confidence interval [CI], 1.2%-3.4%). Of the remaining 275 patients, 240 were initially treated with SRS, and 16 sustained a hemorrhage after SRS (annual bleeding rate, 1.1%; 95% CI, 0.6%-1.8%), but only 2 sustained a hemorrhage after angiographic obliteration (annual bleeding rate, 0.3%; 95% CI, 0.04%-1.2%). Comparing the risk of hemorrhage between the periods before and after SRS, a 53% risk reduction was achieved after SRS (hazard ratio, 0.47; 95% CI, 0.24-0.94; P=0.03), and 85% reduction was achieved after angiographic obliteration (hazard ratio, 0.15; 95% CI, 0.02-0.53; P=0.002). CONCLUSIONS: SRS can significantly reduce the risk of stroke in the patients with small unruptured arteriovenous malformations. To definitively determine the clinical benefits of SRS, a longer follow-up will be necessary. However, based on our results, we can recommend SRS for patients who face a latent risk for stroke from this intractable vascular disease.

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Comparative analysis of arteriovenous malformation grading scales in predicting outcomes after stereotactic radiosurgery

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OBJECTIVE Successful stereotactic radiosurgery (SRS) for the treatment of arteriovenous malformations (AVMs) results in nidus obliteration without new neurological deficits related to either intracranial hemorrhage (ICH) or radiation-induced complications (RICs). In this study the authors compared 5 AVM grading scales (Spetzler-Martin grading scale, radiosurgery-based AVM score [RBAS], Heidelberg score, Virginia Radiosurgery AVM Scale [VRAS], and proton radiosurgery AVM scale [PRAS]) at predicting outcomes after SRS. METHODS The study group consisted of 381 patients with sporadic AVMs who underwent Gamma Knife SRS between January 1990 and December 2009; none of the patients underwent prior radiation therapy. The primary end point was AVM obliteration without a decline in modified Rankin Scale (mRS) score (excellent outcome). Comparison of the area under the receiver operating characteristic curve (AUC) and accuracy was performed between the AVM grading scales and the best linear regression model (generalized linear model, elastic net [GLMnet]). RESULTS The median radiological follow-up after initial SRS was 77 months; the median clinical follow-up was 93 months. AVM obliteration was documented in 297 patients (78.0%). Obliteration was 59% at 4 years and 85% at 8 years. Fifty-five patients (14.4%) had a decline in mRS score secondary to RICs (n = 29, 7.6%) or ICH (n = 26, 6.8%). The mRS score declined by 10% at 4 years and 15% at 8 years. Overall, 274 patients (71.9%) had excellent outcomes. There was no difference between the AUC for the GLMnet (0.69 [95% CI 0.64-0.75]), RBAS (0.68 [95% CI 0.62-0.74]), or PRAS (0.69 [95% CI 0.62-0.74]). Pairwise comparison for accuracy showed no difference between the GLMnet and the RBAS (p = 0.08) or PRAS (p = 0.16), but it did show a significant difference between the GLMnet and the Spetzler-Martin grading system (p < 0.001), Heidelberg score (p < 0.001), and the VRAS (p < 0.001). The RBAS and the PRAS were more accurate when compared with the Spetzler-Martin grading scale (p = 0.03 and p = 0.01), Heidelberg score (p = 0.02 and p = 0.02), and VRAS (p = 0.03 and p = 0.02). CONCLUSIONS SRS provides AVM obliteration without functional decline in the majority of treated patients. AVM grading scales having continuous scores (RBAS and PRAS) outperformed integer-based grading systems in the prediction of AVM obliteration without mRS score decline after SRS.

Clin Neurol Neurosurg. 2015 Jun;133:103-4. Epub 2015 Apr 4.
Microsurgery versus radiosurgery as the definitive intervention for Spetzler-Martin grade III arteriovenous malformations.
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Comment on: Surgical outcomes after classifying Grade III arteriovenous malformations according to Lawton's modified Spetzler-Martin grading system.

Neurol Sci.2014;Epub 2014/12/03
Predicting outcomes from radiosurgery for intracranial arteriovenous malformations: effect of embolization, prior hemorrhage, and nidus anatomy
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World Neurosurg.2014;Epub 2014/09/16
Stereotactic radiosurgery for AVMs with RBAS <1
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Neurosurg Focus.2014;37(3):E3. Epub 2014/09/02

Smoking is a negative predictor of arteriovenous malformation posttreatment obliteration: analysis of vascular risk factors in 774 patients

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Object: Cigarette smoking has been well established as a risk factor in vascular pathology, such as cerebral aneurysms. However, tobacco's implications for patients with cerebral arteriovenous malformations (AVMs) are controversial. The object of this study was to identify predictors of AVM obliteration and risk factors for complications.

Methods: The authors conducted a retrospective analysis of a prospectively maintained database for all patients with AVMs treated using surgical excision, staged endovascular embolization (with N-butyl-cyanoacrylate or Onyx), stereotactic radiosurgery (Gamma Knife or Linear Accelerator), or a combination thereof between 1994 and 2010. Medical risk factors, such as smoking, abuse of alcohol or intravenous recreational drugs, hypercholesterolemia, diabetes mellitus, hypertension, and coronary artery disease, were documented. A multivariate logistic regression analysis was conducted to detect predictors of periprocedural complications, obliteration, and posttreatment hemorrhage.

Results: Of 774 patients treated at a single tertiary care cerebrovascular center, 35% initially presented with symptomatic hemorrhage and 57.6% achieved complete obliteration according to digital subtraction angiography (DSA) or MRI. In a multivariate analysis a negative smoking history (OR 1.9, p = 0.006) was a strong independent predictor of AVM obliteration. Of the patients with obliterated AVMs, 31.9% were smokers, whereas 45% were not (p = 0.05). Multivariate analysis of obliteration, after controlling for AVM size and location (eloquent vs noneloquent tissue), revealed that nonsmokers were more likely (0.082) to have obliterated AVMs through radiosurgery. Smoking was not predictive of treatment complications or posttreatment hemorrhage. Abuse of alcohol or intravenous recreational drugs, hypercholesterolemia, diabetes mellitus, and coronary artery disease had no discernible effect on AVM obliteration, periprocedural complications, or posttreatment hemorrhage.

Conclusions: Cerebral AVM patients with a history of smoking are significantly less likely than those without a smoking history to have complete AVM obliteration on follow-up DSA or MRI. Therefore, patients with AVMs should be strongly advised to quit smoking.

Neurosurg Focus.2014;37(3):E15. Epub 2014/09/02

Stereotactic radiosurgery of intracranial arteriovenous malformations and the use of the K index in determining treatment dose

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Object: The appropriate dose during stereotactic radiosurgery (SRS) of cerebral arteriovenous malformations (AVMs) remains a matter of debate. In the present study, the authors retrospectively evaluated the association of using a prescribed dose calculated utilizing the K index with the obliteration rate of cerebral AVMs after SRS.

Methods: The authors performed a retrospective analysis of the Cleveland Clinic SRS database. All patients undergoing Gamma Knife radiosurgery for cerebral AVMs from 1997 to 2010 were selected. Regression techniques and Kaplan-Meier analyses were used to investigate the effect of divergence from the optimal K index dose on the rate of AVM obliteration.

Results: In the study period 152 patients (mean age 43.6 years; 53.9% of treatments were performed in females) underwent 165 Gamma Knife radiosurgery treatments for AVMs. In a univariate analysis Spetzler-Martin grade (OR 0.63 [95% CI 0.42-0.93]), higher AVM score (OR 0.43 [95% CI 0.27-0.70]), larger AVM volume (OR 0.88 [95% CI 0.82-0.94]), and higher maximum diameter (OR 0.56 [95% CI 0.41-0.77]) were associated with a lower rate of AVM obliteration. Higher margin dose (OR 1.16 [95% CI 1.08- 1.24]) and higher maximum dose (OR 1.08 [95% CI 1.04- 1.13]) were associated with a higher obliteration rate. To further examine the effect of prescribed dose divergence from the calculated K index dose, cases were classified to groups depending on the AVM volume and dose variance from the ideal K index dose. Contingency tables and Kaplan-Meier curves were then created, and no significant differences in rates of obliteration were noted among the different groups.

Conclusions: Gamma Knife radiosurgery for cerebral AVMs remains an effective and safe treatment modality. Smaller AVMs may receive doses less than the calculated K index dose without an apparent effect on obliteration rates.

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Results for a Series of 697 AVMs Treated by Gamma Knife: Influence of Angiographic Features on the Obliteration Rate

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Background: Stereotactic radiosurgery (RS) is an effective tool in treating brain AVMs. Careful study of AVM angiographic characteristics may improve results.

Objective: To report the long-term outcomes of Gamma Knife radiosurgery (GKRS) in brain AVMs focusing on how the angioarchitectural and hemodynamic parameters of AVMs impact the post-radiosurgery results.

Method: Retrospective longitudinal study of 697 consecutive GKRS treatments of brain AVMs in 662 patients, performed at a single center between 1993 and 2005. Mean age: 37 years, median AVM volume: 3.6cc, mean follow-up: 11 years. 45% of patients presented with intracranial hemorrhage, 44% underwent embolization, and 7% multiple RS. AVM characteristics in the RS-planning angiograms were analyzed and their relationship to the post-RS obliteration rate was determined by univariate and multivariate analysis.

Results: The obliteration rate after a single RS was 69.3%, after multiple RS 75%. Positive predictors of obliteration included: compact nidus (OR=3.16, 95%CI: 1.92-5.22), undilatated feeders (OR=0.36, 95%CI: 0.23-0.57), smaller AVM volume (OR=0.95, 95%CI: 0.92-0.99), and higher marginal dose (OR=1.16, 95%CI: 1.06-1.27). Improvement or clinical stability was observed in 89.3% of patients, post-procedure bleeding in 6.1%, and clinical worsening attributable to RS in 3.8%. The annual risk of hemorrhage in the four years following RS was 1.2%.

Conclusion: GKRS yielded a good long-term clinical outcome in most patients. Certain angiographic features of brain AVMs, such as a well-defined nidus and undilatated feeder arteries, contribute to AVM occlusion by RS. GKRS can be regarded as the treatment of choice for AVMs smaller than 6 cc, even after bleeding.

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Is Stereotactic Radiosurgery the Best Treatment Option for Patients with a Radiosurgery-based Arteriovenous Malformation Score </=1?

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Objective: The best management of patients with brain arteriovenous malformations (BAVM) is controversial. The radiosurgery-based AVM score (RBAS) was developed to predict outcomes for BAVM patients having stereotactic radiosurgery (SRS).

Methods: The RBAS is calculated for BAVM patients having SRS at our center as part of our prospectively maintained SRS database [RBAS= (0.1) (AVM volume; cm3) + (0.02) (patient age; years) + (0.5) (AVM location; 0=cerebral/ cerebellar hemispheres/corpus callosum, 1=basal ganglia/ thalamus/brainstem)]. Review of the SRS database from 1990-2009 identified 80 patients with a RBAS </=1 and at least one year of follow-up. The primary endpoint of the study was a decline in Modified Rankin Score (MRS). The mean follow-up after SRS was 68 months (range, 12-133).

Results: The mean patient age was 25.2 years (range, 7-44). Seventy-six patients (95%) had superficially located BAVMs; the mean BAVM volume was 2.3 cm3 (range, 0.1-8.0). The mean RBAS was 0.76 (range, 0.21-1.00). The patients' MRS before SRS was 0 (n=52, 65%), 1 (n=24, 30%), 2 (n=3, 4%), and 3 (n=1, 1%). BAVM obliteration was confirmed in 92% of patients with follow-up beyond 3 years (70/76; 95% CI, 84%-97%). No patient had a

hemorrhage or a radiation-related complication after SRS. The observed rate of MRS decline after SRS was 0% (0/80; 95% CI, 0%-6%).
Conclusions: Stereotactic radiosurgery provided a high rate of obliteration at very low risk for BAVM patients with a RBAS </=1. Patient outcomes after SRS are likely equivalent to resection for younger patients with small-volume BAVM who do not require a craniotomy for clot removal.

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Stereotactic radiosurgery for Spetzler-Martin Grade III arteriovenous malformations. Response
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Radiosurgery for low-grade intracranial arteriovenous malformations
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Object: Low-grade, or Spetzler-Martin (SM) Grades I and II, arteriovenous malformations (AVMs) are associated with lower surgical morbidity rates than higher-grade lesions. While radiosurgery is now widely accepted as an effective treatment approach for AVMs, the risks and benefits of the procedure for low-grade AVMs, as compared with microsurgery, remain poorly understood. The authors of this study present the outcomes for a large cohort of low-grade AVMs treated with radiosurgery.
Methods: From an institutional radiosurgery database comprising approximately 1450 AVM cases, all patients with SM Grade I and II lesions were identified. Patients with less than 2 years of radiological follow-up, except those with complete AVM obliteration, were excluded from analysis. Univariate and multivariate Cox proportional-hazards and logistic regression analyses were used to determine factors associated with obliteration, radiation-induced changes (RICs), and hemorrhage following radiosurgery.
Results: Five hundred two patients harboring low-grade AVMs were eligible for analysis. The median age was 35 years, 50% of patients were male, and the most common presentation was hemorrhage (47%). The median AVM volume and prescription dose were 2.4 cm3 and 23 Gy, respectively. The median radiological and clinical follow-up intervals were 48 and 62 months, respectively. The cumulative obliteration rate was 76%. The median time to obliteration was 40 months, and the actuarial obliteration rates were 66% and 80% at 5 and 10 years, respectively. Independent predictors of obliteration were no preradiosurgery embolization ($p < 0.001$), decreased AVM volume ($p = 0.005$), single draining vein ($p = 0.013$), lower radiosurgery-based AVM scale score ($p = 0.016$), and lower Virginia Radiosurgery AVM Scale (Virginia RAS) score ($p = 0.001$). The annual postradiosurgery hemorrhage rate was 1.4% with increased AVM volume ($p = 0.034$) and lower prescription dose ($p = 0.006$) as independent predictors. Symptomatic and permanent RICs were observed in 8.2% and 1.4% of patients, respectively. No preradiosurgery hemorrhage ($p = 0.011$), a decreased prescription dose ($p = 0.038$), and a higher Virginia RAS score ($p = 0.001$) were independently associated with postradiosurgery RICs.
Conclusions: Spetzler-Martin Grade I and II AVMs are very amenable to successful treatment with stereotactic radiosurgery. While patient, physician, and institutional preferences frequently dictate the final course of treatment, radiosurgery offers a favorable risk-to-benefit profile for the management of low-grade AVMs.

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Stereotactic radiosurgery for Spetzler-Martin Grade III arteriovenous malformations
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Object: The purpose of this study was to define the outcomes and risks of stereotactic radiosurgery (SRS) for Spetzler-Martin (SM) Grade III arteriovenous malformations (AVMs).
Methods: Between 1987 and 2009, SRS was performed in 474 patients with SM Grade III AVMs. The AVMs were categorized by scoring the size (S), drainage (D), and location (L): IIIa was a small AVM (S1D1L1, N = 282); IIIb was a medium/deep AVM (S2D1L0, N = 44); and IIIc was a medium/eloquent AVM (S2D0L1, N = 148). The median target volume was 3.8 ml (range 0.1-26.3 ml) and the margin dose was 20 Gy (range 13-25 Gy). Eighty-one patients (17%) underwent prior embolization, and 58 (12%) underwent prior resection.
Results: At a mean follow-up of 89 months, the total obliteration rates documented by angiography or MRI for all SM Grade III AVMs increased from 48% at 3 years to 69% at 4 years, 72% at 5 years, and 77% at 10 years.

The SM Grade IIIa AVMs were more likely to obliterate than other subgroups. The cumulative rate of hemorrhage was 2.3% at 1 year, 4.4% at 2 years, 5.5% at 3 years, 6.4% at 5 years, and 9% at 10 years. The SM Grade IIIb AVMs had a significantly higher cumulative rate of hemorrhage. Symptomatic adverse radiation effects were detected in 6%.
Conclusions: Treatment with SRS was an effective and relatively safe management option for SM Grade III AVMs. Although patients with residual AVMs remained at risk for hemorrhage during the latency interval, the cumulative 10-year 9% hemorrhage risk in this series may represent a significant reduction compared with the expected natural history.

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Editorial: Stereotactic radiosurgery for Spetzler-Martin Grade III arteriovenous malformations
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Radiosurgery for Spetzler-Martin Grade III arteriovenous malformations
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Object: Intracranial arteriovenous malformations (AVMs) are most commonly classified based on their Spetzler-Martin grades. Due to the composition of the Spetzler- Martin grading scale, Grade III AVMs are the most heterogeneous, comprising 4 distinct lesion subtypes. The management of this class of AVMs and the optimal treatment approach when intervention is indicated remain controversial. The authors report their experience with radiosurgery for the treatment of Grade III AVMs in a large cohort of patients.
Methods: All patients with Spetzler-Martin Grade III AVMs treated with radiosurgery at the University of Virginia over the 20-year span from 1989 to 2009 were identified. Patients who had less than 2 years of radiological follow-up and did not have evidence of complete obliteration during that period were excluded from the study, leaving 398 cases for analysis. The median patient age at treatment was 31 years. The most common presenting symptoms were hemorrhage (59%), seizure (20%), and headache (10%). The median AVM volume was 2.8 cm3, and the median prescription dose was 20 Gy. The median radiological and clinical follow-up intervals were 54 and 68 months, respectively. Univariate and multivariate Cox proportional hazards and logistic regression analysis were used to identify factors associated with obliteration, postradiosurgery radiation-induced changes (RIC), and favorable outcome.
Results: Complete AVM obliteration was observed in 69% of Grade III AVM cases at a median time of 46 months after radiosurgery. The actuarial obliteration rates at 3 and 5 years were 38% and 60%, respectively. The obliteration rate was higher in ruptured AVMs than in unruptured ones ($p < 0.001$). Additionally, the obliteration rate for Grade III AVMs with small size (< 3 cm diameter), deep venous drainage, and location in eloquent cortex was higher than for the other subtypes ($p < 0.001$). Preradiosurgery AVM rupture ($p = 0.016$), no preradiosurgery embolization ($p = 0.003$), increased prescription dose ($p < 0.001$), fewer isocenters ($p = 0.006$), and a single draining vein ($p = 0.018$) were independent predictors of obliteration. The annual risk of postradiosurgery hemorrhage during the latency period was 1.7%. Two patients (0.5%) died of hemorrhage during the radiosurgical latency period. The rates of symptomatic and permanent RIC were 12% and 4%, respectively. Absence of preradiosurgery AVM rupture ($p < 0.001$) and presence of a single draining vein ($p < 0.001$) were independent predictors of RIC. Favorable outcome was observed in 63% of patients. Independent predictors of favorable outcome were no preradiosurgery hemorrhage ($p = 0.014$), increased prescription dose ($p < 0.001$), fewer isocenters ($p = 0.014$), deep location ($p = 0.014$), single draining vein ($p = 0.001$), and lower Virginia radiosurgery AVM scale score ($p = 0.016$).
Conclusions: Radiosurgery for Spetzler-Martin Grade III AVMs yields relatively high rates of obliteration with a low rate of adverse procedural events. Small and ruptured lesions are more likely to become obliterated after radiosurgery than large and unruptured ones.

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Prospective evaluation of preoperative stereotactic radiosurgery followed by delayed resection of a high grade arteriovenous malformation.

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Reports of the utility of preoperative radiation for shrinking large arteriovenous malformations (AVM) in preparation for resection have produced conflicting results, and to our knowledge no prospective studies are available. A 28-year-old man presented with a ruptured right temporal Spetzler-Martin Grade 5 AVM with deep venous drainage, involvement of the internal capsule, deep perforator supply, and a diffuse nidus. He underwent staged embolization, a single Gamma Knife (Elekta AB, Stockholm, Sweden) radiation treatment to the deepest portion of the nidus followed by complete surgical resection 3 years later. He suffered no long-term neurological deficits and has since returned to work symptom-free (modified Rankin Scale score 0). Preoperative radiosurgery is an effective method for downgrading high-grade AVM in preparation for surgery by targeting the deeper portions that abut or involve eloquent territory. To our knowledge this is the first such successful prospective report in the literature.

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A practical grading scale for predicting outcome after radiosurgery for arteriovenous malformations: analysis of 1012 treated patients

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Object The authors performed a study to review outcomes following Gamma Knife radiosurgery for cerebral arteriovenous malformations (AVMs) and to create a practical scale to predict long-term outcome. Methods Outcomes were reviewed in 1012 patients who were followed up for more than 2 years. Favorable outcome was defined as AVM obliteration and no posttreatment hemorrhage or permanent, symptomatic, radiation-induced complication. Preradiosurgery patient and AVM characteristics predictive of outcome in multivariate analysis were weighted according to their odds ratios to create the Virginia Radiosurgery AVM Scale. Results The mean follow-up time was 8 years (range 2-20 years). Arteriovenous malformation obliteration occurred in 69% of patients. Postradiosurgery hemorrhage occurred in 88 patients, for a yearly incidence of 1.14%. Radiation- induced changes occurred in 387 patients (38.2%), symptoms in 100 (9.9%), and permanent deficits in 21 (2.1%). Favorable outcome was achieved in 649 patients (64.1%). The Virginia Radiosurgery AVM Scale was created such that patients were assigned 1 point each for having an AVM volume of 2-4 cm3, eloquent AVM location, or a history of hemorrhage, and 2 points for having an AVM volume greater than 4 cm3. Eighty percent of patients who had a score of 0-1 points had a favorable outcome, as did 70% who had a score of 2 points and 45% who had a score of 3-4 points. The Virginia Radiosurgery AVM Scale was still predictive of outcome after controlling for predictive Gamma Knife radiosurgery treatment parameters, including peripheral dose and number of isocenters, in a multivariate analysis. The Spetzler-Martin grading scale and the Radiosurgery-Based Grading Scale predicted favorable outcome, but the Virginia Radiosurgery AVM Scale provided the best assessment. Conclusions Gamma Knife radiosurgery can be used to achieve long-term AVM obliteration and neurological preservation in a predictable fashion based on patient and AVM characteristics.

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Evaluation of prognostic factors as predictor of AVMS obliteration after Gamma Knife radiosurgery

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BACKGROUND: The reported AVMs obliteration rate after Gamma Knife radiosurgery (GKS) ranges from 70 to 94 %. The objective of the present study was to assess prognostic factors predictive for cerebral AVMs obliteration in 127 patients who underwent GKS. METHODS: The AVMs were classified according to the Spetzler-Martin classification. Twenty-one cases (16.5 %) were classified as grade I, 46 cases (36.2%) as grade II, 51 cases (40.1 %) as grade III, and nine cases (7.1 %) as grade IV-V. The AVMs were deeply located in 16.5 % of patients. The peripheral prescription dose ranged from 16 to 30 Gy (mean 22.3 Gy). The AVMs volume ranged from 0.1 to 13 cc (mean 2.7 cc). RESULTS: In 72 patients out of the 104 (69.2%) with a radiological follow-up, MRI showed the AVM obliteration; in 54 cases (60 %) out of the 90 that performed a DSA, a complete AVM

obliteration was achieved (average closure time 48.5 months). The volume of the nidus (p = 0.001), the prescription dose (p = 0.004), the 2002 Pollock-Flickinger classification (p = 0.031), and their 2008 revised classification (p = 0.025) were found to be statistically significant in predicting the probability of AVM closure. In the multivariate analysis, only the prescription dose was found to be an independent prognostic factor (p = 0.009) for AVM obliteration. CONCLUSIONS: The volume of the nidus and the prescription dose significantly influence the outcome of radiosurgical treatment. The Pollock-Flickinger classification was found to be a reliable scoring system in predicting the AVM closure and an important tool for selection of patients candidate for GKS.

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Multimodality management of Spetzler-Martin Grade III arteriovenous malformations

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Object Grade III arteriovenous malformations (AVMs) are diverse because of their variations in size (S), location in eloquent cortex (E), and presence of central venous drainage (V). Because they may have implications for management and outcome, the authors evaluated these variations in the present study. Methods Between 1984 and 2010, 100 patients with Grade III AVMs were treated. The AVMs were categorized by Spetzler-Martin characteristics as follows: Type 1 = S1E1V1, Type 2 = S2E1V0, Type 3 = S2E0V1, and Type 4 = S3E0V0. The occurrence of a new neurological deficit, functional status (based on modified Rankin Scale [mRS] score) at discharge and follow-up, and radiological obliteration were correlated with demographic and morphological characteristics. Results One hundred patients (49 female and 51 male; age range 5-68 years, mean 35.8 years) were evaluated. The size of AVMs was less than 3 cm in 28 patients, 3-6 cm in 71, and greater than 6 cm in 1; 86 AVMs were located in eloquent cortex and 38 had central drainage. The AVMs were Type 1 in 28 cases, Type 2 in 60, Type 3 in 11, and Type 4 in 1. The authors performed embolization in 77 patients (175 procedures), surgery in 64 patients (74 surgeries), and radiosurgery in 49 patients (44 primary and 5 postoperative). The mortality rate following the management of these AVMs was 1%. Fourteen patients (14%) had new neurological deficits, with 5 (5%) being disabling (mRS score > 2) and 9 (9%) being nondisabling (mRS score </= 2) events. Patients with Type 1 AVMs (small size) had the best outcome, with 1 (3.6%) in 28 having a new neurological deficit, compared with 72 patients with larger AVMs, of whom 13 (18.1%) had a new neurological deficit (p < 0.002). Older age (> 40 years), malformation size > 3 cm, and nonhemorrhagic presentation predicted the occurrence of new deficits (p < 0.002). Sex, eloquent cortex, and venous drainage did not confer any benefit. In 89 cases follow-up was adequate for data to be included in the obliteration analysis. The AVM was obliterated in 78 patients (87.6%), 69 of them (88.5%) demonstrated on angiography and 9 on MRI /MR angiography. There was no difference between obliteration rates between different types of AVMs, size, eloquence, and drainage. Age, sex, and clinical presentation also did not predict obliteration. Conclusions Multimodality management of Grade III AVMs results in a high rate of obliteration, which was not influenced by size, venous drainage, or eloquent location. However, the development of new neurological deficits did correlate with size, whereas eloquence and venous drainage did not affect the neurological complication rate. The authors propose subclassifying the Grade III AVMs according to their size (< 3 and >/= 3 cm) to account for treatment risk.

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Stereotactic radiosurgery for arteriovenous malformations, Part 1: management of Spetzler-Martin Grade I and II arteriovenous malformations

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Object The aim of this paper was to define the outcomes and risks of stereotactic radiosurgery (SRS) for Spetzler-Martin Grade I and II arteriovenous malformations (AVMs). Methods Between 1987 and 2006, the authors performed Gamma Knife surgery in 996 patients with brain AVMs, including 217 patients with AVMs classified as Spetzler-Martin Grade I or II. The median maximum diameter and target volumes were 1.9 cm (range 0.5-3.8 cm) and 2.3 cm(3) (range 0.1-14.1 cm(3)), respectively. The median margin dose was 22 Gy (range 15-27 Gy). Results Arteriovenous malformation obliteration was confirmed by MR imaging in 148 patients and by angiography in 100 patients with a median follow-up of 64 months (range 6-247 months). The actuarial rates of total obliteration determined by angiography or MR imaging after 1 SRS procedure were 58%, 87%, 90%, and 93% at 3, 4, 5, and 10 years, respectively.

The median time to complete MR imaging-determined obliteration was 30 months. Factors associated with higher AVM obliteration rates were smaller AVM target volume, smaller maximum diameter, and greater marginal dose. Thirteen patients (6%) suffered hemorrhages during the latency period, and 6 patients died. Cumulative rates of AVM hemorrhage 1, 2, 3, 5, and 10 years after SRS were 3.7%, 4.2%, 4.2%, 5.0%, and 6.1%, respectively. This corresponded to rates of annual bleeding risk of 3.7%, 0.3%, and 0.2% for Years 0-1, 1-5, and 5-10, respectively, after SRS. The presence of a coexisting aneurysm proximal to the AVM correlated with a significantly higher hemorrhage risk. Temporary symptomatic adverse radiation effects developed in 5 patients (2.3%) after SRS, and 2 patients (1%) developed delayed cysts. Conclusions Stereotactic radiosurgery is a gradually effective and relatively safe option for patients with smaller volume Spetzler-Martin Grade I or II AVMs who decline initial resection.
Hemorrhage after obliteration did not occur in this series. Patients remain at risk for a bleeding event during the latency interval until obliteration occurs. Patients with aneurysms and an AVM warrant more aggressive surgical or endovascular treatment to reduce the risk of a hemorrhage in the latency period after SRS.

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Adverse radiation effects after Gamma Knife Surgery in relation to dose and volume
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INTRODUCTION: The relationship between target volume and adverse radiation effects (AREs) at low prescription doses requires elucidation. The development of AREs in three series of patients treated in the Gamma Knife is analysed in relation to prescription dose and target volume. MATERIALS AND METHODS: There were three groups. In group 1, there were of 275 patients with meningiomas; in group 2, 132 patients with vestibular schwannomas; and in group 3, 107 patients with arteriovenous malformations (AVMs). The minimum follow-up for each group was more than 24 months. All patients were followed up at six monthly intervals. The patients with tumours received a prescription dose of 12 Gy, which was varied to protect normal structures but not in relation to tumour volume per se. The desired AVM prescription dose was 25 Gy, but this was also reduced to protect normal structures and to keep the total dose within certain pre-defined limits. All AREs refer to intra-parenchymal increased perilesional T2 signal on MR irrespective of clinical correlation. RESULTS: There was no relationship between tumour volume and the development of ARE in the tumour groups. There was a highly significant relationship between target volume and the development of ARE for the AVMs with their much higher dose. Radiation-induced clinical trigeminal and facial nerve deficits with both vestibular schwannomas and meningiomas were always associated with an increased T2 signal in the neighbouring brainstem parenchyma. CONCLUSIONS: The relationship between target volume and the risk of adverse radiation effects may not apply with lower prescription doses. Individual radiosensitivity may explain why a minority suffer AREs unrelated to target volume. It is possible that radiation-induced brainstem parenchymal damage with concomitant cranial nerve deficits may be commoner after radiosurgery than is usually thought. If tumour control with lower doses is adequate, radiosurgery could be safely considered for larger targets associated with a high risk from microsurgery.

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[Management of intracranial arteriovenous malformations]
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Intracranial arteriovenous malformations (AVMs) are congenital lesions that can cause serious neurological deficits or even death. They can manifest as intracranial hemorrhage, epileptic seizure, or other symptoms such as headache or tinnitus. They are detected by computed tomography or magnetic resonance imaging. Recently there have been significant developments in the management of AVMs. In this paper, the authors represent an overview of the epidemiology of AVMs and the existing treatment strategies. AVMs are ideally excised by standard microsurgical techniques. The grading scale which was proposed by Spetzler and Martin is widely used to estimate the risk of direct surgery. Stereotactic radiosurgery such as that using a gamma knife is very useful for small lesions located in eloquent areas. Technological advances in endovascular surgery have provided new alternatives in the treatment of AVMs. Currently indications for embolization can be divided into (1) presurgical embolization in large AVMs to occlude deep arterial feeding vessels and (2) embolization before stereotactic

radiosurgery to reduce the size of the nidus. Palliative embolization can be also applied for patients with large, inoperable AVMs who are suffering from progressive neurological deficits secondary to venous hypertension and/or arterial steal phenomenon.

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Clinical and neuroimaging outcome of cerebral arteriovenous malformations after Gamma Knife surgery: analysis of the radiation injury rate depending on the arteriovenous malformation volume

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OBJECT: In this paper the authors analyzed the clinical and neuroimaging outcomes of patients with cerebral arteriovenous malformations (AVMs) after Gamma Knife surgery (GKS), focusing on the analysis of the radiation injury rate depending on the AVM volume. METHODS: Between 1997 and 2004, 277 consecutive patients with cerebral AVMs were treated with GKS. Of these patients, 218 were followed up for >or= 2 years. The mean age was 31 +/- 15 years, the median AVM volume was 3.4 cm3 (range 0.17-35.2 cm3), the median marginal dose was 18.0 Gy (range 10.0-25.0 Gy), and the mean follow-up duration was 44 +/- 20 months. The authors reduced the prescription dose by various amounts, depending on the AVM volume and location as prescribed in the classic guideline to avoid irreversible radiation injuries. RESULTS: The angiographic obliteration rate was 66.4% overall, and it was 81.7, 53.1, and 12.5% for small, medium, and large AVMs, respectively. The overall annual bleeding rate was 1.9%. The annual bleeding rate was 0.44 and 4.64% for small and large AVMs, respectively. Approximately 20% of the patients showed severe postradiosurgery imaging (PRI) changes. The rate of PRI change was 11.4, 33.3, and 9.5% for small, medium, and large AVM volume groups, respectively, and a permanent radiation injury developed in 5.1% of patients. CONCLUSIONS: By using the reduced dose from what is usually prescribed, the authors were able to obtain outcomes in small AVMs that were comparable to the outcomes described in previous reports. However, medium AVMs appear to still be at risk for adverse radiation effects. Last, in large AVMs, the authors were able to attain a tolerable rate of radiation injury; however, the clinical outcomes were quite disappointing following administration of a reduced dose of GKS for large AVMs.

Repeat Radiosurgery

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306 Worse Stereotactic Radiosurgery Outcomes for Intracranial Arteriovenous Malformations After Repeat vs Initial Treatment: A Matched Cohort Study

Ding, D., Xu, Z., Shih, H. H., Starke, R. M., Yen, C. P., Cohen-Inbar, O. and Sheehan, J. P., INTRODUCTION: Incompletely obliterated intracranial arteriovenous malformations (AVMs) after initial treatment with stereotactic radiosurgery (SRS) can be treated with a repeat session of SRS. However, the relative efficacy of repeat vs initial SRS is not well defined. The goal of this retrospective case-control study is to compare the outcomes of repeat vs initial SRS for the treatment of matched cohorts comprising angioarchitecturally similar AVMs. METHODS: We evaluated a prospective database of AVM patients treated with SRS from 1989 to 2013. AVM patients who underwent repeat SRS with radiological follow-up of 2 years or nidus obliteration were selected for analysis and matched, in a 1:1 fashion and blinded to outcome, to previously untreated AVMs that underwent initial SRS. Statistical analyses were performed to compare the outcomes after repeat vs initial SRS. RESULTS: The matching processes yielded 84 patients in each of the repeat and initial SRS cohorts (mean margin doses 20.7 and 20.9 Gy, respectively; P = .74). In the repeat SRS cohort, obliteration was achieved in 67%; the rates of radiologic, symptomatic, and permanent radiation-induced changes (RIC) were 35%, 10%, and 4%, respectively; and the annual post-SRS hemorrhage rate was 3.1%. Compared with the initial SRS cohort, the repeat SRS cohort had significantly lower obliteration rates (P = .038) and higher post-SRS hemorrhage rates (P = .04). The RIC rates of the 2 cohorts were not significantly different. CONCLUSION: Repeat SRS yields considerably poorer outcomes than initial SRS for angioarchitecturally comparable AVMs. Further studies in AVM radiobiology and vascular structure are necessary to elucidate this potentially differential response.

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Stereotactic radiosurgery for arteriovenous malformations, Part 3: outcome predictors and risks after repeat radiosurgery

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Object The object of this study was to evaluate the outcomes and risks of repeat stereotactic radiosurgery (SRS) for incompletely obliterated cerebral arteriovenous malformations (AVMs). Methods Between 1987 and 2006, Gamma Knife surgery was performed in 996 patients with AVMs. During this period, repeat SRS was performed in 105 patients who had incompletely obliterated AVMs at a median of 40.9 months after initial SRS (range 27.5-139 months). The median AVM target volume was 6.4 cm(3) (range 0.2-26.3 cm(3)) at initial SRS but was reduced to 2.3 cm(3) (range 0.1-18.2 cm(3)) at the time of the second procedure. The median margin dose at both initial SRS and repeat SRS was 18 Gy. Results The actuarial rate of total obliteration by angiography or MR imaging after repeat SRS was 35%, 68%, 77%, and 80% at 3, 4, 5, and 10 years, respectively. The median time to complete angiographic or MR imaging obliteration after repeat SRS was 39 months. Factors associated with a higher rate of AVM obliteration were smaller residual AVM target volume ($p = 0.038$) and a volume reduction of 50% or more after the initial procedure ($p = 0.014$). Seven patients (7%) had a hemorrhage in the interval between initial SRS and repeat SRS. Seventeen patients (16%) had hemorrhage after repeat SRS and 6 patients died. The cumulative actuarial rates of new AVM hemorrhage after repeat SRS were 1.9%, 8.1%, 10.1%, 10.1%, and 22.4% at 1, 2, 3, 5, and 10 years, respectively, which translate to annual hemorrhage rates of 4.05% and 1.79% of patients developing new post-repeat-SRS hemorrhages per year for Years 0- 2 and 2-10 following repeat SRS. Factors associated with a higher risk of hemorrhage after repeat SRS were a greater number of prior hemorrhages ($p = 0.008$), larger AVM target volume at initial SRS ($p = 0.010$), larger target volume at repeat SRS ($p = 0.002$), initial AVM volume reduction less than 50% ($p = 0.019$), and a higher Pollock-Flickinger score ($p = 0.010$). Symptomatic adverse radiation effects developed in 5 patients (4.8%) after initial SRS and in 10 patients (9.5%) after repeat SRS. Prior embolization ($p = 0.022$) and a higher Spetzler-Martin grade ($p = 0.004$) were significantly associated with higher rates of adverse radiation effects after repeat SRS. Delayed cyst formation occurred in 5 patients (4.8%) at a median of 108 months after repeat SRS (range 47-184 months). Conclusions Repeat SRS for incompletely obliterated AVMs increases the eventual obliteration rate. Hemorrhage after obliteration did not occur in this series. The best results for patients with incompletely obliterated AVMs were seen in patients with a smaller residual nidus volume and no prior hemorrhages.

General/Other Vascular Malformation Topics

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Stereotactic radiosurgery for cerebral arteriovenous malformations: evaluation of long-term outcomes in a multicenter cohort

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OBJECTIVE In this multicenter study, the authors reviewed the results following Gamma Knife radiosurgery (GKRS) of cerebral arteriovenous malformations (AVMs), determined predictors of outcome, and assessed predictive value of commonly used grading scales based upon this large cohort with long-term follow-up. METHODS Data from a cohort of 2236 patients undergoing GKRS for cerebral AVMs were compiled from the International Gamma Knife Research Foundation. Favorable outcome was defined as AVM obliteration and no posttreatment hemorrhage or permanent symptomatic radiation-induced complications. Patient and AVM characteristics were assessed to determine predictors of outcome, and commonly used grading scales were

assessed. RESULTS The mean maximum AVM diameter was 2.3 cm, with a mean volume of 4.3 cm3. A mean margin dose of 20.5 Gy was delivered. Mean follow-up was 7 years (range 1-20 years). Overall obliteration was 64.7%. Post-GRKS hemorrhage occurred in 165 patients (annual risk 1.1%). Radiation-induced imaging changes occurred in 29.2%; 9.7% were symptomatic, and 2.7% had permanent deficits. Favorable outcome was achieved in 60.3% of patients. Patients with prior nidal embolization (OR 2.1, $p < 0.001$), prior AVM hemorrhage (OR 1.3, $p = 0.007$), eloquent location (OR 1.3, $p = 0.029$), higher volume (OR 1.01, $p < 0.001$), lower margin dose (OR 0.9, $p < 0.001$), and more isocenters (OR 1.1, $p = 0.011$) were more likely to have unfavorable outcomes in multivariate analysis. The Spetzler-Martin grade and radiosurgery-based AVM score predicted outcome, but the Virginia Radiosurgery AVM Scale provided the best assessment. CONCLUSIONS GKRS for cerebral AVMs achieves obliteration and avoids permanent complications in the majority of patients. Patient, AVM, and treatment parameters can be used to predict long-term outcomes following radiosurgery.

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Possible Interaction of Anti-PD-1 Therapy with the Effects of Radiosurgery on Brain Metastases

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Delayed radiation-induced vasculitic leukoencephalopathy related to stereotactic radiosurgery (SRS) of brain metastases has been reported to manifest clinically 9 to 18 months after treatment. Immune-modulating therapies have been introduced to treatment regimens for malignancies with metastatic predilection to the brain. The interaction of these systemic therapies with other modalities of treatment for brain metastases, namely, SRS, has not been fully characterized. We report two patients with metastatic malignancies to the brain who received SRS followed by immunotherapy with monoclonal antibodies (mAb) to programmed death 1 (PD-1). Both patients appeared to have early clinical and radiologic progression of their treated lesions, which was highly suspicious for tumor progression. Both patients underwent surgical resection of their lesions and the material was submitted for histopathologic examination. Pathologic examination in both cases showed predominantly radiation-induced changes characterized by reactive astrocytosis and vascular wall infiltration by T lymphocytes. The accelerated response to SRS in these two patients was temporally related to the initiation of immunotherapy. We propose a possible biologic interaction between SRS and the PD-1 mAbs. Additionally, awareness of this potential occurrence is critical for accurate interpretation and proper management of clinical and radiologic findings in these patients. Cancer Immunol Res; 4(6); 481-7. (c)2016 AACR.

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Integrating bevacizumab and radiation treatment of brain metastasis: is there sense and sensibility in this approach?

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The incidence of brain metastasis has increased over the past decade. Standard treatment options for brain metastases include whole brain radiation therapy (WBRT), stereotactic radiosurgery (SRS) and surgery for patients with operable lesions and either mass effect or need for histologic confirmation of the diagnosis. Patients are living longer due to improvements in systemic therapeutic approaches, included targeted therapies such as inhibition of vascular endothelial growth factor (VEGF) using the monoclonal antibody bevacizumab (Bev). A recent phase I trial (REBECA) investigated adding Bev to whole-brain radiation for patients with brain metastasis from solid tumors. In this Perspectives article, we discuss the results of the REBECA trial in context of advancements in radiation and medical oncology in the era of targeted therapies, and discuss pertinent questions of interest in this field.

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Radiosurgery for Cerebral Arteriovenous Malformations with Associated Arterial Aneurysms

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OBJECTIVE: The radiosurgical outcomes for cerebral arteriovenous malformations (AVM) with AVM-associated arterial aneurysms (AAA) are poorly understood, because many AAAs are embolized before nidal intervention. The aim of this retrospective case-control study is to determine the effect of AAAs on AVM radiosurgery outcomes. METHODS: We evaluated an institutional AVM radiosurgery database from 1989 to 2013. AAAs were classified as intranidal (type I) or prenidal (type II). The case cohort comprised AVMs with patent type I or II AAAs. The control cohort comprised AVMs without AAAs and matched 2:1 to the case cohort. RESULTS: The case cohort comprised 51 AVMs, including 23 with type I and 28 with type II AAAs. The control cohort comprised 102 AVMs without AAAs. The cumulative AVM obliteration, annual postradiosurgery hemorrhage, and radiologically evident radiation-induced changes rates were 67%, 3.3%, and 28%, respectively, for the case cohort, compared with 70%, 2.0%, and 35%, respectively, for the control cohort. The presence of an AAA was not significantly associated with obliteration (P = 0.293), postradiosurgery hemorrhage (P = 0.209), or radiation-induced changes (P = 0.323). The rates of type II AAA occlusion at 3, 5, and 10 years were 46%, 77%, and 95%, respectively. The type II AAA occlusion rate was significantly higher in obliterated AVMs (P = 0.002). CONCLUSIONS: Patent intranidal or prenidal AAAs do not significantly affect AVM radiosurgical outcomes. Occlusion of distal prenidal AAAs commonly occurs after radiosurgery. These findings may support a more conservative stance for embolization before radiosurgery for AVMs with AAAs.

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Trigeminal Neuralgia Caused by Cerebellopontine Angle Arteriovenous Malformation Treated With Gamma Knife Radiosurgery

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Trigeminal neuralgia is a facial pain syndrome characterized as sudden onset and lightening-like sensation over somatosensorial branch(es) of fifth cranial nerve. Rarely, some underlying diseases or disorders could be diagnosed, such as multiple sclerosis, brain tumors, and vascular malformations. The authors present a 47-year-old man with trigeminal neuralgia over left V2 and V3 dermatomes. He had a previous transarterial embolization and long use of carbamazepine with partial response to treatment. Gamma knife radiosurgery (GKR) was planned. A marginal dose of 15 Gy was given to 50% isodose line. His pain was relieved by GKR in 1.5 years. Treatment of posterior fossa arteriovenous malformations causing trigeminal neuralgia, with GKR has a very limited use in the literature. It, however, is obvious that success rate as pain relief, in a very challenging field of functional neurosurgery, is satisfactory. Large series, however, are in need to make a more comprehensive statement about efficacy and safety of the procedure in these pathologies.

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Radiosurgery for Cerebral Arteriovenous Malformations in A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA)-Eligible Patients: A Multicenter Study

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BACKGROUND AND PURPOSE: The benefit of intervention for patients with unruptured cerebral arteriovenous malformations (AVMs) was challenged by results demonstrating superior clinical outcomes with conservative management from A Randomized Trial of Unruptured Brain AVMs (ARUBA). The aim of this multicenter, retrospective cohort study is to analyze the outcomes of stereotactic radiosurgery for ARUBA-eligible patients. METHODS: We combined AVM radiosurgery outcome data from 7 institutions participating in the International Gamma Knife Research Foundation. Patients with >/=12 months of follow-up were screened for ARUBA eligibility criteria. Favorable outcome was defined as AVM obliteration, no postradiosurgery hemorrhage, and no permanently symptomatic radiation-induced changes. Adverse neurological outcome was defined as any new or worsening neurological symptoms or death. RESULTS: The ARUBA-eligible cohort comprised 509 patients (mean age, 40 years). The Spetzler-Martin grade was I to II in 46% and III to IV in 54%. The mean radiosurgical margin dose was 22 Gy and follow-up was 86 months. AVM obliteration was achieved in 75%. The postradiosurgery hemorrhage rate during the latency period was 0.9% per year. Symptomatic and permanent radiation-induced changes occurred in 11% and 3%, respectively. The rates of favorable outcome, adverse neurological outcome, permanent neurological morbidity, and mortality were 70%, 13%, 5%, and 4%, respectively. CONCLUSIONS: Radiosurgery may provide durable clinical benefit in some ARUBA-eligible patients. On the basis of the natural history of untreated, unruptured AVMs in the medical arm of ARUBA, we estimate that a follow-up duration of 15 to 20 years is necessary to realize a potential benefit of radiosurgical intervention for conservative management in unruptured patients with AVM.

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Stereotactic Radiosurgery for Partially Resected Cerebral Arteriovenous Malformations

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OBJECTIVE: Incomplete microsurgical resection of cerebral arteriovenous malformations (AVM) occurs uncommonly. However, such patients harboring postoperative residual nidi remain exposed to the risk of AVM hemorrhage and are therefore reasonable candidates for further intervention. The goals of this retrospective case-control study are to analyze the radiosurgery outcomes for partially resected AVMs and determine the effect of prior resection on AVM radiosurgery outcomes. METHODS: We evaluated a prospective database of AVM patients treated with radiosurgery from 1989-2013. Previously resected AVMs with radiologic follow-up >/=2 years or nidus obliteration were selected for analysis and matched, in a 1:1 fashion and blinded to outcome, to previously unresected AVMs. Statistical analyses were performed to assess relationship between prior resection and AVM radiosurgery outcomes. RESULTS: The matching process yielded 88 patients in each of the previously resected and unresected AVM cohorts. In the resected AVM cohort, the actuarial AVM obliteration rates at 3 and 5 years were 47% and 75%, respectively; the rates of radiologic and symptomatic radiation-induced changes (RICs) were 10% and 3%, respectively; and the annual postradiosurgery hemorrhage risk was 1.1%. The lack of prior AVM resection ($P < 0.001$) and superficial AVM location ($P = 0.009$) were independent predictors of radiologic RIC. The actuarial rates of obliteration ($P = 0.849$) and postradiosurgery hemorrhage ($P = 0.548$) were not significantly different between the resected and unresected AVM cohorts. CONCLUSIONS: Radiosurgery affords a reasonable risk-to-benefit profile for incompletely resected AVMs. For those with a small-volume residual nidus after resection, radiosurgery should be considered an effective alternative to repeat resection.

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Cortical plasticity in patients with cerebral arteriovenous malformations

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The aim of this review is to ascertain the evidence for cortical plasticity in arteriovenous malformation (AVM) patients. Chronic hypoperfusion due to vascular steal from cerebral AVM can result in a translocation of eloquent neurological functions to other brain areas, a phenomenon known as cortical plasticity. We performed a systematic literature review of the studies that have evaluated cortical plasticity in AVM patients. A total of 22 studies from 1996 to 2014 were included for the analyses. The evaluation of cortical plasticity was performed prior to AVM intervention in 109 patients, and during or after AVM intervention in 18. The most commonly assessed neurological functions were motor in 85% and language in 11% of the former cohort, and motor in 78% and language, cognition, and memory each in 39% of the latter cohort. Functional MRI was the most frequently used method for evaluating cortical plasticity, and was performed in 63% of the former and 56% of the latter cohort. In conclusion, cortical plasticity appears to be influenced by both AVM pathogenesis and intervention. Given the limited evidence that is currently available for cortical plasticity in AVM patients, further studies are warranted to determine its incidence and impact on long term clinical outcomes.

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Angiographic, hemodynamic, and histological changes in an animal model of brain arteriovenous malformations treated with Gamma Knife radiosurgery.

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OBJECT: Brain arteriovenous malformations (AVMs) are a major cause of stroke. Many AVMs are effectively obliterated by stereotactic radiosurgery, but such treatment for lesions larger than 3 cm is not as effective. Understanding the responses to radiosurgery may lead to new biological enhancements to this treatment modality. The aim of the present study was to investigate the hemodynamic, morphological, and histological effects of Gamma Knife surgery (GKS) in an animal model of brain AVM.
METHODS: An arteriovenous fistula was created by anastomosing the left external jugular vein to the side of the common carotid artery in 64 male Sprague-Dawley rats (weight 345 ± 8.8 g). Six weeks after AVM creation, 32 rats were treated with a single dose of GKS (20 Gy); 32 animals received sham radiation. Eight irradiated and 8 control animals were studied at each specified time point (1, 3, 6, and 12 weeks) for hemodynamic, morphological, and histological characterization.
RESULTS: Two AVMs showed partial angiographic obliteration at 6 weeks. Angiography revealed complete obliteration in 3 irradiated rats at 12 weeks. Blood flow in the ipsilateral proximal carotid artery ($p < 0.001$) and arterialized jugular vein ($p < 0.05$) was significantly lower in the irradiated group than in the control group. The arterialized vein's external diameter was significantly smaller in GKS-treated animals at 6 ($p < 0.05$) and 12 ($p < 0.001$) weeks. Histological changes included subendothelial cellular proliferation and luminal narrowing in GKS-treated animals. Neither luminal obliteration nor thrombus formation was identified at any of the time points in either irradiated or nonirradiated animals.
CONCLUSIONS: GKS produced morphological, angiographic, and histological changes in the model of AVM as early as 6 weeks after treatment. These results support the use of this model for studying methods to enhance radiation response in AVMs.

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A quantitative analysis of adverse radiation effects following Gamma Knife radiosurgery for arteriovenous malformations.

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OBJECT: The authors review outcomes following Gamma Knife radiosurgery (GKRS) of cerebral arteriovenous malformations (AVMs) and their correlation to postradiosurgery adverse radiation effects (AREs).
METHODS: From a prospective institutional review board-approved database, the authors identified patients with a minimum of 2 years of follow-up and thin-slice T2-weighted MRI sequences for volumetric analysis. A total of 105 AVM patients were included. The authors analyzed the incidence and quantitative changes in AREs

as a function of time after GKRS. Statistical analysis was performed to identify factors related to ARE development and changes in the ARE index.
RESULTS: The median clinical follow-up was 53.8 months (range 24-212.4 months), and the median MRI follow-up was 36.8 months (range 24-212.4 months). 47.6% of patients had an AVM with a Spetzler-Martin grade ≥ III. The median administered margin and maximum doses were 22 and 40 Gy, respectively. The overall obliteration rate was 70.5%. Of patients who showed complete obliteration, 74.4% developed AREs within 4-6 months after GKRS. Late-onset AREs (i.e., > 12 months) correlated to a failure to obliterate the nidus. 58.1% of patients who developed appreciable AREs (defined as ARE index > 8) proceeded to have a complete nidus obliteration. Appreciable AREs were found to be influenced by AVM nidus volume > 3 ml, lobar location, number of draining veins and feeding arteries, prior embolization, and higher margin dose. On the other hand, a minimum ARE index > 8 predicted obliteration ($p = 0.043$).
CONCLUSIONS: ARE development after radiosurgery follows a temporal pattern peaking at 7-12 months after stereotactic radiosurgery. The ARE index serves as an important adjunct tool in patient follow-up and outcome prediction.

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Clinical outcome and complications of gamma knife radiosurgery for intracranial arteriovenous malformations
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We sought to evaluate the outcome of intracranial arteriovenous malformation (AVM) treated with gamma knife radiosurgery (GKRS) (Elekta, Stockholm, Sweden) as a primary treatment as well as an adjunct therapy. GKRS has emerged as an important treatment option for intracranial AVM. However, the long term outcome of GKRS on AVM is not well understood. We performed a retrospective review of 85 patients with AVM from 2000-2012 who received GKRS. Out of 85 patients, 13 had undergone prior embolization. The study population was monitored clinically and radiographically after GKRS treatment. Outcome following GKRS for intracranial AVM showed significant variations in nidus obliteration (obliteration in 67 [79%] patients and increase of nidus size on MRI in 18 [21%] patients). The median time to nidus obliteration was 31 months. Overall two (2.3%) patients had intracranial bleeding and the annual bleeding risk was 1.6% after GKRS. Predictive factors for obliteration of the nidus in patients with AVM were low AVM score, Spetzler-Martin grade I-III and female sex. Seventeen (20%) and one (1.17%) patients underwent repeat GKRS and resection, respectively, after initial GKRS, due to increased size of the nidus and GKRS related cyst formation. Thus, GKRS offers a high obliteration rate of AVM, low risk of intracranial bleeding and neurological morbidity, both as primary modality and as an adjunctive treatment. Therefore, GKRS is an effective treatment option for new patients with AVM as well as an adjuvant therapy in patients with recurrent AVM.

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Draining Vein Shielding in Intracranial Arteriovenous Malformations During Gamma-Knife: A New Way of Preventing Post Gamma-Knife Edema and Hemorrhage
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BACKGROUND: Following gamma knife (GK) therapy for intracranial arteriovenous malformations (AVMs), obliteration of the nidus occurs over several years. During this period, complications like rebleeding have been attributed to early draining vein occlusion. OBJECTIVE: To evaluate if shielding the draining vein(s) during GK therapy prevents early draining vein obliteration and complications following GK therapy. METHODS:: This was a nonrandomized case-control study over 5 years (January 2009-February 2014) and included patients with intracranial AVM who underwent GK therapy at our center. All patients who underwent draining vein shielding by the senior author (D.A.) were included in the test group, and patients who did not undergo draining vein shielding were put in the control group. Patients were followed up for at least 6 months (and every 6 months thereafter) clinically as well as radiologically with computed tomography head scans/magnetic resonance imaging brain scans to check for postradiosurgery imaging (PRI) changes. RESULTS: One hundred eighty-five patients were included in this study, of which 96 were in the control group and 89 were in the test group. Both groups were well matched in demographics, comorbidities, adjuvant treatment, angioarchitecture, and

radiation dosing. Because of shielding, the test group patients received significantly less radiation to the draining vein than the control group (P = .001). On follow-up, a significantly lower number of patients in the test group had new neurological deficits (P = .001), intracranial hemorrhage (P = .03), and PRI changes (P = .002). CONCLUSION: Shielding of the draining vein is a potent new strategy in minimizing PRI and hemorrhage as well as clinical deterioration following GK therapy for intracranial AVMs.

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Gamma Knife surgery for incidental cerebral arteriovenous malformations

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Object: A relatively benign natural course of unruptured cerebral arteriovenous malformations (AVMs) has recently been recognized, and the decision to treat incidentally found AVMs has been questioned. This study aims to evaluate the long-term imaging and clinical outcomes of patients with asymptomatic, incidentally discovered AVMs treated with Gamma Knife surgery (GKS).

Methods: Thirty-one patients, each with an incidentally diagnosed AVM, underwent GKS between 1989 and 2009. The nidus volumes ranged from 0.3 to 11.1 cm3 (median 3.2 cm3). A margin dose between 15 and 26 Gy (median 20 Gy) was used to treat the AVMs. Four patients underwent repeat GKS for still-patent AVM residuals after the initial GKS procedure. Clinical follow-up ranged from 24 to 196 months, with a mean of 78 months (median 51 months) after the initial GKS.

Results: Following GKS, 19 patients (61.3%) had a total AVM obliteration on angiography. In 7 patients (22.6%), no flow voids were observed on MRI but angiographic confirmation was not available. In 5 patients (16.1%), the AVMs remained patent. A small nidus volume was significantly associated with increased AVM obliteration rate. Thirteen patients (41.9%) developed radiation-induced imaging changes: 11 were asymptomatic (35.5%), 1 had only headache (3.2%), and 1 developed seizure and neurological deficits (3.2%). Two patients each had 1 hemorrhage during the latency period (116.5 risk years), yielding an annual hemorrhage rate of 1.7% before AVM obliteration.

Conclusions: The decision to treat asymptomatic AVMs, and if so, which treatment approach to use, remain the subject of debate. GKS as a minimally invasive procedure appears to achieve a reasonable outcome with low procedure-related morbidity. In those patients with incidental AVMs, the benefits as well as the risks of radiosurgical intervention will only be fully defined with long-term follow-up.

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Gamma Knife radiosurgery and arteriovenous malformations. Response

Ding, D., Starke, R. M. and Sheehan, R. M.

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Radiosurgery for ruptured intracranial arteriovenous malformations

Ding, D., Yen, C. P., Starke, R. M., Xu, Z. and Sheehan, J. P.,Department of Neurological Surgery, University of Virginia Health System, Charlottesville, Virginia.

Object: Ruptured intracranial arteriovenous malformations (AVMs) are at a significantly greater risk for future hemorrhage than unruptured lesions, thereby necessitating treatment in the majority of cases. In a retrospective, single-center study, the authors describe the outcomes after radiosurgery in a large cohort of patients with ruptured AVMs. Methods: From an institutional review board-approved, prospectively collected AVM radiosurgery database, the authors identified all patients with a history of AVM rupture. They analyzed obliteration rates in all patients in whom radiological follow-up data were available (n = 639). However, to account for the latency period associated with radiosurgery, only those patients with more than 2 years of radiological follow-up and those with earlier AMV obliteration were included in the analysis of prognostic factors related to obliteration and complications. This resulted in a cohort of 565 patients with ruptured AVMs for whom data were analyzed; these patients had a median radiological follow-up of 57 months and a median age of 29 years. Twenty-one percent of the patients underwent preradiosurgery embolization. The median volume and prescription dose were 2.1 cm3 and 22 Gy, respectively. The Spetzler-Martin grade was III or higher in 56% of patients, the median radiosurgery-based AVM score was 1.08, and the Virginia Radiosurgery AVM Scale (RAS) score was 3 to 4 points in 44%. Survival and regression analyses were performed to determine obliteration rates over time and predictors of obliteration and complications. Results: In the overall population

of 639 patients with ruptured AVMs, the obliteration rate was 11.1% based on MRI only (71 of 639 patients), 56.0% based on angiography (358 of 639), and 67.1% based on combined modalities (429 of 639 patients). In the cohort of patients with 2 years of follow-up or an earlier AVM obliteration, the cumulative obliteration rate was 76% and the actuarial obliteration rates were 41% and 64% at 3 and 5 years, respectively. Multivariate analysis identified the absence of preradiosurgery embolization ($p < 0.001$), increased prescription dose ($p = 0.001$), the presence of a single draining vein ($p = 0.046$), no postradiosurgery-related hemorrhage ($p = 0.007$), and lower Virginia RAS score ($p = 0.020$) as independent predictors of obliteration. The annual risk of a hemorrhage occurring during the latency period was 2.0% and the rate of hemorrhage-related morbidity and mortality was 1.6%. Multivariate analysis showed that decreased prescription dose ($p < 0.001$) and multiple draining veins ($p = 0.003$) were independent predictors of postradiosurgery hemorrhage. The rates of symptomatic and permanent radiation-induced changes were 8% and 2.7%, respectively. In the multivariate analysis, a single draining vein ($p < 0.001$) and higher Virginia RAS score ($p = 0.005$) were independent predictors of radiation-induced changes following radiosurgery. Conclusions: Radiosurgery effectively treats ruptured AVMs with an acceptably low risk-to-benefit ratio. For patients with ruptured AVMs, favorable outcomes are more likely when preradiosurgical embolization is avoided and a higher prescription dose can be delivered.

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Utilization of Cone-Beam Computed Tomographic Angiography in Planning for Gamma Knife Radiosurgery of Arteriovenous Malformations: A Case Series and Early Report

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Background: The effectiveness of Gamma Knife radiosurgery (GKR) for cerebral arteriovenous malformations (AVM) is predicated on inclusion of the entire nidus while excluding normal tissue. As such, GKR may be limited by the resolution and accuracy of the imaging modality used in targeting.

Objective: We present the first case series to demonstrate the feasibility of utilizing ultra-high-resolution C-arm cone beam computed tomography angiography (CBCT-A) in AVM targeting. Methods: From June 2009 to June 2013, CBCT-A was utilized for targeting of all patients with AVMs treated with GKR at our institution. Patients underwent Leksell stereotactic head frame placement followed by catheter-based biplane 2-D digital subtraction angiography (DSA), 3-D rotational angiography (3DRA), as well as CBCT-A. The CBCT-A dataset was used for stereotactic planning for GKR. Patients were followed up at 1, 3, 6, and 12 months, and then annually thereafter. Results: CBCT-A-based targeting was used in twenty-two consecutive patients. CBCT-A provided detailed spatial resolution and sensitivity of nidal angioarchitecture enabling treatment. The average radiation dose to the margin of the AVM nidus corresponding to the 50% percent isodose line was 15.6 Gy. No patient had treatment-associated hemorrhage. At early follow-up (mean=16 months), 84% of patients had a decreasing or obliterated AVM nidus. Conclusion: CBCT-A-guided radiosurgery is feasible and useful because it provides sufficient detailed resolution and sensitivity for imaging brain AVMs.

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Editorial: Gamma Knife radiosurgery and arteriovenous malformations

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Acute Onset of Hemiparesis After Gamma Knife Radiosurgery for Arteriovenous Malformation Caused by Hyperacute Thrombosis of Draining Vein: A Case Report

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Background Complications after gamma knife radiosurgery (GKRS) have been attributed most commonly to radiation-induced damage to the brain. Early occlusion of the draining veins has been postulated as one of the rare causes of complications after GKRS, which often occurs at or beyond 6 months after GKRS.Clinical Presentation We present a very rare incidence of acute onset of hemiparesis caused by a draining vein occlusion within 24 hours after GKRS for arteriovenous malformation. The patient developed hemiparesis within one day

after GKRS, which partially improved with steroids. Radiologic investigations revealed an early occlusion of a draining vein, resulting in occlusive hyperemia and neurologic deficit.Conclusion Early draining vein occlusion is an important cause of postradiosurgery complications, and it can rarely occur within days.

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Gamma Knife radiosurgery and arteriovenous malformations.
Zipfel GJ1, Heros RC., Departments of Neurological Surgery and.
Comment in: Gamma Knife radiosurgery and arteriovenous malformations. Response. [J Neurosurg. 2014]
Comment on: Radiosurgery for Spetzler-Martin Grade III arteriovenous malformations. [J Neurosurg. 2014]

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Benefit of cone-beam computed tomography angiography in acute management of angiographically undetectable ruptured arteriovenous malformations
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Object Ruptured arteriovenous malformations (AVMs) are a frequent cause of intracerebral hemorrhage (ICH). In some cases, compression from the associated hematoma in the acute setting can partially or completely occlude an AVM, making it invisible on conventional angiography techniques. The authors report on the successful use of cone-beam CT angiography (CBCT-A) to precisely identify the underlying angioarchitecture of ruptured AVMs that are not visible on conventional angiography. Methods Three patients presented with ICH for which they underwent examination with CBCT-A in addition to digital subtraction angiography and other imaging modalities, including MR angiography and CT angiography. All patients underwent surgical evacuation due to mass effect from the hematoma. Clinical history, imaging studies, and surgical records were reviewed. Hematoma volumes were calculated. Results In all 3 cases, CBCT-A demonstrated detailed anatomy of an AVM where no lesion or just a suggestion of a draining vein had been seen with other imaging modalities. Magnetic resonance imaging demonstrated enhancement in 1 patient; CT angiography demonstrated a draining vein in 1 patient; 2D digital subtraction angiography and 3D rotational angiography demonstrated a suggestion of a draining vein in 2 cases and no finding in the third. In the 2 patients in whom CBCT-A was performed prior to surgery, the demonstrated AVM was successfully resected without evidence of a residual lesion. In the third patient, CBCT-A allowed precise targeting of the AVM nidus using Gamma Knife radiosurgery. Conclusions Cone-beam CT angiography should be considered in the evaluation and subsequent treatment of ICH due to ruptured AVMs. In cases in which the associated hematoma compresses the AVM nidus, CBCT-A can have higher sensitivity and anatomical accuracy than traditional angiographic modalities, including digital subtraction angiography.

Stroke.2013;44(2):437-41. Epub 2013/01/05
The Risk of Stroke or Clinical Impairment After Stereotactic Radiosurgery for ARUBA-Eligible Patients
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BACKGROUND AND PURPOSE: The best management of patients with unruptured brain arteriovenous malformations (BAVM) is controversial. In this study, we analyzed the stroke rate and functional outcomes of patients having stereotactic radiosurgery (SRS) for unruptured BAVM using the same eligibility criteria and primary end points as the ARUBA trial. METHODS: Retrospective observational study of 174 ARUBA-eligible patients having SRS from 1990 to 2005. RESULTS: The median follow-up after SRS was 64 months. Fifteen patients (8.7%) had a hemorrhagic stroke at a median of 21 months after SRS. Six patients (3.5%) had a focal neurological deficit and 4 patients died (2.3%). The risk of stroke or death was 10.3% at 5 years and 11.5% at 10 years. Twelve additional patients (6.9%) had a focal neurological deficit from either radiation-related complications (n=7) or subsequent resection (n=5). The risk of patients' having clinical impairment (modified Rankin Score >/=2) was 8.4% at 5 years and 12.0% at 10 years. Increasing BAVM volume was associated with both stroke or death (hazard ratio=1.06; 95% confidence interval, 1.0-1.11; P=0.04) and clinical impairment (hazard ratio=1.06; 95% confidence interval, 1.01-1.09; P=0.01). The 10-year risk of stroke or death and clinical impairment for patients with BAVM </=5.6 cm(3) was 5% and 4%, respectively. CONCLUSIONS: The observed risk of stroke or death after SRS was approximately 2% per year for the first 5 years after SRS, declining to 0.2%

annually for years 6 to 10. Patients with small volume BAVM may benefit from SRS compared with the natural history of unruptured BAVM over the planned follow-up interval of the ARUBA trial (5-10 years).

World Neurosurg.2013;Epub 2013/02/14

An Updated Assessment of the Risk of Radiation Induced Neoplasia Following Radiosurgery of Arteriovenous Malformations

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OBJECT: Gamma Knife radiosurgery (GKRS) is a minimally invasive technique employed in the treatment of intracranial arteriovenous malformations (AVM's). Patients experience a low incidence of complications following treatment. As the long-term follow-up data became available, some late adverse effects have been reported. However, the exact incidence of radiosurgically induced neoplasia is not known. METHODS: At UVA, imaging and clinical outcomes of 1309 patients with intracranial AVM's treated with GKRS have been reviewed. AVM patients underwent magnetic resonance imaging (MRI's) every 6 months for 2 years and then annually following GKRS. When the nidi were no longer visible on MRI, angiography was performed to verify the obliteration of AVM's. Patients were thereafter recommended to continue MRI's every 3-5 years to detect any long-term complications. A subset of 812, 358, and 78 patients had neuro-imaging and clinical follow-up of at least 3, 10, and 15 years respectively. RESULTS: The authors report the occurrence of 3 cases of radiosurgically induced neoplasia. More than 10 years after GKRS, 2 patients were found to have an incidental, uniformly enhancing, dural based mass lesion near the site of the AVM with radiological characteristics of a meningioma. As the lesions have shown no evidence of mass effect, they are being followed with serial neuro-imaging. A third patient was found to have neurological decline from a tumor in immediate proximity to an AVM previously treated with proton beam radiosurgery and GKRS. The patient underwent resection demonstrating a high grade glioma. The 3, 10, and 15-year incidence of a radiation- induced tumor is 0% (0/812), 0.3% (1/358), and 2.6% (2/78) respectively. The cumulative rate of radiosurgically induced tumors in those with a minimum of 10 year follow up is 3 in 4692 person-years or 64 in 100,000 person-years. Thus, patients had a 0.64% chance of developing a radiation induced tumor within 10 or more years following GKRS. If we calculate rates based on a subset of 78 patients with neuro-imaging and clinical follow-up of at least 15 years, the cumulative rate was 3.4%. These are the 2(nd), 3(rd), and 5(th) reported cases of radiation induced tumors following GKRS for an AVM. CONCLUSIONS: Although radiosurgery is generally considered a safe modality in the treatment of AVM's, radiation induced neoplasia is a rare but serious adverse event. The possibility of GKRS induced tumors underscores the necessity of long-term follow-up in AVM patients receiving radiosurgery.

Canadian Journal of Neurological Sciences.2011;38(6):851-7. Epub 2011/10/28

Gamma knife for cerebral arteriovenous malformations at a single centre

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BACKGROUND: We report the results of a consecutive series of patients treated with Gamma Knife (GK) Surgery for cerebral arteriovenous malformations (AVMs). METHODS: We retrospectively reviewed 69 patients treated with GK for cerebral AVMs between November 2003 and April 2009, recording clinical data, treatment parameters, and AVM obliteration rates in order to assess our effectiveness with GK in treating these lesions. RESULTS: Ten patients were lost to follow-up. Presentations included: seizure (24), hemorrhage (18), persistent headache (12), progressing neurological signs (10), and incidental (9). In 24 patients (34.8%) treatment planning consisted of digital subtraction angiography (DSA), magnetic resonance imaging (MRI), and computed tomogram (CT) angiography (CTA). Currently we rely predominantly on CTA and/or MRI scanning only. Fourty-one patients have been followed for a minimum of 3 years; average age 40.9 yr., 58.5% males. Average dose at the 50% isodose line was 20.3 Gy (range 16 to 26.4 Gy). Obliteration was observed in 87.8% by MRI, CT, or DSA. Not all obliteration was confirmed by DSA. Complications occurred in 12 of 59 (20.3%) patients, and in 11 of 41 (26.8%) with 3 year follow-up. Major (temporary) complications for the 59 included symptomatic cerebral edema (7), seizure (2), and hemorrhage (1). Major permanent complications occurred in one patient suffering a cranial nerve V deafferentation, and in two patients suffering a hemorrhage. CONCLUSION: GKS for cerebral AVM's offers an effective and safe method of treatment, with low permanent complication rate.

Stereotactic and Functional Neurosurgery.2011;89(2):96-102. Epub 2011/02/05

Surgical treatment for late complications following gamma knife surgery for arteriovenous malformations

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BACKGROUND: To establish the surgical indications and strategy for late complications following gamma knife surgery (GKS) for arteriovenous malformations (AVMs). METHODS: Ten male and 7 female patients aged 17-52 years (mean 28.0 years) were retrospectively identified among 686 patients who underwent GKS for AVM at our hospital. Ten patients showed cyst formation (group A), 2 patients had expanding hematoma (group B), and 5 patients had both cyst and expanding hematoma (group C). RESULTS: The mean nidus volume was 10.1 ml (range 0.1-36 ml), and the mean prescription dose at the nidus margin was 19.9 Gy (range 18-28 Gy). Complete obliteration of the nidus was obtained in 12 patients, partial obliteration in 4, and no change in 1. Cyst formation (group A) was asymptomatic in 5 patients, and symptomatic in 5 patients, manifesting as headache, hemianopia, aphasia, and motor weakness.

Expanding hematoma (groups B and C) was associated with surrounding brain edema and was symptomatic in all 7 patients. Cyst opening in 1 patient and placement of an Ommaya reservoir in 2 patients were necessary in group A. Both patients in group B underwent craniotomy. Four of the 5 patients in group C required craniotomy. Another patient in group C was lost to follow-up and the final outcome was unknown. CONCLUSIONS: Cyst formation is one of the late complications of GKS for AVM. Some cysts show spontaneous regression but others gradually increase in size and become symptomatic, although relatively large asymptomatic cysts are also known. Predicting the future course of a cyst is difficult. Surgery such as placement of an Ommaya reservoir should be considered for symptomatic cases. Expanding hematoma always increases in size and becomes symptomatic, so removal by craniotomy is necessary. Surrounding brain edema decreases rapidly after surgery and neurological symptoms quickly resolv

Brain Nerve.2010;62(5):539-43. Epub 2010/05/11

[Symptomatic radiation necrosis 10 years after gamma knife surgery for arteriovenous malformations: a case report]

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We present a case of symptomatic radiation necrosis after gamma knife surgery for arteriovenous malformations (AVMs). Initially, at the age of 30 years the patient was treated with gamma knife surgery. Angiography performed 2 years after radiation therapy revealed that the AVMs were completely obliterated. Five years later, the patient had a generalized convulsion and a computed tomography (CT) scan showed a cystic formation in the irradiated area. The patient was treated with a cyst-peritoneal (CP) shunt. Thereafter, the patient seemed to be cured, but 5 years after CP shunt treatment, the patient had right hemiparesis, agraphia, and right hemianopsia. Magnetic resonance imaging (MRI) revealed radiation necrosis in the left parietooccipital region and midline shift of the brain. The patient was operated on and the hyalinized nidus and CP shunt tube were removed. The patient fully recovered from the symptoms and resumed work.

International Journal of Radiation Oncology, Biology, Physics.2011;80(2):354-61. Epub 2010/04/20

The radiosurgical treatment of arteriovenous malformations: obliteration, morbidities, and performance status

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OBJECTIVE: This study examined the single-center treatment outcomes of arteriovenous malformations (AVMs) of the brain using stereotactic radiosurgery, with regard to obliteration, predictive factors, morbidities, and patient performance status. PATIENTS AND METHODS: 127 patients were treated between 1990 and 2008 by use of linear accelerator or Gamma Knife. Their median age was 37 years, the median AVM volume was 7.3 cc (range, 0.014-113.13 cc), and the median follow-up duration was 42 months (range, 6-209 months). Forty-two percent of patients presented with intracranial hemorrhage, 31% received embolization, and 8% underwent prior resection. Thirty-one percent of patients received more than one round of radiosurgery. RESULTS: 64% of patients had complete obliteration confirmed by magnetic resonance imaging or angiography. Positive predictors of obliteration included pretreatment hemorrhage ($p = 0.042$), smaller AVM volume (odds ratio =

1.25; 95% CI, 1.03-1.52), and larger marginal dose (odds ratio = 0.292; 95% CI, 0.100-0.820), whereas embolization ($p < 0.001$) was a negative predictor. The annual risk of hemorrhage after radiosurgery was 2.2%, and the risk of death as a result of hemorrhage was 0.6-1.3%. Eleven percent of patients reported new or worsened neurologic symptoms. Radiosurgery was effective in treating AVM-related headaches ($p < 0.001$) but did not improve the performance status of patients. CONCLUSIONS: Stereotactic radiosurgery is an effective tool in the treatment of AVMs and amelioration of AVM-related headaches, but it did not affect the patients' performance status. Factors affecting obliteration include prior hemorrhage, marginal dose, prior embolization, and AVM volume. Risk of hemorrhage persists in the latency period after radiosurgery, and it remains finite even after complete obliteration.

Acta Neurochirurgica.2010;152(5):803-15. Epub 2010/01/08

Operative intervention for delayed symptomatic radionecrotic masses developing following stereotactic radiosurgery for cerebral arteriovenous malformations--case analysis and literature review

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CASE REPORT: We report two cases of operative intervention that was beneficial in the treatment of delayed symptomatic radionecrotic masses that had developed following stereotactic radiosurgery (SRS) using the gamma knife (GK) for the treatment of cerebral arteriovenous malformations (AVM).

DISCUSSION: Case 1 involved a small craniotomy for decompression of a large cerebral multiloculated cyst, which had become symptomatic 84 months following gamma knife treatment for a left frontal lobe AVM. Case 2 involved surgical excision of an occipital radionecrotic mass 72 months following GK treatment for an occipital AVM. This patient had suffered from longstanding symptomatic cerebral oedema, which on occasions had become life threatening. Case 2 is also the first report of a radionecrotic mass occurring post-SRS for an AVM, which conversely appeared to demonstrate increased uptake on single photon emission computed tomography (SPECT) scan. The first literature review of such delayed symptomatic radionecrotic lesions is presented. There appears to be a late onset of symptoms (average 55 months, range 12-111 months) associated with such radionecrosis. Drainage of such cysts or excision of the mass lesion appears to be consistently beneficial to the patients and appears to be uncomplicated. CONCLUSION: We recommend early surgical intervention for such delayed symptomatic radionecrotic masses that do not resolve following non-operative management. We also recommend caution in interpretation of SPECT scan results when attempting to differentiate radionecrosis from neoplasia.

Neurosurgery.2010;66(1):121-9; discussion 129-30. Epub 2009/12/22

Endovascular treatment increases but gamma knife radiosurgery decreases angiogenic activity of arteriovenous malformations: an in vivo experimental study using a rat cornea model

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OBJECTIVE: To compare the angiogenic potentials of embolized, gamma knife-treated or untreated cerebral arteriovenous malformations (AVMs), using a rat cornea angiogenesis model. METHODS: Tissue samples from cerebral AVM patients who were either untreated or had previously been treated with embolization or gamma knife radiosurgery and who had undergone operations for hemorrhage at the Neurosurgery Department or the Neurological Sciences Institute of Marmara University were used. For the macroscopic evaluation of angiogenesis, tissue samples were inoculated in a micropocket created on the rat eye, and the level of angiogenic activity was graded macroscopically for 15 days, with glioblastoma multiforme and normal brain artery tissues serving as positive and negative controls, respectively. For the other part of the experiment, eyes of another set of rats were inoculated with the study samples only using the same cornea angiogenesis model, in which microvessel count and vascular endothelial growth factor assessment was done at days 3, 7, 11, and 15. RESULTS: Based on our macroscopic findings in the cornea angiogenesis model, embolized AVMs exhibited the highest angiogenic activity, followed by untreated AVMs and gamma knife-treated AVMs. Evaluations of vascular endothelial growth factor expression and microvessel counts showed a similar relation among the 3 tissue groups with regard to the level of angiogenic activity, supporting the results of macroscopic examinations. CONCLUSION: This study, for the first time, provides experimental semiquantitative data to

compare the angiogenic potentials of embolized and gamma knife-treated AVM tissues. Embolization may increase angiogenic activity, and gamma knife radiosurgery may decrease it when compared with activity in previously untreated AVMs. These data can be useful to understand why recurrence of AVMs after angiographically demonstrated endovascular occlusion is common but after gamma knife occlusion is rare.

Journal of Neurosurgery.2008;109 Suppl(51-6. Epub 2009/01/10

Treatment of arteriovenous malformations using Gamma Knife surgery: the experience at the University of Washington from 2000 to 2005

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OBJECT: The purpose of this study was to examine the efficacy and toxicity of treating arteriovenous malformations (AVMs) with the model 3C Gamma Knife at the University of Washington Medical Center. METHODS: Ninety-five evaluable patients with 99 treatable AVMs were treated at the University of Washington Medical Center from April 2000 through June 2005. The median patient age at the time of treatment was 40 years (range 6-68 years). The male to female patient ratio was 0.98:1. The median AVM volume treated was 3.8 cm(3) (range 0.12-32 cm(3)). Forty-four percent of the patients had hemorrhaged prior to treatment. The median peripheral Gamma Knife surgery dose was 20 Gy with a median of 12 isocenters treated. The median follow-up duration was 38 months (range 3-91 months).

Eighty-one percent of the patients had no previous stereotactic radiosurgery (SRS), whereas the remaining 19% had previously been treated with linear accelerator-based SRS. RESULTS: The Kaplan- Meier estimated 6-year AVM obliteration rate for the entire cohort was 71.4%. The Kaplan-Meier estimated 6-year obliteration rate was 72% for patients having no prior SRS and 54.5% for those undergoing repeat SRS. The median time to AVM obliteration was 47 months, with 90% of the obliterations occurring between 24 and 58 months. Eight patients (7.4%) experienced late toxicities. There were 2 fatal bleeds and 13 (13.8%) nonfatal bleeds after Gamma Knife surgery. CONCLUSIONS: Gamma Knife surgery is an effective treatment for AVMs, resulting in an excellent obliteration rate with acceptable toxicity.

Journal of Neurosurgery.2008;109 Suppl(2-7. Epub 2009/01/10

Complications of Gamma Knife surgery: an early report from 2 Canadian centers

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OBJECT: Gamma Knife surgery (GKS) is used to treat benign and malignant brain tumors, arteriovenous malformations, trigeminal neuralgia, and other conditions. Patients experience reduced neurological morbidity from GKS compared with open microneurosurgery, but risks of radiation injury and technical limitations persist. The authors report treatment complications from the early experience of 2 Canadian GKS programs in Toronto and Sherbrooke. METHODS: In Toronto, a prospective administrative database was searched for adverse events and incomplete treatment administrations. In Sherbrooke, data were acquired by chart review. Patients were accrued until August 1, 2007, and a total of 973 patients were included in this report. RESULTS: During the radiosurgical procedure, 19 patients (2%) suffered anxiety or syncopal episodes, and 2 patients suffered acute coronary events. Treatments were incompletely administered in 12 patients (1.2%). Severe pain was a delayed complication: 8 patients suffered unexpected headaches, and 9 patients developed severe facial pain. New motor deficits developed in 11 patients, including edema-induced ataxia in 4 and one case of facial weakness after treatment of a vestibular schwannoma. Four patients required shunt placement for symptomatic hydrocephalus, and 16 patients suffered delayed seizures. CONCLUSIONS: Gamma Knife surgery is a minimally invasive treatment modality for many intracranial diseases. Treatment is not risk free, and some patients will develop complications; these are likely to decrease as institutional experience matures. Expanding availability and indications necessitate discussion of these risks with patients considering treatment.

J Korean Neurosurg Soc.2008;43(6):265-9. Epub 2008/12/20

Retrospective analysis on 76 cases of cerebral arteriovenous malformations treated by gamma knife radiosurgery

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OBJECTIVE: Outcome of gamma knife radiosurgery (GKS) in the consecutive 100 cases with cerebral arteriovenous malformations (AVMs) was analyzed. METHODS: Data from initial 100 patients treated with GKS in the authors' institute were reviewed retrospectively. Spetzler-Martin grade at diagnosis were I in 18 patients, II in 27, III in 36, IV in 11, and V in 8. Thirty-five patients had experienced previous bleeding, 27 patients presented with seizure, and 31 patients presented with headache. The mean volume of the lesion was 4.3 cm(3) (0.1-29.3 cm(3)). The median radiation dose delivered to the margin was 20.0 Gy (13-32 Gy). Mean follow-up period was 37.5 months (5-63 months). RESULTS: Angiographic follow-up was performed in 48 patients at least 2 years after GKS. Sixteen patients were lost in follow up following 2 years from GKS. Twenty-eight of 48 patients (58%) showed complete obliteration and 20 patients (42%) showed partial obliteration. Seven patients presented with post-GKS hemorrhage.

Adverse radiation effect (ARE) was observed at follow-up MRI in 25 of 76 patients, and it was symptomatic in 5 patients. Complete obliteration was confirmed in 24 of 31 (77%) patients with volume less than 4 cm(3), meanwhile only 4 of 17 (24%) patients with volume of 4 cm(3) or more showed complete obliteration. Complete obliteration rate was 67% with 20 Gy or higher marginal dose, 63% with 15-20 Gy, and 17% with less than 15 Gy. CONCLUSION: GKS can provide high rates of obliteration with acceptable risk of morbidity in a subgroup of small AVMs. However, overall outcome in whole spectrum of AVMs, in which large proportion of cases have unfavorable characteristics for radiosurgery, is much worse. More effective therapeutic strategy needs to be developed for large AVMs that are difficult to be managed with current available treatment modalities.

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Radiosurgery facilitates resection of brain arteriovenous malformations and reduces surgical morbidity

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OBJECTIVE: Stereotactic radiosurgery makes brain arteriovenous malformations (AVM) more manageable during their microsurgical resection. To better characterize these effects, we compared results of microsurgical resection of radiated (RS) and nonradiated (RS) AVMs to demonstrate that previous radiosurgery facilitates surgery and decreases operative morbidity. METHODS: From our series of 344 patients who underwent AVM resections at the University of California, San Francisco (1997- 2007), 21 RS patients were matched with 21 RS patients based on pretreatment clinical and AVM characteristics. Matching was blinded to outcomes, which were assessed with the modified Rankin Scale. RESULTS: Mean AVM volume was reduced by 78% ($P < 0.01$), and Spetzler-Martin grades were reduced in 52% of RS patients ($P < 0.001$). Preoperative embolization was used less in RS than in RS patients ($P < 0.001$). Mean operative time ($P < 0.01$), blood loss ($P < 0.05$), and length of hospital stay ($P < 0.05$) were lower in the RS group. Surgical morbidity was 14% higher in RS patients, and they demonstrated significant worsening in modified Rankin Scale scores after surgery, whereas RS patients did not ($P < 0.01$). RS patients deteriorated between AVM diagnosis and surgery owing to hemorrhages during the latency period ($P < 0.05$). CONCLUSION: Previous radiosurgery facilitates AVM microsurgery and decreases operative morbidity. Radiosurgery is recommended for unruptured AVMs that are not favorable for microsurgical resection. Microsurgical resection is recommended for radiated AVMs that are not completely obliterated after the 3-year latency period but are altered favorably for surgery, even in asymptomatic patients. Prompt resection of persistent AVMs should be considered to avoid the risk of postlatency hemorrhage and to optimize patient outcomes.

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Gamma knife radiosurgery for arteriovenous malformations: the Furukawa experience

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The Furukawa experience treating 534 patients with cerebral arteriovenous malformations using gamma knife radiosurgery (GKRS) is summarized. By repeating radiosurgery for any residual nidus after the first GKRS, the rates of cumulative complete obliteration 7 years after this initial GKRS, according to four volume categories (< or =1, 4 > or = >1, 10 > or = > 4, > 10cm3), were 92, 89, 68 and 43%, respectively.

Bleeding after GKRS was observed in 8.1% of the patients and was more frequently seen in patients with a large nidus and history of bleeding two or more times before GKRS. Cyst formation was recognized in 4.7% of patients, two thirds of which required some form of surgical intervention. Refinement of the total GKRS system contributed to earlier and more effective nidus obliteration.

Neurosurgery.2008;62(5):1129-38; discussion 138-9. Epub 2008/06/27

Radiation arteriopathy in the transgenic arteriovenous fistula model

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OBJECTIVE: The transgenic arteriovenous fistula model, surgically constructed with transgenic mouse aorta interposed in common carotid artery-to-external jugular vein fistulae in nude rats, has a 4-month experimental window because patency and transgenic phenotype are lost over time. We adapted this model to investigate occlusive arteriopathy in brain arteriovenous malformations after radiosurgery by radiating grafted aorta before insertion in the fistula. We hypothesized that high-dose radiation would reproduce the arteriopathy observed clinically within the experimental time window and that deletions of endoglin (ENG) and endothelial nitric oxide synthase (eNOS) genes would modify the radiation response. METHODS: Radiation arteriopathy in the common carotid arteries of 171 wild-type mice was examined with doses of 25, 80, 120, or 200 Gy (Experiment 1). Radiation arteriopathy in 68 wild-type arteriovenous fistulae was examined histologically and morphometrically with preoperative radiation doses of 0, 25, or 200 Gy (Experiment 2). Radiation arteriopathy in 51 transgenic arteriovenous fistulae (36 ENG and 15 eNOS knock-out fistulae) was examined using preoperative radiation doses of 0, 25, or 200 Gy (Experiment 3). RESULTS: High-dose radiation (200 Gy) of mouse common carotid arteries induced only mild arteriopathy (mean score, 0.66) without intimal hyperplasia and with high mortality (68%). Radiation arteriopathy in wild-type arteriovenous fistulae was severe (mean score, 3.5 at 200 Gy), with intimal hyperplasia and medial disruption at 3 months, decreasing luminal areas with increasing dose, and no mortality. Arteriopathy was robust in transgenic arteriovenous fistulae with ENG +/- and with eNOS +/-, with thick intimal hyperplasia in the former and distinct smooth muscle cell proliferation in the latter. CONCLUSION: The transgenic arteriovenous fistula model can be adapted to rapidly reproduce radiation arteriopathy observed in resected brain arteriovenous malformations after radiosurgery. High radiation doses accelerate the progression of arteriopathy to fit the 4-month time limitation of the model, allowing transgenic tissues to retain their phenotypes throughout the experimental window. Modified radiation responses in ENG and eNOS knock-out fistulae indicate that arteriopathy after arteriovenous malformation radiosurgery might potentially be enhanced by altered gene expression.

Prog Neurol Surg.2007;20(212-9. Epub 2007/02/24

Histopathological changes in cerebral arteriovenous malformations following Gamma Knife radiosurgery

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Histological, immunohistochemical and electron microscopic investigations were carried out in a series of surgical pathology material that was removed from 7 patients. They were harboring cerebral arteriovenous malformations (AVMs) that had been previously treated with Leksell Gamma Knife radiosurgery, and presented subsequent bleeding 10-52 months after treatment. Light microscopic studies revealed a spindle cell proliferation in the connective tissue stroma and in the subendothelial region of the irradiated AVM vessels. The histological, immunohistochemical and ultrastructural characteristics of the spindle cell population in the Leksell Gamma Knife-treated AVMs are similar to those designated as myofibroblasts in wound healing processes and pathological fibromatoses. Considering that similar cell modifications have not been demonstrated in control, nonirradiated AVM specimens, these myofibroblasts might contribute to the shrinking process and final occlusion of AVMs after radiosurgery.

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Gamma Knife treatment for cerebral arteriovenous malformations

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One of the earliest indications for Gamma Knife treatment, radiosurgery for cerebral arteriovenous malformations, has stood the test of time. While initially only the ideal cases (small, compact nidus in a non-eloquent site) were chosen, increasingly larger, more complex AVMs were treated. Combination treatment with embolisation and surgery enables most lesions to be treated with success and remarkably low complication rate. This paper is a brief overview of the experience gained in Sheffield.

Interv Neuroradiol.2006;12(3):189-202. Epub 2006/09/15
Neurovascular radiosurgery
Soderman, M., Guo, W. Y., Karlsson, B., Pelz, D. M., Ulfarsson, E. and Andersson, T.,Dept of Neuroradiology, Karolinska University Hospital, Stockholm, Sweden - michael.soderman@karolinska.se.
Summary: This article focuses on the treatment of neurovascular diseases, in particular brain arteriovenous malformations (BAVMs), with radiosurgery. The target group for this review is physicians who manage patients with neurovascular diseases, but are not actively engaged in radiosurgery. Radiosurgery for BAVMs is an established treatment with clearly defined risks and benefits. The efficacy of radiosurgery for dural arteriovenous shunts (DAVSs) is probably similar but the treatment has not yet gained the same acceptance. Radiosurgical treatment of cavernomas (cavernous hemangiomas) remains controversial. Well founded predictive models for BAVM radiosurgery show: *The probability of obliteration depends on the dose of radiation given to the periphery of the BAVM. *The risk of adverse radiation effects depends on the total dose of radiation, i.e. the amount of energy imparted into the tissue. The risk is greater in centrally located lesions. The risk of damage to brainstem nucleii and cranial nerves must be added to the risk predicted from current outcome models. *The risk of hemorrhage during the time span before obliteration depends on the BAVM volume, the dose of radiation to the periphery of the lesion and the age of the patient. Central location is a probably also a risk factor.

Cavernous Malformations

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Pathological response of cavernous malformations following radiosurgery
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Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.
OBJECT: Stereotactic radiosurgery (SRS) is a therapeutic option for repeatedly hemorrhagic cavernous malformations (CMs) located in areas deemed to be high risk for resection. During the latency period of 2 or more years after SRS, recurrent hemorrhage remains a persistent risk until the obliterative process has finished. The pathological response to SRS has been studied in relatively few patients. The authors of the present study aimed to gain insight into the effect of SRS on CM and to propose possible mechanisms leading to recurrent hemorrhages following SRS. METHODS: During a 13-year interval between 2001 and 2013, bleeding recurred in 9 patients with CMs that had been treated using Gamma Knife surgery at the authors' institution. Microsurgical removal was subsequently performed in 5 of these patients, who had recurrent hemorrhages between 4 months and 7 years after SRS. Specimens from 4 patients were available for analysis and used for this report. RESULTS: Histopathological analysis demonstrated that vascular sclerosis develops as early as 4 months after SRS. In the samples from 2 to 7 years after SRS, sclerotic vessels were prominent, but there were also vessels with incomplete sclerosis as well as some foci of neovascularization. CONCLUSIONS: Recurrent bleeding after SRS for CM could be related to incomplete sclerosis of the vessels, but neovascularization may also play a role.

Surg Neurol Int. 2015 May 14;6(Suppl 5):S249-57. eCollection 2015.
Radiosurgery for symptomatic cavernous malformations: A multi-institutional retrospective study in Japan.
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BACKGROUND: A group study for symptomatic cavernous malformation (CM) treated with gamma knife (GK) surgery was performed.

METHODS: A total of 298 cases collected from 23 GK centers across Japan were included. Hemorrhage was the most common manifestation, followed by seizures and neurological deficits. Most of the lesions were located in the brainstem and basal ganglia, followed by the cerebral or cerebellar hemispheres. The CMs, which had a mean diameter of 14.8 mm, were treated using GK surgery with a mean marginal dose of 14.6 Gy.

RESULTS: In terms of hemorrhage-free survival (HFS), a marked dissociation was confirmed between the hemorrhage and seizure groups, while no obvious difference was noted between sexes. Superficial CMs located in cerebellum or lobar regions responded to the treatment better than deeply located CMs in the basal ganglia or brainstem. No significant difference of dose-dependent response was seen for three different ranges of marginal dose: Less than 15 Gy, between 15 and 20 Gy, and more than 20 Gy. Complications were more frequent after a marginal dose of over 15 Gy and in patients with lesions more than 15 mm in diameter. The rates of annual hemorrhage were estimated to be 7.4% during the first 2 years after radiosurgery and 2.8% thereafter. The overall hemorrhage rate after radiosurgery was 4.4%/year/patient.

CONCLUSION: The risk of hemorrhage is considerably reduced after GK treatment. The HFS as well as annual hemorrhage rate after GK treatment was apparently superior to that after conservative treatment for symptomatic CMs. To optimize the success of GK treatment, it is important to reduce the incidence of complications.

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Pathological response of cavernous malformations following radiosurgery.

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OBJECT: Stereotactic radiosurgery (SRS) is a therapeutic option for repeatedly hemorrhagic cavernous malformations (CMs) located in areas deemed to be high risk for resection. During the latency period of 2 or more years after SRS, recurrent hemorrhage remains a persistent risk until the obliterative process has finished. The pathological response to SRS has been studied in relatively few patients. The authors of the present study aimed to gain insight into the effect of SRS on CM and to propose possible mechanisms leading to recurrent hemorrhages following SRS.

METHODS: During a 13-year interval between 2001 and 2013, bleeding recurred in 9 patients with CMs that had been treated using Gamma Knife surgery at the authors' institution. Microsurgical removal was subsequently performed in 5 of these patients, who had recurrent hemorrhages between 4 months and 7 years after SRS. Specimens from 4 patients were available for analysis and used for this report.

RESULTS: Histopathological analysis demonstrated that vascular sclerosis develops as early as 4 months after SRS. In the samples from 2 to 7 years after SRS, sclerotic vessels were prominent, but there were also vessels with incomplete sclerosis as well as some foci of neovascularization.

CONCLUSIONS: Recurrent bleeding after SRS for CM could be related to incomplete sclerosis of the vessels, but neovascularization may also play a role.

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Radiosurgery and cavernous malformations.

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Comment in: Response. [J Neurosurg. 2015]

Comment on: Pathological response of cavernous malformations following radiosurgery. [J Neurosurg. 2015]

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Radiosurgery for cerebral cavernomas.
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The role of stereotactic radiosurgery (SRS) in the management of cerebral cavernomas (CCMs) remains controversial. However, during the last decade the increasing knowledge on natural history and numerous publications from SRS centers using modern treatment protocols has been changing the initial resistance of the neurosurgical community. Unfortunately, the quality of publications on CCM SRS remains heterogeneous. Controversies arise from the lack of control groups, the different definition of hemorrhage, heterogeneous patient populations, and poor definition of treatment protocols. The key for proper interpretation of results is the understanding of the natural history of CCMs, which is varied both according to anatomical location and the presence or absence of previous hemorrhage. Hemispheric lesions appear to be more benign with lower annual bleed rate and risk of persisting disability, whereas those found in the thalamus, basal ganglia and brainstem typically have higher rebleed risk resulting in higher cumulative morbidity following subsequent hemorrhages. However, we are still unable at presentation to predict the future behavior of an individual lesion. In the present paper we critically review and analyze the modern SRS literature on CCMs. The expanding number of available data with current treatment protocols strongly supports the initial intuition that SRS is an effective treatment alternative for deep-seated CCMs with multiple hemorrhages reducing pretreatment annual rebleed rates from 32% pre-treatment to 1.5% within 2 years after treatment (N.=197). Moreover, it appears to stabilize lesions with no more than one bleed, and it is also effective for CCMs causing therapy resistant epilepsy especially if applied within 3 years after presentation. In modern SRS series the rate of persisting adverse radiation effects is low, resulting only in mild morbidity even in deep-seated lesions (4.16%, N.=376), and morbidity caused by post-treatment hemorrhages is also low (5.3%, N.=132). Admittedly, there is no high quality evidence to define the relative roles of microsurgery, SRS and wait-and-see policy in the management of detected CCMs at present. However, based on increasing positive experience, we recommend early SRS soon after presentation in neurologically intact or minimally disabled patients harboring deep-seated CCMs, because waiting for the cumulative morbidity of the natural history to justify an otherwise low-risk intervention does not serve the patient well.

Clin Neurol Neurosurg.2015; Epub 2015/02/11
Controversies in the management of brainstem cavernous malformations: Role of stereotactic radiosurgery
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Clin Neurol Neurosurg. 2015 Apr;131:88-9. doi: 10.1016/j.clineuro.2015.01.019. Epub 2015 Jan 28.
Controversies in the management of brainstem cavernous malformations: role of stereotactic radiosurgery.
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Comment on: Gamma knife radiosurgery of the symptomatic brain stem cavernous angioma with low marginal dose. [Clin Neurol Neurosurg. 2014]

Zhong Nan Da Xue Xue Bao Yi Xue Ban.2014;39(12):1320-5. Epub 2014/12/30
[Therapeutic effect of gamma knife on intracranial cavernous angioma]
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Objective: To evaluate the therapeutic effect of gamma knife on patients with intracranial cavernous angioma (CA).
Methods: The medical records of 122 patients (134 lesions) who underwent radiosurgery were reviewed retrospectively. Results: The average follow-up period was 43 months. No patient died. One patient underwent CA resection. In patients with epilepsy, 83% patients showed alleviation of seizures. About 44% of the lesions

shrank in size after treatment with gamma knife radiosurgery (59/134). Seven cases had hemorrhage again after radiosurgery, and the overall annual hemorrhage rate was 1.6%. Edema was found in 11.5% patients (14/122) and all patients showed improvement aft er treatment. Conclusion: Gamma knife is a safe treatment for CA, which could obviously improve the symptoms of epilepsy. Gamma knife radiosurgery is the fi rst option for the treatment of cavernous sinus angiomas.

Acta Neurochir (Wien).2015;157(1):51-2. Epub 2014/11/14

Stereotactic radiosurgery for cavernous malformations: prejudice from ignorance

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Effect of stereotactic radiosurgery on the hemorrhage risk of cerebral cavernous malformations: fact or fiction?

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Gamma knife radiosurgery for brainstem cavernous malformations: should a patient wait for the rebleed?

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Background: The effectiveness of stereotactic radiosurgery (SRS) for cavernous malformation (CM) has not been fully assessed. Consequently, observation is usually recommended when a bleeding CM is initially discovered. Recurrent bleeding occurs with CMs, and these repeat hemorrhages can result in additional morbidity. Methods: From 1992 to 2011, 49 patients with brainstem CMs were treated with Gamma Knife radiosurgery (GKS). We classified patients into two groups: Group A (n = 31), patients who underwent GKS for a CM following a single symptomatic bleed, and group B (n = 18), patients who underwent GKS for a CM following two or more symptomatic bleeds. The mean marginal dose of radiation was 13.1 Gy (range 9.0-16.8 Gy): 12.8 Gy in group A and 13.7 Gy in group B. The mean follow-up period was 64.0 months (range 1-171 months). Results: In group A, the annual hemorrhage rate (AHR) following GKS was 7.06 % within the first 2 years and 2.03 % after 2 years. In group B, four patients (22.2 %) developed new or worsening neurologic deterioration as a result of repeat hemorrhages. In group B, the AHR was 38.36 % prior to GKS, 9.84 % within the first two years, and 1.50 % after two years. There was no statistically significant difference in the AHRs at each follow-up period after GKS between the two groups. Adverse radiation effects (AREs) developed in a total of four patients (8.2 %); among them, one patient (2.0 %) developed a permanent case of diplopia. No mortality occurred in this series. Conclusion: In this study, GKS was demonstrated to be a safe and effective alternative treatment for brain stem CMs that resulted in a reduction in the AHR. Consequently, we suggest that even CM patients who have suffered only a single bleed should not be contraindicated for SRS.

World Neurosurg.2014;Epub 2014/01/21

Microsurgery and Radiosurgery for Brainstem Cavernomas: Effective and Complementary Treatment Options

Frischer, J. M., Gatterbauer, B., Holzer, S., Stavrou, I., Gruber, A., Novak, K., Wang, W. T., Reinprecht, A., Mert, A., Trattnig, S., Mallouhi, A., Kitz, K. and Knosp, E.,Medical University Vienna, Department of Neurosurgery, Vienna, Austria. Electronic address: josa.frischer@meduniwien.ac.at.

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Background: Treatment options for brainstem cavernous malformations (BSCMs) are still controversially discussed.

Objective: To evaluate treatment options for BSCM we provide the results of a center with long-standing experience in microsurgical resection and Gamma Knife radiosurgical (GKRS) treatment of BSCMs. Methods:

67 symptomatic patients with BSCMs were treated microsurgically (n = 29) or radiosurgically (n = 38). Patients were followed-up for a minimum of 2 years (median: 7.7 years). A recent follow-up was performed. Results: Surgically treated patients had mainly large superficially seated lesions, experienced preoperative hemorrhages more often and presented with higher preoperative modified Rankin Scale (mRS) scores. Radiosurgically treated patients harbored smaller deep-seated lesions, thus reflecting a selection bias. In both treatment groups, patients presented with significantly better mRS scores at follow-up than prior to intervention. Overall annual preoperative hemorrhage rates were 3.2% in microsurgery patients and 2.3% in radiosurgery patients. In the preoperative observation period, the re-hemorrhage rate was 25.1% for microsurgery patients and 7.2% for radiosurgery patients. Hemorrhage rate after GKRS dropped significantly to 0.6% after 2 years. The postoperative hemorrhage rate was 8.8% but only for microsurgery patients with residual lesions. Advancements in microsurgical techniques improved surgical outcomes, resulting in a high total excision rate in the modern era. Conclusion: In the treatment of BSCM, patient selection and timing of surgery are crucial. If applied in a multidisciplinary neurosurgical center, microsurgery and radiosurgery are complimentary treatment options both resulting in reduced bleeding rates and improvement of clinical outcome.

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Treatment of cavernoma: an evidence-based dilemma?

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Acta Neurochir Suppl.2013;116(107-11. Epub 2013/02/19

Gamma knife radiosurgery of brain cavernomas

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PURPOSE: Radiosurgery of cavernomas should prevent rebleeding, growth of the lesion, and deterioration of clinical symptoms. However, there is no direct diagnostic tool to verify the endpoints of treatment. At present, the positive effects of radiosurgery are identified by clinical observation and analysis of imaging changes on magnetic resonance imaging during a sufficiently long follow-up period. METHODS: Between 1992 and 2000, a total of 112 patients with brain cavernomas were treated with Gamma Knife radiosurgery at our center. In all, 59 patients experienced bleeding before radiosurgery; the remainder did not. The median age of patients was 42 years, the median volume of the cavernomas was 0.9 cm(3), and the median applied marginal dose was 16 Gy. RESULTS: After a 2-year latent interval after treatment (median follow-up 84 months), the risk of bleeding in the group of patients with bleeding before radiosurgery had decreased from 3.7 % to 0.2 %. For the patients without bleeding before radiosurgery, the annual risk of bleeding was 0.8 %. The cavernoma size decreased in 53.0 % of cases and increased in 6.4 %. Epilepsy, if present before the treatment, was alleviated in 45 % of cases. The risks of temporary or permanent morbidity caused by radiosurgery were 14.6 % and 0.9 %, respectively. CONCLUSION: Radiosurgery of cavernomas was associated with a low risk of permanent morbidity. The risk of rebleeding after the 2-year latent interval after radiosurgery had decreased. Treatment of cavernomas with no history of bleeding was halted at our center.

J Clin Neurosci.2009;16(7):945-9. Epub 2009/04/04

Different responses of cavernous malformations and arteriovenous malformations to radiosurgery

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The vascular structure of cavernous malformations (CMs) and arteriovenous malformations (AVMs) is different and they have differing clinical responses to radiosurgery. The structural differences of irradiated and non-irradiated CMs and AVMs were examined to clarify their differential responses to radiosurgery. CMs showed a greater ratio of intraluminal diameter to vessel wall thickness and a lack of subendothelial fibroblasts, myofibroblasts and smooth muscle cells compared with AVMs. Partial proteinaceous clots (19-22% of lumen) formed in CM sinusoids after radiosurgery but complete vaso- occlusion did not occur for up to 6 years after radiosurgery. In contrast, complete vaso-occlusion (91- 98% of lumen) by fibrin thrombi that are permanent clots was observed in AVM vessels. Radiation- induced neuronal loss, neurofibrillary degeneration of neurons

and myelin fragmentation were typical in the surrounding brain tissue of the irradiated lesions. The different structure and cellular composition of CMs and AVMs is likely to influence their responses to radiosurgery.

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Pathological considerations to irradiation of cavernous malformations

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Stereotactic radiosurgery is a controversial treatment modality in the management of cerebral cavernous malformations (CVMs). Systematic pathological studies of irradiated specimens probably could help to resolve the controversy. Light microscopic investigation of a surgically resected thalamic CVM 1 year after 40-Gy irradiation revealed endothelial cell destruction in the cavernous channels, and marked fibrosis with scar tissue formation in the connective stroma of the lesion. These histopathological findings were similar to those described in arteriovenous malformations after Gamma Knife surgery, and suggest that the ionizing effect of radiation energy evokes vascular and connective tissue stroma changes in CVMs as well.

Dural Arteriovenous Fistula

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Paradoxical exacerbation of symptoms with obstruction of the venous outflow after gamma knife radiosurgery for treatment of a dural arteriovenous fistula of the cavernous sinus

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A 59-year-old female presented with progressive right proptosis, chemosis and ocular pain. An imaging work-up including conventional catheter angiography showed a right-sided dural arteriovenous fistula of the cavernous sinus, which drained into the right superior petrosal sinus, right superior ophthalmic vein, and right inferior ophthalmic vein, and cortical venous reflux was seen via the right petrosal vein in the right posterior fossa. After failure of transvenous embolization, the patient underwent Gamma Knife radiosurgery (GKRS). At one month after GKRS, she developed increasing ocular pain and occipital headache. Repeat angiography showed partial obliteration of the fistula and loss of drainage via the superior and inferior ophthalmic veins with severe congestion, resulting in slow flow around the right cerebellar hemisphere. Prompt transarterial embolization relieved the patient's ocular symptoms and headache. We report on a case of paradoxical exacerbation of symptoms resulting from obstruction of the venous outflow after GKRS for treatment of a dural arteriovenous fistula of the cavernous sinus.

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Radiosurgery for dural arterio-venous fistulas: A review

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Dural arteriovenous fistulas (dAVFs) are vascular lesions involving direct connections between intracranial dural arteries and venous sinuses. The goal of treatment of these vascular lesions is to alleviate symptoms and prevent future hemorrhage. While endovascular embolization remains the primary method of treatment and obliteration of dAVF recently, stereotactic radiosurgery (SRS) has been used as a treatment modality in select dAVF either alone or in conjunction with endovascular embolization. Considering recent studies examining dAVFs natural history and possible therapeutic interventions, the authors provide a concise review of the literature and discuss the indications, efficacy, and safety of SRS in the management of dAVFs.

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Gamma Knife radiosurgery for the management of intracranial dural arteriovenous fistulas

Pan, D. H., Lee, C. C., Wu, H. M., Chung, W. Y., Yang, H. C. and Lin, C. J.,Department of Neurosurgery, Taipei Veterans General Hospital, No. 201 Shi-Pai Rd., Sec. 2, Taipei, Taiwan. hcpan@vghtpe.gov.tw BACKGROUND: This report presents our 15-year experience with Gamma Knife radiosurgery (GKS) for the treatment of 321 patients with dural arteriovenous fistulas (DAVFs) in different locations. METHODS: The most common locations of DAVFs were the cavernous sinus (206 cases) and transverse-sigmoid sinus (72 cases), which together accounted for 86.6 % of cases. In all, 54 patients had undergone embolization or surgery prior to radiosurgery, and the other patients underwent GKS as the primary treatment. During GKS, radiation was confined to the involved sinus wall, which was considered the true nidus of the DAVF. Target volume ranged from 0.8 to 52 cm(3). Marginal and maximum doses to the nidus ranged from 14 to 25 Gy and from 25 to 36 Gy, respectively. RESULTS: The mean follow-up time was 28 months (range 2-149 months). In 264 of 321 patients (82 %) available for follow-up study, 173 (66 %) showed complete obliteration of DAVFs with symptomatic resolution, 87 (33 %) had partial obliteration, 2 (0.8 %) had stationary status, 1 (0.4 %) had progression, and 1 (0.4 %) died from a new hemorrhagic episode. Complications were found in only two (0.8 %) patients, one with venous hemorrhage and one with focal brain edema after GKS. CONCLUSIONS: GKS is a safe, effective treatment for DAVFs. It provides a minimally invasive therapeutic option for patients who harbor less-aggressive DAVFs but who suffer from intolerable clinical symptoms. For some aggressive DAVFs with extensive venous hypertension or hemorrhage, multimodal treatment with combined embolization or surgery is necessary.

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[Radiosurgery for intracranial dural arteriovenous fistulas--indications for limitations for gamma knife treatment]

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We summarize the results of gamma knife treatment for dural arterivenous fistula (DAVF), are report our study. Since the early 1990s, DAVFs have been treated in the same manner as arteriovenous malformations (AVMs), i.e., by radiosurgery, performed with or without embolization. DAVFs in the cavernous sinus, transverse-sigmoid sinus, and cerebellar tent were treated with a marginal dose of 18 to 20 Gy. The current obliteration rates of DAVF reported in literature are not low when compared with those of AVM. Excellent DAVF obliteration rates were observed in our study, which were similar to those reported in the literature. In fact, complete response (CR) was observed in 9 cases, partial response (PR) in 9 cases, and partical obliteration in 6 cases during the mean follow-up of 27 months. Moreover, considerable neurological improvements were noted, which apparently began at an early stage post radiosurgery. Bleeding was observed 2 cases associated with cortical reflux during the follow-up. In conclusion, radiosurgery for DAVF is very useful for both the obliteration of the fistula and for the improvement of clinical signs. However, prior to performing radiosurgery, the lesions with cortical reflux should be interrupted by initially treated with surgery or embolization.