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# Leksell Gamma Knife<sup>®</sup> Radiosurgery Bibliography

Arteriovenous Malformation

**2012–2020**

≥ 30 patient cohorts

[1] Stereotactic radiosurgery with versus without prior Onyx embolization for brain arteriovenous malformations.

*J Neurosurg.* 2020 Dec 11:1-9.

Chen CJ, Ding D, Lee CC, Kearns KN, Pomeranec JJ, Cifarelli CP, Arsanious DE, Liscak R, Hanuska J, Williams BJ, Yusuf MB, Woo SY, Ironside N, Burke RM, Warnick RE, Trifiletti DM, Mathieu D, Mureb M, Benjamin C, Kondziolka D, Feliciano CE, Rodriguez-Mercado R, Cockroft KM, Simon S, Mackley HB, Zammar SG, Patel NT, Padmanaban V, Beatson N, Saylany A, Lee JYK, Sheehan JP  
PMID: 33307527 DOI: 10.3171/2020.7.JNS201731

**OBJECTIVE:** Investigations of the combined effects of neoadjuvant Onyx embolization and stereotactic radiosurgery (SRS) on brain arteriovenous malformations (AVMs) have not accounted for initial angioarchitectural features prior to neuroendovascular intervention. The aim of this retrospective, multicenter matched cohort study is to compare the outcomes of SRS with versus without upfront Onyx embolization for AVMs using de novo characteristics of the pre-embolized nidus. **METHODS:** The International Radiosurgery Research Foundation AVM databases from 1987 to 2018 were retrospectively reviewed. Patients were categorized based on AVM treatment approach into Onyx embolization (OE) and SRS (OE+SRS) or SRS alone (SRS-only) cohorts and then propensity score matched in a 1:1 ratio. The primary outcome was AVM obliteration. Secondary outcomes were post-SRS hemorrhage, all-cause mortality, radiological and symptomatic radiation-induced changes (RICs), and cyst formation. Comparisons were analyzed using crude rates and cumulative probabilities adjusted for competing risk of death. **RESULTS:** The matched OE+SRS and SRS-only cohorts each comprised 53 patients. Crude rates (37.7% vs 47.2% for the OE+SRS vs SRS-only cohorts, respectively; OR 0.679,  $p = 0.327$ ) and cumulative probabilities at 3, 4, 5, and 6 years (33.7%, 44.1%, 57.5%, and 65.7% for the OE+SRS cohort vs 34.8%, 45.5%, 59.0%, and 67.1% for the SRS-only cohort, respectively; subhazard ratio 0.961,  $p = 0.896$ ) of AVM obliteration were similar between the matched cohorts. The secondary outcomes of the matched cohorts were also similar. Asymptomatic and symptomatic embolization-related complication rates in the matched OE+SRS cohort were 18.9% and 9.4%, respectively. **CONCLUSIONS:** Pre-SRS AVM embolization with Onyx does not appear to negatively influence outcomes after SRS. These analyses, based on de novo nidus characteristics, thereby refute previous studies that found detrimental effects of Onyx embolization on SRS-induced AVM obliteration. However, given the risks incurred by nidus embolization using Onyx, this neoadjuvant intervention should be used judiciously in multimodal treatment strategies involving SRS for appropriately selected large-volume or angioarchitecturally high-risk AVMs.

[2] Radiosurgery for unruptured brain arteriovenous malformations in the pre-ARUBA era: long-term obliteration rate, risk of hemorrhage and functional outcomes.

*Sci Rep.* 2020 Dec 8;10(1):21427.

Peciu-Florianu I, Leroy HA, Drumez E, Dumot C, Aboukais R, Touzet G, Leclerc X, Blond S, Lejeune JP, Reyns N

PMID: 33293642 DOI: 10.1038/s41598-020-78547-0

The management of non-hemorrhagic arteriovenous malformations (AVMs) remains a subject of debate, even more since the ARUBA trial. Here, we report the obliteration rate, the risk of hemorrhage and the functional outcomes after Gamma Knife radiosurgery (GKRS) as first-line treatment for non-hemorrhagic AVMs treated before the ARUBA publication, in a reference university center with multimodal AVM treatments available. We retrospectively analyzed data from a continuous series of 172 patients harboring unruptured AVMs treated by GKRS as first-line treatment in our Lille University Hospital, France, between April 2004 and December 2013. The primary outcome was obliteration rate. Secondary outcomes were the hemorrhage rate, the modified Rankin Scale (mRS), morbidity and epilepsy control at last follow-up. The minimal follow-up period was of 3 years. Median age at presentation was 40 years (IQR 28; 51). Median follow-up was 8.8 years (IQR 6.8; 11.3). Median target volume was 1.9 cm<sup>3</sup> (IQR 0.8-3.3 cm<sup>3</sup>), median Spetzler-Martin grade: 2 (IQR 1-2), median Pollock-Flickinger score:

1.07 (IQR 0.82-2.94), median Virginia score: 1 (IQR 1-2). Median treatment dose was 24 Gy at 50% isodose line. Twenty-three patients underwent a second GKRS after a median time of 58 months after first GKRS. The overall obliteration rate was of 76%, based primarily on cerebral angiography and/or rarely only upon MRI. Hemorrhage during the post-treatment follow-up was reported in 18 (10%) patients (annual risk of 1.1%). Transient post-GKRS morbidity was reported in 14 cases (8%) and persistent neurological deficit in 8 (4.6%) of patients. At last follow-up, 86% of patients had a mRS  $\leq 1$ . Concerning patients with pretherapeutic epilepsy, 84.6% of them were seizure-free at last follow-up. GKRS as first-line therapeutic option for unruptured cerebral AVMs achieves high obliteration rates (76%) while maintaining a high-level patient's autonomy. All hemorrhagic events occurred during the first 4 years after the initial GKRS. In cases with epilepsy, there was 84.6% seizure free at last follow-up. Permanent morbidity was reported in only 4.6%.

[3] Dynamic conformal arcs-based single-isocenter VMAT planning technique for radiosurgery of multiple brain metastases.

*Med Dosim.* 2020 Dec 7. pii: S0958-3947(20)30161-8.

Pokhrel D, Palmiero AN, Bernard ME, Clair WS

PMID: 33303353 DOI: 10.1016/j.meddos.2020.11.005

Multiple small beamlets in the delivery of highly modulated single-isocenter HyperArc VMAT plan can lead to dose delivery errors associated with small-field dosimetry, which can be a major concern for stereotactic radiosurgery for multiple brain lesions. Herein, we describe and compare a clinically valuable dynamic conformal arc (DCA)-based VMAT (DCA-VMAT) approach for stereotactic radiosurgery of multiple brain lesions using flattening filter free beams to minimize this effect. Original single-isocenter HyperArc style VMAT and DCA-VMAT plans were created on 7 patients with 2 to 8 brain lesions (total 35 lesions) for 10 MV-flattening filter free beam. 20 Gy was prescribed to each lesion. For identical planning criteria, DCA-VMAT utilizes user-controlled field aperture shaper before VMAT optimization. Plans were evaluated for conformity and target coverage, low- and intermediate dose spillages to brain volume that received more than 30% (V30%) and 50% (V50%) of prescription dose. Additionally, mean brain dose, V8, V12 and maximal dose to adjacent organs-at-risk (OAR) including hippocampi were reported. Total monitor units, beam modulation factor, treatment delivery efficiency, and accuracy were recorded. Comparing with original VMAT, DCA-VMAT plans provided similar tumor dose, target coverage and conformity, yet tighter radio-surgical dose distribution with lower dose to normal brain V30% ( $p=0.009$ ), V50% ( $p=0.05$ ) and other OAR including lower dose to hippocampi. Lower total number of monitor units and smaller beam modulation factor reduced beam on time by 2.82 min ( $p < 0.001$ ), on average (maximum up to 3.8 min). Beam delivery accuracy was improved by 8%, on average ( $p < 0.001$ ) and maximum up to 13% in some cases for DCA-VMAT plans. This novel DCA-VMAT approach provided excellent plan quality, reduced dose to normal brain, and other OAR while significantly reducing beam-on time for radiosurgery of multiple brain lesions-improving patient compliance and clinic workflow. It also provided less MLC modulation through the targets-potentially minimizing small field dosimetry errors as demonstrated by quality assurance results. Incorporating DCA-based VMAT optimization in HyperArc module for radiosurgery of multiple brain lesions merits future investigation.

[4] Outcomes of stereotactic radiosurgery for hemorrhagic arteriovenous malformations with or without prior resection or embolization.

*J Neurosurg.* 2020 Dec 4:1-9.

Kawashima M, Hasegawa H, Shin M, Shinya Y, Ishikawa O, Koizumi S, Katano A, Nakatomi H, Saito N

PMID: 33276336 DOI: 10.3171/2020.7.JNS201502

**OBJECTIVE:** The major concern about ruptured arteriovenous malformations (rAVMs) is recurrent hemorrhage, which tends to preclude stereotactic radiosurgery (SRS) as a therapeutic modality for these brain malformations. In this study, the authors aimed to clarify the role of SRS for rAVM as a stand-alone

modality and an adjunct for a remnant nidus after surgery or embolization. **METHODS:** Data on 410 consecutive patients with rAVMs treated with SRS were analyzed. The patients were classified into groups, according to prior interventions: SRS-alone, surgery and SRS (Surg-SRS), and embolization and SRS (Embol-SRS) groups. The outcomes of the SRS-alone group were analyzed in comparison with those of the other two groups. **RESULTS:** The obliteration rate was higher in the Surg-SRS group than in the SRS-alone group (5-year cumulative rate 97% vs 79%,  $p < 0.001$ ), whereas no significant difference was observed between the Embol-SRS and SRS-alone groups. Prior resection (HR 1.78, 95% CI 1.30-2.43,  $p < 0.001$ ), a maximum AVM diameter  $\leq 20$  mm (HR 1.81, 95% CI 1.43-2.30,  $p < 0.001$ ), and a prescription dose  $\geq 20$  Gy (HR 2.04, 95% CI 1.28-3.27,  $p = 0.003$ ) were associated with a better obliteration rate, as demonstrated by multivariate Cox proportional hazards analyses. In the SRS-alone group, the annual post-SRS hemorrhage rates were 1.5% within 5 years and 0.2% thereafter and the 10-year significant neurological event-free rate was 95%; no intergroup difference was observed in either outcome. The exclusive performance of SRS (SRS alone) was not a risk for post-SRS hemorrhage or for significant neurological events based on multivariate analyses. These results were also confirmed with propensity score-matched analyses. **CONCLUSIONS:** The treatment strategy for rAVMs should be tailored with due consideration of multiple factors associated with the patients. Stand-alone SRS is effective for hemorrhagic AVMs, and the risk of post-SRS hemorrhage was low. SRS can also be favorably used for residual AVMs after initial interventions, especially after failed resection.

#### [5] Does the Diffuseness of the Nidus Affect the Outcome of Stereotactic Radiosurgery in Patients with Unruptured Cerebral Arteriovenous Malformations?

*Stereotact Funct Neurosurg.* 2020 Dec 2:1-10.

Yang HC, Peng SJ, Lee CC, Wu HM, Chen YW, Lin CJ, Shiau CY, Guo WY, Pan DH, Liu KD, Chung WY, Lin YY

PMID: 33264796 DOI: 10.1159/000510683

**BACKGROUND:** We proposed an algorithm to automate the components within the identification of components within the nidus of cerebral arteriovenous malformations (AVMs) which may be used to analyze the relationship between its diffuseness and treatment outcomes following stereotactic radiosurgery (SRS). **OBJECTIVES:** to determine the impact of the diffuseness of the AVM nidus on SRS outcomes. **METHODS:** This study conducted regular follow-ups of 209 patients with unruptured AVMs who underwent SRS. The diffuseness of the AVM nidus was estimated by quantifying the proportions of vascular nidal component, brain parenchyma, and cerebrospinal fluid in T2-weighted MRIs. We used Cox regression analysis to characterize the association between nidal diffuseness and treatment outcomes in terms of obliteration rate and radiation-induced change (RICs) rate following SRS. **RESULTS:** The median AVM volume was 20.7 cm<sup>3</sup>. The median duration of imaging follow-up was 51 months after SRS. The overall AVM obliteration rate was 68.4%. RICs were identified in 156 of the 209 patients (74.6%). The median proportions of the nidus of AVM and brain parenchyma components within the prescription isodose range were 30.2 and 52.2%, respectively. Cox regression multivariate analysis revealed that the only factor associated with AVM obliteration rate after SRS was AVM volume. However, a larger AVM volume ( $>20$  mL) and a larger proportion of brain parenchyma ( $>50\%$ ) within the prescription isodose range were both correlated with a higher RIC rate following SRS. **CONCLUSIONS:** The diffuseness of the nidus indeed appears to affect the RIC rate following SRS in patients with unruptured AVMs.

#### [6] Haemorrhage rates of ruptured and unruptured brain arteriovenous malformation after radiosurgery: a nationwide population-based cohort study.

*BMJ Open.* 2020 Oct 13;10(10):e036606.

Chye CL, Wang KW, Chen HJ, Yeh SA, Tang JT, Liang CL

PMID: 33051231 DOI: 10.1136/bmjopen-2019-036606

**OBJECTIVES:** The present nationwide population-based cohort study aims to assess the effectiveness of gamma knife radiosurgery (GKS) on ruptured

and unruptured brain arteriovenous malformations (AVMs) by evaluating the haemorrhage rates. **DESIGN:** A nationwide, retrospective cohort study. **SETTING:** Taiwan National Health Insurance Research Database (NHIRD). **PARTICIPANTS:** An observational study of 1515 patients who were diagnosed with brain AVMs between 1997 and 2013 from the Taiwan NHIRD. **PRIMARY OUTCOME AND SECONDARY OUTCOME MEASURES:** We performed a survival analysis using the Kaplan-Meier method. Multivariate Cox proportional hazards regression models were used to explore the relationship between treatment modalities (GKS vs non-GKS) and haemorrhage, adjusted for age and sex. **RESULTS:** The GKS and non-GKS groups included 317 and 1198 patients, respectively. Patients in the GKS group (mean $\pm$ SD, 33.08 $\pm$ 15.48 years of age) tended to be younger than those in the non-GKS group (37.40 $\pm$ 17.62) ( $p < 0.001$ ). The 15-year follow-up revealed that the rate of bleeding risk was lower in the GKS group than in the non-GKRS group (adjusted HR (aHR) 0.61; 95% CI 0.40 to 0.92). The bleeding risk of ruptured AVMs was significantly lower in GKS group than in the non-GKS group (aHR 0.34; 95% CI 0.19 to 0.62). On the other hand, the bleeding risk of unruptured AVMs was higher in the GKS group than in the non-GKS group (aHR 1.95; 95% CI 1.04 to 3.65). In the unruptured AVM group, the incidence of bleeding was significantly higher among patients in the GKS group that were of  $>40$  years of age (aHR 3.21; 95% CI 1.12 to 9.14). **CONCLUSIONS:** GKS is safe and it reduces the risk of haemorrhage in patients with ruptured AVMs. The administration of GKS to patients with unruptured AVMs who are above the age of 40 years old male might increase the risk of haemorrhage.

#### [7] Changes in Clinical Presentation and Treatment Over Time in Patients with Unruptured Intracranial Arteriovenous Malformations.

*World Neurosurg.* 2020 Sep;141:e261-e265.

Naylor RM, Flemming KD, Brinjikji W, Brown RD Jr, Chiu S, Lanzino G

PMID: 32442730 DOI: 10.1016/j.wneu.2020.05.094

**OBJECTIVE:** Treatment of unruptured intracranial arteriovenous malformations (AVMs) has become controversial since the ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations) study was published in 2014. We sought to analyze changes in the demographics, clinical presentation, and treatment strategies in 2 patient cohorts from the same institution separated by 40 years. **METHODS:** We retrospectively reviewed the electronic medical records for a consecutive series of patients with unruptured intracranial AVMs seen at the Mayo Clinic between 2003 and 2017 and compared them with a previously published historical cohort from the same institution seen between 1974 and 1985. **RESULTS:** There were 273 patients in the contemporary cohort, of which discovery of the AVM was incidental in 123 (45.1%), a 3.5-fold increase compared with the 13.1% out of 168 patients in the historical cohort ( $P < 0.0001$ ). Consequently, the percentage of patients with seizures as the presenting symptom leading to the diagnosis of AVM decreased from 57.7% in the historical cohort to 28.9% in the contemporary cohort ( $P < 0.0001$ ). Interventional treatment was utilized in 220 (81.5%) contemporary patients compared with 49 (29.2%) historical patients ( $P < 0.0001$ ). **CONCLUSIONS:** Compared to 40 years ago, more patients are presenting with incidentally discovered intracranial AVMs and are undergoing interventional treatment. Better understanding of the natural history, developments in endovascular therapy, and stereotactic radiosurgery, as well as improvements in microsurgical techniques have led to a substantial increase in patients undergoing invasive treatment.

#### [8] Stagnant Venous Outflow Predicts Brain Arteriovenous Malformation Obliteration After Gamma Knife Radiosurgery Without Prior Intervention.

*Neurosurgery.* 2020 Aug 1;87(2):338-347.

Hu YS, Lee CC, Wu HM, Yang HC, Lin TM, Luo CB, Guo WY, Chung WY, Lin CJ

PMID: 31792505 DOI: 10.1093/neuros/nyz507

**BACKGROUND:** Gamma Knife radiosurgery (GKRS) obliterates 65% to 82% of brain arteriovenous malformations (BAVMs). **OBJECTIVE:** To explore the impact of hemodynamics on GKRS outcomes. **METHODS:** We retrospectively (2011-2017) included 98 patients with BAVMs who had received GKRS alone.

Two evaluators, blinded to the outcomes, analyzed the pre-GKRS angiography and magnetic resonance images to obtain the morphological characteristics and quantitative digital subtraction angiography (QDSA) parameters. The venous stasis index was defined as the inflow gradient divided by the absolute value of the outflow gradient. Patients' follow-up magnetic resonance or digital subtraction angiography images were evaluated for the presence of complete obliteration (CO). Cox regression and Kaplan-Meier analyses were conducted to determine the correlations between the parameters and outcomes. **RESULTS:** Among the 98 patients, 63 (63.4%) achieved CO after GKRS at a median latency period of 31 mo. In multivariable analyses with adjustments for age and sex, increased BAVM volume (hazard ratio (HR) 0.949,  $P = .022$ ) was an independent characteristic predictor, and venous stenosis (HR 2.595,  $P = .009$ ), venous rerouting (HR 0.375,  $P = .022$ ), and larger stasis index (HR 1.227,  $P = .025$ ) were independent angiographic predictors of CO. BAVMs with a stasis index of  $>1.71$  had a higher 36-mo probability of CO than those with a stasis index of  $\leq 1.71$  (61.1% vs 26.7%,  $P < .001$ ). **CONCLUSION:** BAVMs with a larger stasis index, indicating more stagnant venous outflow, may predict obliteration after GKRS. QDSA analysis may help in predicting BAVM treatment outcomes and making therapeutic decisions.

#### [9] Radiosurgery for Unruptured Intervention-Naive Pediatric Brain Arteriovenous Malformations.

*Neurosurgery.* 2020 Aug 1;87(2):368-376.

Chen CJ, Lee CC, Kano H, Kearns KN, Ding D, Tzeng SW, Atik AF, Joshi K, Huang PP, Kondziolka D, Ironside N, Mathieu D, Iorio-Morin C, Grills IS, Quinn TJ, Siddiqui ZA, Marvin K, Feliciano C, Starke RM, Faramand A, Barnett G, Lunsford LD, Sheehan JP

PMID: 31942635 DOI: 10.1093/neuros/nyz558

**BACKGROUND:** Long-term data regarding stereotactic radiosurgery (SRS) as a standalone therapy for unruptured pediatric brain arteriovenous malformations (AVMs) are incompletely defined. **OBJECTIVE:** To evaluate, in a multicenter, retrospective cohort study, the outcomes after SRS for unruptured, intervention-naive pediatric AVMs. **METHODS:** To retrospectively analyze the International Radiosurgery Research Foundation pediatric AVM database from 1987 to 2018. Pediatric patients with unruptured, previously untreated AVMs who underwent SRS were included. The primary endpoint was a composite of hemorrhagic stroke, death, or permanently symptomatic radiation-induced changes.

**RESULTS:** The study cohort comprised 101 patients (mean follow-up 80.8 mo). The primary endpoint occurred in 14%, comprising hemorrhagic stroke, death, and permanent radiation-induced changes in 6%, 3%, and 8%, respectively. Estimated probabilities of the primary endpoint were 5.2%, 10.8%, and 23.0% at 2, 5, and 10 yr, respectively. Estimated probabilities of AVM obliteration at 5 and 10 yr were 64% and 82%, respectively. Single SRS treatment ( $P = .007$ ) and higher margin dose ( $P = .005$ ) were predictors of obliteration. Subgroup analysis of Spetzler-Martin grade I-III AVMs estimated primary endpoint probabilities of 3.7%, 8.4%, and 18.7% at 2, 5, and 10 yr, respectively. **CONCLUSION:** Treatment of unruptured, intervention-naive AVMs in the pediatric population with SRS carries an approximately 2% annual risk of morbidity and mortality, which appears to plateau after 10 yr. The poorly described natural history of pediatric AVMs renders any comparison of SRS vs conservative management imperfect.

#### [10] Clinical outcome following cerebral AVM hemorrhage.

*Acta Neurochir (Wien).* 2020 Jul;162(7):1759-1766.

Karlsson B, Jokura H, Yang HC, Yamamoto M, Martinez R, Kawagishi J, Guo WY, Beute G, Chung WY, Soderman M, Yeo TT

PMID: 32385636 DOI: 10.1007/s00701-020-04380-z

**BACKGROUND:** A significant difference exists between the published results reporting the clinical outcome following brain arteriovenous malformation (AVM) ruptures. Information about the outcome following hemorrhage in an AVM population treated with radiosurgery could provide additional information to assess the risk of mortality and morbidity following an AVM hemorrhage.

**METHODS:** Clinical outcome was studied in 383 patients, the largest patient

population yet studied, who suffered from a symptomatic hemorrhage after Gamma Knife(R) surgery (GKS) but before confirmed AVM obliteration. The impact of different patient, AVM, and treatment parameters on the clinical outcome was analyzed. The aim was to generate outcome predictions by comparing our data to and combining them with earlier published results. **RESULTS:** No relation was found between clinical outcome and treatment parameters, indicating that the results are applicable also on untreated AVMs. Twenty-one percent of the patients died, 45% developed or experienced worsening of neurological sequelae, and 35% recovered completely after the hemorrhage. Old age was a predictor of poor outcome. Sex, AVM location, AVM volume, and history of prior hemorrhage did not influence the outcome. The mortality rate was comparable to earlier published prospective data, but higher than that found in retrospective studies. **CONCLUSIONS:** The mortality rates in earlier published retrospective series as well as in studies focusing on clinical outcome following AVM hemorrhage significantly underestimate the risk for a mortal outcome following an AVM hemorrhage. Based on our findings, an AVM rupture has around 20% likelihood to result in mortality, 45% likelihood to result in a minor or major deficit, and 35% likelihood of complete recovery. The findings are probably applicable also for AVM ruptures in general. The cumulative mortality and morbidity rates 25 years after diagnosis were estimated to be around 40% in a patient with a patent AVM.

#### [11] Bibliometric analysis of the top-100 most cited articles on the radiosurgical management of cerebral arteriovenous malformation.

*Surg Neurol Int.* 2020 Dec 29;11:477.

Alkhabiry A, Almutairi OT, Elarjani T, Bafaquh M, Alassaf H, Alturki AY  
PMID: 33500815 DOI: 10.25259/SNI\_760\_2020

**BACKGROUND:** Radiosurgery is an effective, alternative treatment modality in managing patients with cerebral arteriovenous malformations (AVMs). The present study aims to highlight the scholarly impact of the top-100 most cited articles on the radiosurgical management of AVMs. **METHODS:** A title-specific search using the keyword "arteriovenous malformation" was conducted in the Scopus database. The outcome of the search was rearranged based on the citations count. Articles were categorized into four entities; clinical, gamma knife radiosurgery, linear accelerator (LINAC) radiosurgery, and proton beam radiosurgery. The exclusion criteria were applied to spinal or non-intracranial AVM, conference papers, non-English articles predominantly discussing the endovascular or microsurgical management. **RESULTS:** The top-100 articles on the radiosurgical management of AVM were published between 1972 and 2016. Approximately one-third of the publications were produced between 1995 and 2000. The average citations per year for all papers were seven. The most-studied entity was pertinent to the clinical application of gamma knife radiosurgery in AVM (68%). The United States was the most active country in studying the radiosurgical application in AVM. The Journal of Neurosurgery published approximately one-third of the most-cited articles in the list. The top-3 most contributing authors, publishing 80% of articles in the list, were Lunsford et al. **CONCLUSION:** The radiosurgical management of AVMs evolved significantly throughout the years. Identifications of the publication trends facilitate the acquisition of evidence-based articles for authors investigating various radiosurgical techniques in the treatment of AVMs.

#### [12] Evaluation of the radiosurgical treatment of cerebral arteriovenous malformations: a retrospective single-center analysis of three decades.

*Journal of neurointerventional surgery.* 2020;12(4):401-406

Hirschmann D, Goebel P, Witte FH, Gatterbauer B, Wang WT, Dodier P, Bavinszki G, Ertl A, Marik W, Mallouhi A, Roetzer T, Dorfer C, Eisner W, Gruber A, Kitz K, Frischer JM

PMID: 31558656 DOI: 10.1136/neurintsurg-2019-015332

**BACKGROUND:** Gamma Knife radiosurgery (GKRS) in the treatment of arteriovenous malformations (AVMs) is still controversially discussed. **OBJECTIVE:** To present long-term follow-up data on patients after Gamma Knife radiosurgery for cerebral AVMs. **METHODS:** Overall, 516 patients received radiosurgery

for cerebral AVMs between 1992 and 2018 at our department, of whom 265 received radiosurgery alone and 207 were treated with a combined endovascular-radiosurgical approach. Moreover, 45 patients were treated with a volume-staged approach. Two eras were analyzed, the pre-modern era between 1992 and 2002 and the modern era thereafter. **RESULTS:** In GKRS-only treated patients, median time to nidus occlusion was 3.8 years. Spetzler-Ponce (SP) class was a significant predictor for time to obliteration in the whole sample. Median time to obliteration for the combined treatment group was 6.5 years. Patients in the pre-modern era had a significantly higher obliteration rate than those treated in the modern era. Overall, the calculated yearly hemorrhage risk in the observation period after first GKRS was 1.3%. Permanent post-radiosurgical complications occurred in 4.9% of cases but did not differ between the treatment groups or treatment eras. The obliteration rate was significantly lower and the hemorrhage rate was higher in volume-staged treated patients than in conventionally treated patients. **CONCLUSION:** GKRS is an effective treatment option for SP class A and B cerebral AVMs. After combined endovascular-radiosurgical treatment, the outcome of selected SP class C AVMs aligns with that of SP class B lesions. Both the combined therapy and radiosurgery alone constitute sound methods for treatment of cerebral AVMs.

**[13] Stereotactic radiosurgery for pediatric brain arteriovenous malformations: long-term outcomes.**

*Journal of neurosurgery. Pediatrics.* 2020;:1-9

Chen CJ, Lee CC, Kano H, Kearns KN, Ding D, Tzeng SW, Atik A, Joshi K, Barnett GH, Huang PP, Kondziolka D, Mathieu D, Iorio-Morin C, Grills IS, Quinn TJ, Siddiqui ZA, Marvin K, Feliciano C, Faramand A, Lunsford LD, Sheehan JP  
PMID: 32032957 DOI: 10.3171/2019.12.PEDS19595

**OBJECTIVE:** Contrary to the better described obliteration- and hemorrhage-related data after stereotactic radiosurgery (SRS) of brain arteriovenous malformations (AVMs) in pediatric patients, estimates of the rarer complications, including cyst and tumor formation, are limited in the literature. The aim of the present study was to assess the long-term outcomes and risks of SRS for AVMs in pediatric patients (age < 18 years). **METHODS:** The authors retrospectively analyzed the International Radiosurgery Research Foundation pediatric AVM database for the years 1987 to 2018. AVM obliteration, post-SRS hemorrhage, cyst formation, and tumor formation were assessed. Cumulative probabilities, adjusted for the competing risk of death, were calculated. **RESULTS:** The study cohort comprised 539 pediatric AVM patients (mean follow-up 85.8 months). AVM obliteration was observed in 64.3% of patients, with cumulative probabilities of 63.6% (95% CI 58.8%-68.0%), 77.1% (95% CI 72.1%-81.3%), and 88.1% (95% CI 82.5%-92.0%) over 5, 10, and 15 years, respectively. Post-SRS hemorrhage was observed in 8.4% of patients, with cumulative probabilities of 4.9% (95% CI 3.1%-7.2%), 9.7% (95% CI 6.4%-13.7%), and 14.5% (95% CI 9.5%-20.5%) over 5, 10, and 15 years, respectively. Cyst formation was observed in 2.1% of patients, with cumulative probabilities of 5.5% (95% CI 2.3%-10.7%) and 6.9% (95% CI 3.1%-12.9%) over 10 and 15 years, respectively. Meningiomas were observed in 2 patients (0.4%) at 10 and 12 years after SRS, with a cumulative probability of 3.1% (95% CI 0.6%-9.7%) over 15 years. **CONCLUSIONS:** AVM obliteration can be expected after SRS in the majority of the pediatric population, with a relatively low risk of hemorrhage during the latency period. Cyst and benign tumor formation after SRS can be observed in 7% and 3% of patients over 15 years, respectively. Longitudinal surveillance for delayed neoplasia is prudent despite its low incidence.

**[14] More II It than Meets the Eye: Outcomes After Single-Fraction Stereotactic Radiosurgery in a Case Series of Low-Grade Arteriovenous Malformations.**

*Operative neurosurgery (Hagerstown, Md.).* 2020;18(2):136-144

Graffeo CS, Link MJ, Stafford SL, Garces YI, Foote RL, Pollock BE  
PMID: 31250901 DOI: 10.1093/ons/18(2)136

**BACKGROUND:** Surgical resection is typically cited as the optimal treatment of patients with Spetzler-Martin Grade I-II arteriovenous malformation (AVM).

**OBJECTIVE:** To report our experience with single-fraction stereotactic radiosurgery (SRS) for Spetzler-Martin Grade I-II AVM. **METHODS:** A prospectively maintained registry was reviewed for patients with nonsyndromic Spetzler-Martin Grade I-II AVM having SRS from 1990 to 2011. Patients with <24 mo of follow-up or prior radiotherapy/SRS were excluded, resulting in a study population of 173 patients. Actuarial analysis was performed using the Kaplan-Meier method, and Cox proportional hazards modeling was performed with excellent outcomes (obliteration without new deficits) as the dependent variable. **RESULTS:** Median post-SRS follow-up was 68 mo (range, 24-275). AVM obliteration was achieved in 132 (76%) after initial SRS. Eleven additional patients achieved obliteration after repeat SRS for an overall obliteration rate of 83%. The rate of obliteration was 60% at 4 yr and 78% at 8 yr. Post-SRS hemorrhage occurred in 7 patients (4%), resulting in 3 minor deficits (2%) and 1 death (<1%). Radiation-induced complications occurred in 5 patients (3%), resulting in minor deficits only. One hundred and thirty-seven patients (79%) had excellent outcomes at last follow-up.

**CONCLUSION:** SRS is a safe and effective treatment for patients with Spetzler-Martin Grade I-II AVM. Selection bias is likely a contributing factor to explain the superior outcomes generally noted in reported series of microsurgery for patients with low grade AVM.

**[15] Curative treatment for low-grade arteriovenous malformations.**

*Journal of neurointerventional surgery.* 2020;12(1):48-54

Wang A, Mandigo GK, Feldstein NA, Sisti MB, Connolly ES, Solomon RA, Lavine SD, Meyers PM

PMID: 31300533 DOI: 10.1136/neurintsurg-2019-015115

**BACKGROUND:** Spetzler-Martin (SM) grade I-II (low-grade) arteriovenous malformations (AVMs) are often considered safe for microsurgery or radiosurgery. The adjunctive use of preoperative embolization to reduce surgical risk in these AVMs remains controversial. **OBJECTIVE:** To assess the safety of combined treatment of grade I-II AVMs with preoperative embolization followed by surgical resection or radiosurgery, and determine the long-term functional outcomes.

**METHODS:** With institutional review board approval, a retrospective analysis was carried out on patients with ruptured and unruptured SM I-II AVMs between 2002 and 2017. Details of the endovascular procedures, including number of arteries supplying the AVM, number of branches embolized, embolic agent(s) used, and complications were studied. Baseline clinical and imaging characteristics were compared. Functional status using the modified Rankin Scale (mRS) before and after endovascular and microsurgical treatments was compared. **RESULTS:** 258 SM I-II AVMs (36% SM I, 64% SM II) were identified in patients with a mean age of 38 +/- 17 years. 48% presented with hemorrhage, 21% with seizure, 16% with headache, 10% with no symptoms, and 5% with clinical deficits. 90 patients (68%) in the unruptured group and 74 patients (59%) in the ruptured group underwent presurgical embolization (p = 0.0013). The mean number of arteries supplying the AVM was 1.44 and 1.41 in the unruptured and ruptured groups, respectively (p = 0.75). The mean number of arteries embolized was 2.51 in the unruptured group and 1.82 in the ruptured group (p = 0.003). n-Butyl cyanoacrylate and Onyx were the two most commonly used embolic agents. Four complications were seen in four patients (4/164 patients embolized): two peri-/postprocedural hemorrhage, one dissection, and one infarct. All patients undergoing surgery had a complete cure on postoperative angiography. Patients were followed up for a mean of 55 months. Good long-term outcomes (mRS score <= 2) were seen in 92.5% of patients with unruptured AVMs and 88.0% of those with ruptured AVMs. Permanent neurological morbidity occurred in 1.2%. **CONCLUSIONS:** Curative treatment of SM I-II AVMs can be performed using endovascular embolization with microsurgical resection or radiosurgery in selected cases, with very low morbidity and high cure rates. Compared with other published series, these outcomes suggest that preoperative embolization is a safe and effective adjunct to definitive surgical treatment. Long-term follow-up showed that patients with low-grade AVMs undergoing surgical resection or radiosurgery have good functional outcomes.

**[16] Re-Evaluation of the Size Limitation in Single-Session Stereotactic Radiosurgery for Brain Arteriovenous Malformations: Detailed Analyses on the Outcomes with Focusing on Radiosurgical Doses.**

*Neurosurgery.* 2019;86(5):685-696

Hasegawa H, Hanakita S, Shin M, Sugiyama T, Kawashima M, Takahashi W, Ishikawa O, Nakatomi H, Saito N

PMID: 31322166 DOI: 10.1093/neuros/nyz280

**BACKGROUND:** Single-session stereotactic radiosurgery (SRS) for large arteriovenous malformations (AVMs)  $\geq 10$  mL remains controversial, which is considered as the current size limitation. **OBJECTIVE:** To reconsider the size limitation of SRS for AVMs by profoundly analyzing dose-volume relationship. **METHODS:** Data on 610 consecutive patients with AVM treated with SRS using regular (18-22 Gy) or low ( $< 18$  Gy) prescription doses were retrospectively analyzed. AVMs were classified into 4 groups: small ( $< 5$  mL), medium ( $\geq 5$  and  $< 10$  mL), medium-large ( $\geq 10$  and  $< 15$  mL), and large ( $\geq 15$  mL). The maximum volumes were 22.5 mL (regular-dose group) and 23.5 mL (low-dose group). **RESULTS:** When treated with regular doses, the cumulative 6-yr obliteration rates for each of the 4 AVM groups were 86%, 80%, 87%, and 79%, respectively; the cumulative 10-yr significant neurological event (SNE) rates were 2.6%, 3.9%, 6.8%, and 5.3%, respectively. Regarding large AVMs, regular-dose SRS resulted in marginally better obliteration rate (6-yr cumulative rate, 79% vs 48%,  $P = .111$ ) and significantly lower SNE (5-yr cumulative rate, 5% vs 31%,  $P = .038$ ) and post-SRS hemorrhage rate (8-yr cumulative rate, 0% vs 54%,  $P = .002$ ) compared to low-dose SRS. Multivariate analyses revealed that regular-dose SRS significantly contributed to increase in the obliteration rate and decrease in SNEs and hemorrhage. **CONCLUSION:** The outcomes for large AVMs were generally favorable when treated with ablative doses. Single-session SRS could be acceptable for AVMs up to approximately 20 mL if treated with ablative doses.

**[17] Dose response and architecture in volume staged radiosurgery for large arteriovenous malformations: A multi-institutional study.**

*Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology.* 2019;144:180-188

Seymour ZA, Chan JW, Sneed PK, Kano H, Lehocky CA, Jacobs RC, Ye H, Chytka T, Liscak R, Lee CC, Yang HC, Ding D, Sheehan J, Feliciano CE, Rodriguez-Mercado R, Chiang VL, Hess JA, Sommaruga S, McShane B, Lee J, Vasas LT, Kaufmann AM, Grills I, McDermott MW

PMID: 31835173 DOI: 10.1016/j.radonc.2019.09.019

**BACKGROUND:** Optimal treatment paradigm for large arteriovenous malformations (AVMs) is controversial. Volume-staged stereotactic radiosurgery (VS-SRS) provides an effective option for these high-risk lesions, but optimizing treatment for these recalcitrant and rare lesions has proven difficult. **METHODS:** This is a multi-centered retrospective review of patients treated with a planned prospective volume staging approach to stereotactically treat the entire nidus of an AVM with volume stages separated by intervals of 3-6 months. A total of 9 radiosurgical centers treated 257 patients with VS-SRS between 1991 and 2016. We evaluated near complete response (nCR), obliteration, cure, and overall survival. **RESULTS:** With a median age of 33 years old at the time of first SRS volume stage, patients received 2-4 total volume stages and a median follow up of 5.7 years after VS-SRS. The median total AVM nidus volume was 23.25cc (range: 7.7-94.4cc) with a median margin dose per stage of 17Gy (range: 12-20Gy). Total AVM volume, margin dose per stage, compact nidus, lack of prior embolization, and lack of thalamic location involvement were all associated with improved outcomes. Dose  $\geq 17.5$ Gy was strongly associated with improved rates of nCR, obliteration, and cure. With dose  $\geq 17.5$ Gy, 5- and 10-year cure rates were 33.7% and 76.8% in evaluable patients compared to 23.7% and 34.7% of patients with 17Gy and 6.4% and 20.6% with  $< 17$ Gy per volume-stage ( $p = 0.004$ ). Obliteration rates in diffuse nidus architecture with  $< 17$ Gy were particularly poor with none achieving obliteration compared to 32.3% with doses  $\geq 17$ Gy at 5 years ( $p = 0.007$ ). Comparatively, lesions with a compact nidus architecture exhibited obliteration rates at 5 years were 10.7% vs 9.3% vs 26.6% for dose  $> 17$ Gy vs 17Gy vs  $\geq 17.5$ Gy.

**CONCLUSION:** VS-SRS is an option for upfront treatment of large AVMs. Higher dose was associated with improved rates of nCR, obliteration, and cure suggesting that larger volumetric responses may facilitate salvage therapy and optimize the chance for cure.

**[18] Short Term Effectiveness of Gamma Knife Radiosurgery in the Management of Brain Arteriovenous Malformation.**

*Open access Macedonian journal of medical sciences.* 2019;7(19):3221-3224

Arkawazi BMF, Faraj MK, Al-Attar Z, Hussien HAA

PMID: 31949520 DOI: 10.3889/oamjms.2019.802

**AIM:** To evaluate the short-term effectiveness of Gamma knife radiosurgery as a modality of treatment of brain arteriovenous malformation. **METHODS:** Sixty-three patients with arteriovenous brain malformations underwent Gamma knife radiosurgery included in this prospective study between April 2017 and September 2018 with clinical and radiological with MRI follow up was done at three months and six months post-Gamma knife radiosurgery. By the end of the 12th-month post-Gamma knife radiosurgery, the patients were re-evaluated using digital subtraction angiography co-registered with M.R.I. During the 12 months follow up, CT scan or MRI was done at any time if any one of the patients' condition deteriorated or developed signs and symptoms of complications. The mean volume of the arteriovenous malformations treated was 26.0  $\pm$  5 cm(3) (range 12.5-39.5 cm(3)) in The Neurosciences Hospital, Baghdad/Iraq. **RESULTS:** By the end of the 12th month of follow up, the overall obliteration of the arteriovenous malformations was seen in six patients only (9.5%), while shrinkage was noticed in 57 patients (90.5%). Improvement or clinical stability was found in 24 out of 39 patients (61.5%) presented with epilepsy as a chief complaint before Gamma knife radiosurgery and 21 out of 24 patients (87.0%) complained of a headache before Gamma knife radiosurgery. Post-Gamma knife radiosurgery bleeding was found in only three patients (5.0%). **CONCLUSION:** Even with the short term follow up, Gamma knife radiosurgery has an excellent clinical outcome in most patients with arteriovenous brain malformations. The clinical symptoms like headache and seizure were either diminished or controlled with the same medical treatment dose before Gamma knife radiosurgery. Long term clinical and radiological follow up is recommended.

**[19] Stereotactic Radiosurgery for Unruptured Versus Ruptured Pediatric Brain Arteriovenous Malformations.**

*Stroke.* 2019;50(10):2745-2751

Chen CJ, Lee CC, Ding D, Tzeng SW, Kearns KN, Kano H, Atik A, Ironside N, Joshi K, Huang PP, Kondziolka D, Mathieu D, Iorio-Morin C, Grills IS, Quinn TJ, Siddiqui Z, Marvin K, Feliciano C, Faramand A, Starke RM, Barnett G, Lunsford LD, Sheehan JP

PMID: 31387513 DOI: 10.1161/STROKEAHA.119.026211

**BACKGROUND AND PURPOSE:** The effects of prior hemorrhage on stereotactic radiosurgery (SRS) outcomes for pediatric arteriovenous malformations (AVMs) are not well defined. The aim of this multicenter, retrospective cohort study is to compare the SRS outcomes for unruptured versus ruptured pediatric AVMs. **METHODS:** The International Radiosurgery Research Foundation pediatric AVM database from 1987 to 2018 was reviewed retrospectively. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes. Associations between prior hemorrhage and outcomes were adjusted for baseline differences, inverse probability weights, and competing risks. **RESULTS:** The study cohort comprised 153 unruptured and 386 ruptured AVMs. Favorable outcome was achieved in 48.4% and 60.4% of unruptured and ruptured AVMs, respectively (adjusted odds ratio, 1.353;  $P = 0.190$ ). Cumulative AVM obliteration probabilities were 51.2%, 59.4%, 64.2%, and 70.0% for unruptured and 61.0%, 69.3%, 74.0%, and 79.3% for ruptured AVMs at 4, 6, 8, and 10 years, respectively (subhazard ratio, 1.311;  $P = 0.020$ ). Cumulative post-SRS hemorrhage probabilities were 4.5%, 5.6%, 5.6%, and 9.8% for unruptured and 4.7%, 6.1%, 6.1%, and 10.6% for ruptured AVMs at 4, 6, 8, and 10 years, respectively (subhazard ratio, 1.086;  $P = 0.825$ ). Probabilities of AVM obliteration

(adjusted subhazard ratio, 0.968;  $P=0.850$ ) and post-SRS hemorrhage (adjusted subhazard ratio, 1.663;  $P=0.251$ ) were comparable between the 2 cohorts after inverse probability weight adjustments. Symptomatic (15.8% versus 8.1%; adjusted odds ratio, 0.400;  $P=0.008$ ) and permanent (9.2% versus 5.0%; adjusted odds ratio, 0.441;  $P=0.045$ ) radiation-induced change were more common in unruptured AVMs. **CONCLUSIONS:** The overall outcomes after SRS for unruptured versus ruptured pediatric AVMs are comparable. However, symptomatic and permanent radiation-induced change occur more frequently in pediatric patients with unruptured AVMs.

#### [20] Gamma Knife Radiosurgery for ARUBA-Eligible Patients with Unruptured Brain Arteriovenous Malformations.

*Journal of Korean medical science.* 2019;34(36):e232

Kim BS, Yeon JY, Kim JS, Hong SC, Shin HJ, Lee JI

PMID: 31538418 DOI: 10.3346/jkms.2019.34.e232

**BACKGROUND:** A randomized trial of unruptured brain arteriovenous malformations (ARUBA) reported superior outcomes in conservative management compared to interventional treatment. There were numerous limitations to the study. This study aimed to investigate the efficacy of gamma knife radiosurgery (GKS) for patients with brain arteriovenous malformations (AVMs) by comparing its outcomes to those of the ARUBA study. **METHODS:** We retrospectively reviewed ARUBA-eligible patients treated with GKS from June 2002 to September 2017 and compared against those in the ARUBA study. AVM obliteration and hemorrhage rates, and clinical outcomes following GKS were also evaluated. **RESULTS:** The ARUBA-eligible cohort comprised 264 patients. The Spetzler-Martin grade was Grade I to II in 52.7% and III to IV in 47.3% of the patients. The mean AVM nidus volume, marginal dose, and follow-up period were 4.8 cm(3), 20.8 Gy, and 55.5 months, respectively. AVM obliteration was achieved in 62.1%. The annual hemorrhage rate after GKS was 3.4%. A stroke or death occurred in 14.0%. The overall stroke or death rate of the ARUBA-eligible cohort was significantly lower than that of the interventional arm of the ARUBA study ( $P < 0.001$ ) and did not significantly differ from that of the medical arm in the ARUBA study ( $P = 0.601$ ). **CONCLUSION:** GKS was shown to achieve a favorable outcome with low procedure-related morbidity in majority of the ARUBA-eligible patients. The outcome after GKS in our patients was not inferior to that of medical care alone in the ARUBA study. It is suggested that GKS is rather superior to medical care considering the short follow-up duration of the ARUBA study.

#### [21] The impact of preradiosurgery embolization on intracranial arteriovenous malformations: a matched cohort analysis based on de novo lesion volume.

*Journal of neurosurgery.* 2019;:1-12

Hung YC, Mohammed N, Eluvathingal Muttikkal TJ, Kearns KN, Li CE, Narayan A, Schlesinger D, Xu Z, Sheehan JP

PMID: 31470409 DOI: 10.3171/2019.5.JNS19722

**OBJECTIVE:** The benefits and risks of pre-stereotactic radiosurgery (SRS) embolization have been reported in different studies. The goal of this study was to compare the long-term outcome of arteriovenous malformations (AVMs) treated with and without pre-SRS embolization. **METHODS:** A database including 1159 patients with AVMs who underwent SRS was reviewed. The embolized group was selected by including AVMs with pre-SRS embolization, maximal diameter  $> 30$  mm, and estimated volume  $> 8$  ml. The nonembolized group was defined as AVMs treated by SRS alone with matched de novo nidus volume. Outcomes including incidences of favorable clinical outcome (obliteration without hemorrhage, cyst formation, worsening, or new seizures), obliteration, adverse effects, and angioarchitectural complexity were evaluated. **RESULTS:** The study cohort comprised 17 patients in the embolized group (median AVM volume 17.0 ml) and 35 patients in the nonembolized group (median AVM volume 13.1 ml). The rates of obliteration (embolized cohort: 33%, 44%, and 56%; nonembolized cohort: 32%, 47%, and 47% at 4, 6, and 10 years, respectively) and favorable outcome were comparable between the 2 groups. However, the embolized group had a significantly higher incidence of repeat SRS (41% vs 23%,  $p = 0.012$ ) and

total procedures (median number of procedures 4 vs 1,  $p < 0.001$ ), even with a significantly higher margin dose delivered at the first SRS (23 Gy vs 17 Gy,  $p < 0.001$ ). The median angioarchitectural complexity score was reduced from 7 to 5 after embolization. Collateral flow and neovascularization were more frequently observed in the embolized nonobliterated AVMs. **CONCLUSIONS:** Both embolization plus SRS and SRS alone were effective therapies for moderately large (8-39 ml) AVMs. Even with a significantly higher prescription dose at the time of initial SRS, the embolized group still required more procedures to reach final obliteration. The presence of collateral flow and neovascularization could be risk factors for a failure to obliterate following treatment.

#### [22] Seizure Presentation in Patients with Brain Arteriovenous Malformations Treated with Stereotactic Radiosurgery: A Multicenter Study.

*World neurosurgery.* 2019;126:e634-e640

Chen CJ, Shabo LM, Ding D, Ironside N, Kano H, Mathieu D, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Grills IS, Barnett G, Lunsford LD, Sheehan JP  
PMID: 30831294 DOI: 10.1016/j.wneu.2019.02.104

**BACKGROUND:** Seizures are the second most common clinical presentation in patients with brain arteriovenous malformations (AVMs) and the most common presentation of unruptured AVMs. The aim of the present multicenter, retrospective cohort study was to identify the predictors of seizure presentation in patients with AVM who had undergone stereotactic radiosurgery (SRS). **METHODS:** We performed a retrospective review of patients with AVM who had been treated with SRS at 8 participating International Radiosurgery Research Foundation sites. The patient and AVM characteristics were compared between those with and without seizure presentation in univariable and multivariable models. A subgroup analysis of patients with cortical AVMs was performed. **RESULTS:** The study cohort included 2333 patients with AVM, including 419 (18%) with and 1914 (82%) without a seizure presentation. Previous AVM resection (odds ratio [OR], 7.65;  $P = 0.001$ ), a lack of previous AVM hemorrhage (OR, 0.004;  $P < 0.001$ ), a cortical AVM location (OR, 1559.42;  $P < 0.001$ ), a lower Spetzler-Martin grade (OR, 0.51;  $P = 0.007$ ), and a higher Virginia radiosurgery AVM score (OR, 1.46;  $P = 0.008$ ) were independent predictors of seizure presentation. The rate of seizure presentation in patients with cortical AVMs was 27%. Previous AVM resection (OR, 8.36;  $P < 0.001$ ), a lack of previous AVM hemorrhage (OR, 0.004;  $P < 0.001$ ), and temporal AVM location (OR, 4.15;  $P < 0.001$ ) were independent predictors of seizure presentation for cortical AVMs. **CONCLUSION:** We identified multiple factors associated with seizure presentation in patients with AVM to undergo SRS. Previous AVM resection, a cortical AVM location, and a lack of previous AVM hemorrhage were the strongest predictors of pre-SRS seizures. The Spetzler-Martin grade and Virginia radiosurgery AVM score might have a role in seizure risk stratification. For cortical AVMs, a temporal lobe location was predictive of seizure presentation.

#### [23] Long-Term Outcomes for Pediatric Patients with Brain Arteriovenous Malformations Treated with Gamma Knife Radiosurgery, Part 1: Analysis of Nidus Obliteration Rates and Related Factors.

*World neurosurgery.* 2019;126:e1518-e1525

Hasegawa T, Kato T, Naito T, Tanei T, Torii J, Ishii K, Tsukamoto E

PMID: 30922904 DOI: 10.1016/j.wneu.2019.03.176

**OBJECTIVE:** Little is known about long-term outcomes for pediatric brain arteriovenous malformations (AVMs) treated with Gamma Knife radiosurgery (GKRS). This study investigated annual hemorrhage rates and nidus obliteration rates, and the factors affecting them, in pediatric AVMs treated with GKRS. **METHODS:** We examined 189 pediatric AVM patients (age  $\leq 15$  years) who underwent GKRS and had at least 12 months of follow-up. The Spetzler-Martin (S-M) grade was I in 29 patients (15%), II in 57 (30%), III in 82 (43%), IV in 16 (9%), and V in 5 (3%). The median treatment volume was 2.2 cm(3), and the median marginal dose was 20 Gy. **RESULTS:** The mean follow-up period was 136 months. During a cumulative latency period to nidus obliteration of 813 years, 23 hemorrhages occurred, resulting in an annual post-GKRS hemorrhage rate of

2.8%. The cumulative hemorrhage rates after GKRS were 3.3%, 8.5%, and 11.9% at 3, 5, and 10 years, respectively. Higher S-M grade was significantly associated with intracranial hemorrhages during the latency period ( $P < 0.001$ ). The actuarial nidus obliteration rates with repeated GKRS were 64% and 81% at 5 and 10 years, respectively. Absence of pre-GKRS embolization ( $P = 0.023$ ) and higher marginal dose ( $P = 0.029$ ) were significant factors predicting nidus obliteration.

**CONCLUSIONS:** GKRS is a reasonable treatment option in pediatric AVMs to prevent future hemorrhages. Because higher S-M grade AVMs are more likely to hemorrhage during the latency period, a combined therapy with endovascular embolization should be considered to prevent AVM rupture.

[24] Long-Term Outcomes for Pediatric Patients with Brain Arteriovenous Malformations Treated with Gamma Knife Radiosurgery, Part 2: The Incidence of Cyst Formation, Encapsulated Hematoma, and Radiation-Induced Tumor. *World neurosurgery*. 2019;126:e1526-e1536

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

PMID: 30922905 DOI: 10.1016/j.wneu.2019.03.177

**OBJECTIVE:** Long-term data about the incidence of late adverse radiation effects (AREs) in pediatric brain arteriovenous malformations (AVMs) treated with Gamma Knife radiosurgery (GKRS) are lacking. This study addresses the incidence of late AREs, including cyst formation (CF), chronic encapsulated hematoma (CEH), and radiation-induced tumor, in pediatric patients with AVM treated with GKRS. **METHODS:** This is a single-institutional study involving pediatric patients with AVM who underwent GKRS between 1991 and 2014. Among 201 pediatric patients with AVM (age  $\leq 15$  years), 189 who had at least 12 months of follow-up were assessed in this study. The median treatment volume was 2.2 cm<sup>3</sup>, and the median marginal dose was 20 Gy. **RESULTS:** The mean follow-up period was 136 months. During the follow-up period, symptomatic radiation-induced perilesional edema was found in 5 patients (3%), CFs in 7 patients (4%), CEHs in 7 patients (4%), and radiation-induced tumors in 2 patients (1%). The cumulative incidences of late AREs including CF, CEH, and radiation-induced tumor were 1.2% at 5 years, 5.2% at 8 years, 6.1% at 10 years, 7.2% at 15 years, and 17.0% at 20 years. In the multivariate analysis, treatment volume alone was a significant factor for late AREs ( $P < 0.001$ ; hazard ratio, 1.111). **CONCLUSIONS:** GKRS is a reasonable treatment option for pediatric AVMs to prevent future intracranial hemorrhages, particularly in the eloquent regions. However, considerable attention should be paid to late AREs such as CFs, CEHs, and radiation-induced tumors because of longer life expectancy in pediatric patients.

[25] Correlation of Appearance of MRI Perinidal T2 Hyperintensity Signal and Eventual Nidus Obliteration Following Photon Radiosurgery of Brain AVMs: Combined Results of LINAC and Gamma Knife Centers.

*Journal of neurological surgery. Part A, Central European neurosurgery*. 2019;80(3):187-197

Abdelaziz O, Shereen A, Inoue T, Hirai H, Shima A

PMID: 30895568 DOI: 10.1055/s-0039-1678710

**BACKGROUND:** A wide variety of radiologic changes occur within and adjacent to the nidus of arteriovenous malformations (AVMs) after stereotactic radiosurgery (SRS). Our objective was to study the magnetic resonance imaging (MRI)-defined changes following photon radiosurgery of AVMs and specifically to correlate the appearance of a perinidal T2 hyperintensity signal with the eventual angiographic obliteration of an AVM nidus in response to SRS treatment. **MATERIAL AND METHODS:** This retrospective study was conducted on 62 patients with brain AVMs who received photon SRS treatments between 2004 and 2017, using either a technique based on a linear accelerator at the Alexandria LINAC Radiosurgery Center in Egypt (21 patients/AVMs) or a technique based on a gamma unit at the Koto Memorial Gamma Knife Center in Japan (41 patients/AVMs). All patients included in the study had serial clinical and radiologic follow-ups for  $\geq 2$  years after SRS treatments. **RESULTS:** In the combined study series of 62 patients/AVMs treated with photon SRS, the follow-up MRIs revealed that

50 AVMs (80.6%) showed nonvisualized nidus and 12 AVMs (19.4%) showed decreased nidus size. Radiation-induced changes, defined as appearance of perinidal T2 hyperintensities in post-SRS MRIs, occurred in 34 patients (54.8%). Of the 35 patients with available follow-up angiographic studies, 30 AVMs (85.7%) demonstrated complete nidus obliteration at a mean of 36 months (range: 8-66 months) after SRS. Of the 30 AVMs with both MRI evidence of a nonvisualized nidus and angiographic verification of complete nidus obliteration, 20 AVMs (66.7%) were associated with prior MRI evidence of the appearance of a perinidal T2 hyperintensity signal at an average of 12 months (range: 6-45 months) after SRS. Of the five AVMs with both MRI evidence of decreased nidus size and angiographic verification of partial nidus obliteration, four AVMs (80%) showed perinidal T2 hyperintensity signal on post-SRS follow-up MRIs. Lower Spetzler-Martin grade ( $p = 0.013$ ), smaller AVM volume ( $p = 0.017$ ), and appearance of post-SRS perinidal T2 hyperintensity signal ( $p = 0.007$ ) were the statistically significant independent predictors of AVM obliteration. The appearance of perinidal T2 hyperintensity signal in the post-SRS MRIs had a sensitivity of 66.7%, a specificity of 20%, and an overall accuracy of 60% in predicting the eventual obliteration of the AVM nidus. **CONCLUSIONS:** The present study may help improve our current understanding of the mechanisms behind the radiation-induced tissue changes following AVM SRS. Because the SRS-induced hemodynamic changes within the AVM nidus initiate the cascade of the subsequent formation of perinidal vasogenic brain edema, the appearance of perinidal high T2 signal in the follow-up MRIs after SRS would be a valuable indicator of the AVM response to SRS. The development of perinidal hyperintensity was the strongest predictive factor of AVM obliteration ( $p = 0.007$ ), with relatively high sensitivity (66.7%) and accuracy (60%) and fairly low specificity (20%), as a prognostic sign of eventual complete angiographic obliteration of the AVM nidus following SRS.

[26] Morphologic Change of Flow-Related Aneurysms in Brain Arteriovenous Malformations after Stereotactic Radiosurgery.

*AJNR. American journal of neuroradiology*. 2019;40(4):675-680

Tsuei YS, Luo CB, Fay LY, Yang HC, Guo WY, Wu HM, Chung WY, Teng MMH  
PMID: 30948381 DOI: 10.3174/ajnr.A6018

**BACKGROUND AND PURPOSE:** The natural history of flow-related aneurysms after obliteration of brain arteriovenous malformations is poorly understood. The purpose of this study was to evaluate the angioarchitecture and morphologic change in flow-related aneurysms after gamma knife surgery of brain arteriovenous malformations. **MATERIALS AND METHODS:** During a 12-year period, 823 patients with brain arteriovenous malformations underwent gamma knife surgery at our institution with complete peritherapeutic angiographic evaluation. From this population, a series of 72 patients (8.8%) with 111 flow-related aneurysms were enrolled (1.5 aneurysms per patient). There were 43 men and 29 women; ages ranged from 18 to 72 years (mean, 43 years). The morphologic change of flow-related aneurysms was longitudinally evaluated before and after obliteration of brain arteriovenous malformations. After gamma knife surgery, angiographic follow-up varied from 26 to 130 months (mean, 58 months). **RESULTS:** All flow-related aneurysms were small (mean, 4.1 mm; range, 2-9 mm). There were 72 proximal flow-related aneurysms (mean size, 4.3 mm) and 39 distal flow-related aneurysms (mean size, 3.7 mm). Spontaneous thrombosis occurred more frequently in distal flow-related aneurysms than in proximal flow-related aneurysms ( $P < .001$ ). Smaller flow-related aneurysms ( $< 5$  mm) tended to spontaneously occlude after obliteration of brain arteriovenous malformations ( $P = .036$ ). Two patients had ruptures of proximal flow-related aneurysms at 27- and 54-month follow-ups, respectively. **CONCLUSIONS:** Spontaneous thrombosis occurred more frequently in distal flow-related aneurysms due to occlusion or normalization of distal feeders. Smaller flow-related aneurysms also tended to spontaneously thrombose after obliteration of brain arteriovenous malformations. The rate of flow-related aneurysm rupture in our series was similar to that of natural intradural aneurysms.



[27] Microsurgery Versus Stereotactic Radiosurgery for Brain Arteriovenous Malformations: A Matched Cohort Study.

*Neurosurgery.* 2019;84(3):696-708

Chen CJ, Ding D, Wang TR, Buell TJ, Ilyas A, Ironside N, Lee CC, Kalani MY, Park MS, Liu KC, Sheehan JP

PMID: 29762746 DOI: 10.1093/neuros/nyy174

**BACKGROUND:** Microsurgery (MS) and stereotactic radiosurgery (SRS) remain the preferred interventions for the curative treatment of brain arteriovenous malformations (AVM), but their relative efficacy remains incompletely defined.

**OBJECTIVE:** To compare the outcomes of MS to SRS for AVMs through a retrospective, matched cohort study. **METHODS:** We evaluated institutional databases of AVM patients who underwent MS and SRS. MS-treated patients were matched, in a 1:1 ratio based on patient and AVM characteristics, to SRS-treated patients. Statistical analyses were performed to compare outcomes data between the 2 cohorts. The primary outcome was defined as AVM obliteration without a new permanent neurological deficit. **RESULTS:** The matched MS and SRS cohorts were each comprised of 59 patients. Both radiological (85 vs 11 mo;  $P < .001$ ) and clinical (92 vs 12 mo;  $P < .001$ ) follow-up were significantly longer for the SRS cohort. The primary outcome was achieved in 69% of each cohort. The MS cohort had a significantly higher obliteration rate (98% vs 72%;  $P = .001$ ), but also had a significantly higher rate of new permanent deficit (31% vs 10%;  $P = .011$ ). The posttreatment hemorrhage rate was significantly higher for the SRS cohort (10% for SRS vs 0% for MS;  $P = .027$ ). In subgroup analyses of ruptured and unruptured AVMs, no significant differences between the primary outcomes were observed.

**CONCLUSION:** For patients with comparable AVMs, MS and SRS afford similar rates of deficit-free obliteration. Nidal obliteration is more frequently achieved with MS, but this intervention also incurs a greater risk of new permanent neurological deficit.

[28] Radiosurgical treatment of arteriovenous malformations in a retrospective study group of 33 children: the importance of radiobiological scores.

*Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery.* 2019;35(2):301-308

Capitaino JF, Panni P, Gallotti AL, Gigliotti CR, Scmazzone F, Acerno S, Del Vecchio A, Mortini P

PMID: 30474715 DOI: 10.1007/s00381-018-4008-2

**PURPOSE:** Arteriovenous malformations' (AVMs) obliteration depends on several factors; among the many factors that must be considered to obtain a high rate of obliteration and a low rate of complications, Flickinger-Pollock Score (FPS) seems to have an important role but still have to be validated in the pediatric population while Paddick-Conformity Index (PCI) still has no demonstration of its utility on the outcome and is considered only as a treatment quality marker. **METHODS:** We retrospectively analyzed 33 consecutive children (2-18 years) with an AVM, treated with stereotactic radiosurgery Gamma Knife (SRS-GK) from 2001 to 2014 in our institution. We assess angiographic (DSA) Obliteration Rate (OR) as well FPS and PCI to draw conclusions. **RESULTS:** DSA-OR was 60.6% with a rate of hemorrhage of 0%. median target volume (TV) was 3.60 cc (mean 4.32 +/- 3.63; range 0.15-14.2), median PD was 22 Gy (mean 21.4 +/- 2.6; range 16.5-25). Median percentage of coverage was 98% (mean 97 +/- 3; range 84-100). The median modified FPS was 0.78 (mean 0.89 +/- 0.52; range 0.21-2.1) and highly correlate with OR ( $p = 0.01$ ). The median PCI was 0.65 (mean 0.65 +/- 0.14; range 0.34-0.95) A PCI lower than 0.57 highly correlates with final OR ( $p = 0.02$ ). **CONCLUSION:** SRS-GK was safe and gradually effective in children. A prescription dose-like that used in adult population (i.e. > 18 and between 20 and 25 Gy) is essential to achieve obliteration. A PD of 23 Gy and 22 Gy did impact OR, respectively ( $p = 0.02$ ) and ( $p = 0.05$ ). FPS and PCI are valuable scores that seem to correlate with the OR also in the pediatric population although further prospective studies are needed to confirm these observations.

## 2018

[29] Seizure control after radiosurgery for cerebral arteriovenous malformations: a 25-year experience.

*Journal of neurosurgery.* 2018;131(6):1763-1772

Niranjan A, Kashkoush A, Kano H, Monaco EA, Flickinger JC, Lunsford LD  
PMID: 30554186 DOI: 10.3171/2018.7.JNS18304

**OBJECTIVE:** Seizures are the second-most common presenting symptom in patients with lobar arteriovenous malformations (AVMs). However, few studies have assessed the long-term effect of stereotactic radiosurgery (SRS) on seizure control. The authors of this study assess the outcome of SRS for these patients to identify prognostic factors associated with seizure control. **METHODS:** Patients with AVM who presented with a history of seizure and underwent SRS at the authors' institution between 1987 and 2012 were retrospectively assessed. The total cohort included 155 patients with a mean follow-up of 86 months (range 6-295 months). Primary outcomes assessed were seizure frequency, antiepileptic drug regimen, and seizure freedom for 6 months prior to last follow-up. **RESULTS:** Seizure-free status was achieved in 108 patients (70%), with an additional 23 patients (15%) reporting improved seizure frequency as compared to their pre-SRS status. The median time to seizure-free status was estimated to be 12 months (95% CI 0-27 months) as evaluated via Kaplan-Meier survival analysis. The mean seizure frequency prior to SRS was 14.2 (95% CI 5.4-23.1) episodes per year. Although not all patients tried, the proportion of patients successfully weaned off all antiepileptic drugs was 18% (28/155 patients). On multivariate logistic regression, focal impaired awareness seizure type (also known as complex partial seizures) and superficial venous drainage were significantly associated with a decreased odds ratio for seizure-free status at last follow-up (OR 0.37 [95% CI 0.15-0.92] for focal impaired awareness seizures; OR 0.36 [95% CI 0.16-0.81] for superficial venous drainage). The effects of superficial venous drainage on seizure outcome were nonsignificant when excluding patients with < 2 years of follow-up. AVM obliteration did not correlate with long-term seizure freedom ( $p = 0.202$ , chi-square test). **CONCLUSIONS:** This study suggests that SRS improves long-term seizure control and increases the likelihood of being medication free, independently of AVM obliteration. Patients with focal impaired awareness seizures were less likely to obtain long-term seizure relief.

[30] Effect of Advanced Age on Stereotactic Radiosurgery Outcomes for Brain Arteriovenous Malformations: A Multicenter Matched Cohort Study.

*World neurosurgery.* 2018;119:e429-e440

Chen CJ, Ding D, Kano H, Mathieu D, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Sheehan DE, Grills IS, Barnett G, Lunsford LD, Sheehan JP

PMID: 30071340 DOI: 10.1016/j.wneu.2018.07.178

**BACKGROUND:** The effect of age on adult brain arteriovenous malformation (AVM) outcomes after stereotactic radiosurgery (SRS) remains unclear. The aim of this study is to compare AVM outcomes between elderly (age  $\geq 60$  years) and nonelderly adult patients. **METHODS:** We retrospectively reviewed pooled data comprising patients who underwent SRS for AVMs between 1987 and 2014 at 8 centers participating in the International Gamma Knife Research Foundation. Adult (age  $\geq 18$  years) patients with  $\geq 12$  months follow-up were dichotomized into elderly and nonelderly cohorts, and matched in a 1:1 ratio. Favorable outcome was AVM obliteration without permanent symptomatic radiation-induced changes (RIC) or post-SRS hemorrhage. **RESULTS:** The study cohort consisted of 1845 patients (188 elderly vs. 1657 nonelderly) who met the inclusion criteria, and subsequent matching resulted in 181 patients in each cohort. In the matched cohorts, rates of obliteration (54.7% vs. 64.6%;  $P = 0.054$ ) favorable outcome (51.4% vs. 61.3%;  $P = 0.056$ ) were no different between the elderly and nonelderly cohorts. The rates of post-SRS hemorrhage (9.9% vs. 5.5%;  $P = 0.115$ ), RIC (26.5% vs. 30.9%;  $P = 0.353$ ), symptomatic RIC (9.4% vs. 9.4%;  $P = 1.000$ ), and permanent symptomatic RIC (3.3% vs. 2.2%;  $P = 0.750$ ) were also not significantly different between the elderly and nonelderly cohorts. Elderly patients

with AVM did have a significantly higher rate of all-cause mortality (27.7% vs. 5.5%;  $P < 0.001$ ). **CONCLUSIONS:** Advanced age does not seem to significantly affect obliteration or complication rates after SRS for AVMs. Although the decision to recommend intervention for AVMs in the elderly population is multifactorial, SRS may be a viable modality when treatment is deemed appropriate.

**[31] Delayed cyst formation after stereotactic radiosurgery for brain arteriovenous malformations.**

*Journal of neurosurgery.* 2018;129(4):937-946

Pomeraniec IJ, Ding D, Starke RM, Liu KC, Mrachek EK, Lopes MB, Sheehan JP  
PMID: 29192860 DOI: 10.3171/2017.6.JNS17559

**OBJECTIVE:** Stereotactic radiosurgery (SRS) is a commonly employed treatment modality for brain arteriovenous malformations (AVMs). However, due to the low frequency of delayed cyst formation after AVM SRS, as well as the prolonged time interval between treatment and its occurrence, the characteristics of post-SRS cyst formation are not well defined. Therefore, the aims of this retrospective cohort study are to determine the rate of cyst formation after SRS for AVMs, identify predictive factors, and evaluate the clinical sequelae of post-SRS cysts.

**METHODS:** The authors analyzed an SRS database for AVM patients who underwent SRS at the University of Virginia and identified those who developed post-SRS cysts. Statistical analyses were performed to determine predictors of post-SRS cyst formation and the effect of cyst formation on new or worsening seizures after SRS. **RESULTS:** The study cohort comprised 1159 AVM patients treated with SRS; cyst formation occurred in 17 patients (post-SRS cyst rate of 1.5%). Compared with patients who did not develop post-SRS cysts, those with cyst formation were treated with a greater number of radiosurgical isocenters (mean 3.8 vs 2.8,  $p = 0.047$ ), had a longer follow-up (mean 132 vs 71 months,  $p < 0.001$ ), were more likely to develop radiological radiation-induced changes (RIC) (64.7% vs 36.1%,  $p = 0.021$ ), and had a longer duration of RIC (57 vs 21 months,  $p < 0.001$ ). A higher number of isocenters ( $p = 0.014$ ), radiological RIC ( $p = 0.002$ ), and longer follow-up ( $p = 0.034$ ) were found to be independent predictors of post-SRS cyst formation in the multivariate analysis. There was a trend toward a significant association between cyst formation and new or worsening seizures in univariate analysis ( $p = 0.054$ ). **CONCLUSIONS:** Patients with greater nidus complexity appear to be more prone to post-SRS cyst formation. The findings of this study emphasize the importance of long-term follow-up for patients who have undergone AVM SRS, even after nidus obliteration is achieved. Post-SRS cysts may be epileptogenic, although seizure outcomes after AVM SRS are multifactorial.

**[32] Treatment Outcomes of A Randomized Trial of Unruptured Brain Arteriovenous Malformation-Eligible Unruptured Brain Arteriovenous Malformation Patients.**

*Neurosurgery.* 2018;83(3):548-555

Lang M, Moore NZ, Rasmussen PA, Bain MD  
PMID: 29040773 DOI: 10.1093/neuros/nyx506

**BACKGROUND:** The guideline for treating unruptured brain arteriovenous malformations (ubAVMs) remains controversial. A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA) reported lower risk of stroke or death with conservative management compared to interventional treatment. There were numerous limitations to the study, including short follow-up period and disproportionate number of patients treated with surgery and embolization.

**OBJECTIVE:** To evaluate whether treatment of ARUBA-eligible patients have acceptable outcomes at our institution. **METHODS:** Retrospective analysis was performed on 673 patients with brain AVMs treated at our institution between 2001 and 2014. One hundred five patients were ARUBA eligible and included in the study. Patients were divided into the microsurgery or Gamma Knife Radiosurgery (GKS; Elekta, Stockholm, Sweden) arm depending on their final treatment. Mean follow-up period was 43 mo (range 4-136 mo). Primary outcome was stroke or death. **RESULTS:** A total of 8 (7.6%) patients had a stroke or died. The overall risk of stroke or death was 11.4% (5 of 44 patients) for the microsurgery arm and 4.9% (3 of 61 patients) for the GKS arm. The annual rates of stroke or

death were 2.1%, 4.0%, and 1.2% for the entire patient cohort, microsurgery arm, and GKS arm, respectively. AVM obliteration rates at the end of the follow-up period were 95.5% and 47.5% for the microsurgery and GKS arms, respectively. **CONCLUSION:** We report a lower overall risk of stroke or death in our ARUBA-eligible patients following treatment than ARUBA. Our results suggest that microsurgery and GKS may be appropriate treatments for patients with ubAVM.

**[33] Multimodal management of arteriovenous malformations of the basal ganglia and thalamus: factors affecting obliteration and outcome.**

*Journal of neurosurgery.* 2018;131(2):410-419

Madhugiri VS, Teo MKC, Westbroek EM, Chang SD, Marks MP, Do HM, Levy RP, Steinberg GK

PMID: 30117771 DOI: 10.3171/2018.2.JNS172511

**OBJECTIVE:** Arteriovenous malformations (AVMs) of the basal ganglia and thalamus are particularly difficult lesions to treat, accounting for 3%-13% of all AVMs in surgical series and 23%-44% of malformations in radiosurgery series. The goal of this study was to report the results of multimodal management of basal ganglia and thalamic AVMs and investigate the factors that influence radiographic cure and good clinical outcomes. **METHODS:** This study was a retrospective analysis of a prospectively maintained database of all patients treated at the authors' institution. Clinical, radiological, follow-up, and outcome data were analyzed. Univariate and multivariate analyses were conducted to explore the influence of various factors on outcome. **RESULTS:** The results and data analysis pertaining to 123 patients treated over 32 years are presented. In this cohort, radiographic cure was achieved in 50.9% of the patients. Seventy-five percent of patients had good clinical outcomes (stable or improved performance scores), whereas 25% worsened after treatment. Inclusion of surgery and radiosurgery independently predicted obliteration, whereas nidus diameter and volume predicted clinical outcomes. Nidus volume/diameter and inclusion of surgery predicted the optimal outcome, i.e., good clinical outcomes with lesion obliteration. **CONCLUSIONS:** Good outcomes are possible with multimodal treatment in these complex patients. Increasing size and, by extension, higher Spetzler-Martin grade are associated with worse outcomes. Inclusion of multiple modalities of treatment as indicated could improve the chances of radiographic cure and good outcomes.

**[34] Stereotactic Radiosurgery for Pediatric Versus Adult Brain Arteriovenous Malformations.**

*Stroke.* 2018;49(8):1939-1945

Chen CJ, Ding D, Kano H, Mathieu D, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Grills IS, Barnett G, Lunsford LD, Sheehan JP  
PMID: 30002149 DOI: 10.1161/STROKEAHA.118.022052

**BACKGROUND AND PURPOSE:** The aim of this international, multicenter, retrospective matched cohort study is to directly compare the outcomes after stereotactic radiosurgery (SRS) for brain arteriovenous malformations (AVM) in pediatric versus adult patients. **METHODS:** We performed a retrospective review of patients with AVM who underwent SRS at 8 institutions participating in the International Gamma Knife Research Foundation from 1987 to 2014. Patients were categorized into pediatric (<18 years of age) and adult ( $\geq 18$  years of age) cohorts and matched in a 1:1 ratio using propensity scores. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes. **RESULTS:** From a total of 2191 patients who were eligible for inclusion in the overall study cohort, 315 were selected for each of the matched cohorts. There were no significant differences between matched pediatric versus adult cohorts with respect to the rates of favorable outcome (59% versus 58%;  $P=0.936$ ), AVM obliteration (62% versus 63%;  $P=0.934$ ), post-SRS hemorrhage (9% versus 7%;  $P=0.298$ ), radiological radiation-induced changes (26% versus 26%;  $P=0.837$ ), symptomatic radiation-induced changes (7% versus 9%;  $P=0.383$ ), or permanent radiation-induced changes (2% versus 3%;  $P=0.589$ ). The all-cause mortality rate was significantly lower in the matched pediatric cohort (3% versus 10%;  $P=0.003$ ). **CONCLUSIONS:** The outcomes

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

**[35] Stereotactic radiosurgery for Spetzler-Martin Grade IV and V arteriovenous malformations: an international multicenter study.**

*Journal of neurosurgery.* 2018;129(2):498-507

Patibandla MR, Ding D, Kano H, Xu Z, Lee JYK, Mathieu D, Whitesell J, Pierce JT, Huang PP, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Almodovar L, Grills IS, Silva D, Abbassy M, Missios S, Barnett GH, Lunsford LD, Sheehan JP  
PMID: 28885118 DOI: 10.3171/2017.3.JNS162635

**OBJECTIVE:** Due to the complexity of Spetzler-Martin (SM) Grade IV-V arteriovenous malformations (AVMs), the management of these lesions remains controversial. The aims of this multicenter, retrospective cohort study were to evaluate the outcomes after single-session stereotactic radiosurgery (SRS) for SM Grade IV-V AVMs and determine predictive factors. **METHODS:** The authors retrospectively pooled data from 233 patients (mean age 33 years) with SM Grade IV (94.4%) or V AVMs (5.6%) treated with single-session SRS at 8 participating centers in the International Gamma Knife Research Foundation. Pre-SRS embolization was performed in 71 AVMs (30.5%). The mean nidus volume, SRS margin dose, and follow-up duration were 9.7 cm<sup>3</sup>, 17.3 Gy, and 84.5 months, respectively. Statistical analyses were performed to identify factors associated with post-SRS outcomes. **RESULTS:** At a mean follow-up interval of 84.5 months, favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes (RIC) and was achieved in 26.2% of patients. The actuarial obliteration rates at 3, 7, 10, and 12 years were 15%, 34%, 37%, and 42%, respectively. The annual post-SRS hemorrhage rate was 3.0%. Symptomatic and permanent RIC occurred in 10.7% and 4% of the patients, respectively. Only larger AVM diameter ( $p = 0.04$ ) was found to be an independent predictor of unfavorable outcome in the multivariate logistic regression analysis. The rate of favorable outcome was significantly lower for unruptured SM Grade IV-V AVMs compared with ruptured ones ( $p = 0.042$ ). Prior embolization was a negative independent predictor of AVM obliteration ( $p = 0.024$ ) and radiologically evident RIC ( $p = 0.05$ ) in the respective multivariate analyses. **CONCLUSIONS:** In this multi-institutional study, single-session SRS had limited efficacy in the management of SM Grade IV-V AVMs. Favorable outcome was only achieved in a minority of unruptured SM Grade IV-V AVMs, which supports less frequent utilization of SRS for the management of these lesions. A volume-staged SRS approach for large AVMs represents an alternative approach for high-grade AVMs, but it requires further investigation.

**[36] A Comprehensive Study of Symptomatic Late Radiation-Induced Complications After Radiosurgery for Brain Arteriovenous Malformation: Incidence, Risk Factors, and Clinical Outcomes.**

*World neurosurgery.* 2018;116:e556-e565

Hasegawa H, Hanakita S, Shin M, Sugiyama T, Kawashima M, Takahashi W, Shojima M, Ishikawa O, Nakatomi H, Saito N  
PMID: 29772363 DOI: 10.1016/j.wneu.2018.05.038

**OBJECTIVE:** Stereotactic radiosurgery is widely used to treat brain arteriovenous malformation; however, detailed information on late radiation-induced complications (LRICs) is scarce. The goal of the present study was to characterize the incidence, risk factors, and clinical outcomes of LRICs based on our long-term follow-up data. **METHODS:** The outcomes of consecutive patients who underwent stereotactic radiosurgery for arteriovenous malformations at our institution in 1990-2010 were analyzed. Cyst formation/encapsulated hematoma (CF/EH) and radiation-induced tumor were defined as LRICs. Cumulative incidence rates were calculated using the Kaplan-Meier method. Risk factors for CF/EH were analyzed using a Cox proportional hazard model. **RESULTS:** A total of 581 patients with mean and median follow-up periods of 11.8 and 10.1 years,

respectively (range, 2.0-26.7 years), were analyzed. CF/EH was observed in 30 patients (5.2%). The median time to progression was 11.8 years (range, 1.9-23.9 years). Cumulative incidence rates were 0.8%, 2.8%, 7.6%, and 9.7% at 5, 10, 15, and 20 years, respectively. A multivariate analysis showed that lobar location and maximal diameter  $\geq 22$  mm were significant risk factors for CF/EH. Overall, the functional outcomes were mild, moderate, and severe/fatal in 26 (87%), 1 (3%), and 3 (10%) patients, respectively. Radiation-induced tumor was confirmed in only 1 patient (0.17%). **CONCLUSIONS:** An increased nidus size and lobar location are risk factors for CF/EH. Although the CF/EH incidence is low, some LRICs develop after long periods. Extended follow-up is warranted, particularly of patients with risk factors.

**[37] How to improve obliteration rates during volume-staged stereotactic radiosurgery for large arteriovenous malformations.**

*Journal of neurosurgery.* 2018;:1-8

Kano H, Flickinger JC, Nakamura A, Jacobs RC, Tonetti DA, Lehoccky C, Park KJ, Yang HC, Niranjan A, Lunsford LD  
PMID: 30028266 DOI: 10.3171/2018.2.JNS172964

**OBJECTIVE:** The management of large-volume arteriovenous malformations (AVMs) with stereotactic radiosurgery (SRS) remains challenging. The authors retrospectively tested the hypothesis that AVM obliteration rates can be improved by increasing the percentage volume of an AVM that receives a minimal threshold dose of radiation. **METHODS:** In 1992, the authors prospectively began to stage anatomical components in order to deliver higher single doses to AVMs  $> 15$  cm<sup>3</sup> in volume. Since that time 60 patients with large AVMs have undergone volume-staged SRS (VS-SRS). The median interval between the first stage and the second stage was 4.5 months (2.8-13.8 months). The median target volume was 11.6 cm<sup>3</sup> (range 4.3-26 cm<sup>3</sup>) in the first-stage SRS and 10.6 cm<sup>3</sup> (range 2.8-33.7 cm<sup>3</sup>) in the second-stage SRS. The median margin dose was 16 Gy (range 13-18 Gy) for both SRS stages. **RESULTS:** AVM obliteration after the initial two staged volumetric SRS treatments was confirmed by MRI alone in 4 patients and by angiography in 11 patients at a median follow-up of 82 months (range 0.4-206 months) after VS-SRS. The post-VS-SRS obliteration rates on angiography were 4% at 3 years, 13% at 4 years, 23% at 5 years, and 27% at 10 years. In multivariate analysis, only  $\geq 20$ -Gy volume coverage was significantly associated with higher total obliteration rates confirmed by angiography. When the margin dose is  $\geq 17$  Gy and the 20-Gy SRS volume included  $\geq 63\%$  of the total target volume, the angiographically confirmed obliteration rates increased to 61% at 5 years and 70% at 10 years. **CONCLUSIONS:** The outcomes of prospective VS-SRS for large AVMs can be improved by prescribing an AVM margin dose of  $\geq 17$  Gy and adding additional isocenters so that  $\geq 63\%$  of the internal AVM dose receives more than 20 Gy.

**[38] Gamma knife radiosurgery for arteriovenous malformations: general principles and preliminary results in a Swiss cohort.**

*Swiss medical weekly.* 2018;148:w14602

Raboud M, Tuleasca C, Maeder P, Schiappacasse L, Marguet M, Daniel RT, Levivier M  
PMID: 29611866 DOI: 10.4414/sm.w.2018.14602

**INTRODUCTION:** Arteriovenous malformations (AVMs) are a type of vascular malformation characterized by an abnormal connection between arteries and veins, bypassing the capillary system. This absence of capillaries generates an elevated pressure (hyperdebit), in both the AVM and the venous drainage, increasing the risk of rupture. Management modalities are: observation, microsurgical clipping, endovascular treatment and radiosurgery. The former can be used alone or in the frame of a multidisciplinary approach. We review our single-institution experience with gamma knife radiosurgery (GKR) over a period of 5 years. **MATERIALS AND METHODS:** The study was open-label, prospective and nonrandomised. Fifty-seven consecutive patients, benefitting from 64 GKR treatments, were included. All were treated with Leksell Gamma Knife Perfexion (Elekta Instruments, AB, Sweden) between July 2010 and August 2015. All underwent stereotactic multimodal imaging: standard digital subtraction

angiography, magnetic resonance imaging and computed tomography angiography. We report obliteration rates, radiation-induced complications and haemorrhages during follow-up course. **RESULTS:** The mean age was 46 years (range 13-79 years). The mean follow-up period was 36.4 months (median 38, range 12-75 months). Most common pretherapeutic clinical presentation was haemorrhage (50%). The most common Pollock-Flickinger score was between 1.01 and 1.5 (46%) and Spetzler-Martin grade III (46%). In 39 (60.1%) of cases, GKR was performed as upfront therapeutic option. The mean gross target volume (GTV) was 2.3 ml (median 1.2, range 0.03-11.3 ml). Mean marginal dose was 22.4 Gy (median 24, range 18-24 Gy). The mean prescription isodose volume (PIV) was 2.9 ml (median 1.8, range 0.065-14.6 ml). The overall obliteration rates (all treatments combined) at 12, 24, 36, 48 and 60 months were 4.8, 16.9%, 37.4, 63.6 and 78.4%, respectively. The main predictive factors for complete obliteration were: higher mean marginal dose (23.3 vs 21.0 Gy), lower GTV (mean 1.5 vs 3.5 ml) and absence of previous embolisation (at 60 months 61.8% prior embolisation compared with 82.4% without prior embolisation) (for all  $p < 0.05$ ). Eight (14%) patients experienced complications after GKR. Overall definitive morbidity rate was 3.1%. No patient died from causes related to GKR. However, during the obliteration period, one case of extremely rare fatal haemorrhage occurred. **CONCLUSION:** Radiosurgery is a safe and effective treatment modality for intracranial AVMs in selected cases. It can be used as upfront therapy or in the frame of a combined management. Obliteration rates are high, with minimal morbidity. The treatment effect is progressive and subsequent and regular clinical and radiological follow-up is needed to evaluate this effect.

**[39] Comparison of the Long-term Efficacy and Safety of Gamma Knife Radiosurgery for Arteriovenous Malformations in Pediatric and Adult Patients.**

*Neurologia medico-chirurgica.* 2018;58(6):231-239

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

PMID: 29769453 DOI: 10.2176/nmc.st.2018-0008

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

**[40] The benefit of radiosurgery for ARUBA-eligible arteriovenous malformations: a practical analysis over an appropriate follow-up period.**

*Journal of neurosurgery.* 2018;128(6):1850-1854

Tonetti DA, Gross BA, Atcheson KM, Jankowitz BT, Kano H, Monaco EA, Niranjana A, Flickinger JC, Lunsford LD

PMID: 28665253 DOI: 10.3171/2017.1.JNS162962

**OBJECTIVE:** The authors of this study found that, given the latency period required for arteriovenous malformation (AVM) obliteration after stereotactic radiosurgery (SRS), a study with limited follow-up cannot assess the benefit of

SRS for unruptured AVMs. **METHODS:** The authors reviewed their institutional experience with "ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations)-eligible" AVMs treated with SRS between 1987 and 2016, with the primary outcome defined as stroke (ischemic or hemorrhagic) or death (AVM related or AVM unrelated). Patients with at least 3 years of follow-up in addition to those who experienced stroke or died during the latency period were included. Secondary outcome measures included obliteration rates, patients with new seizure disorders, and those with new focal deficits without stroke. **RESULTS:** Of 233 patients included in this study, 32 had a stroke or died after SRS over the mean 8.4-year follow-up (14%). Utilizing the 10% stroke or death rate at a mean 2.8-year follow-up for untreated AVMs in ARUBA, the rate in the authors' study is significantly lower than that anticipated at the 8.4-year follow-up for an untreated cohort (14% vs 30%,  $p = 0.0003$ ). Notwithstanding obliteration, in this study, annualized rates of hemorrhage and stroke or death after 3 years following SRS were 0.4% and 0.8%, respectively. The overall obliteration rate was 72%; new seizure disorders, temporary new focal deficits without stroke, and permanent new focal deficits without stroke occurred in 2% of patients each. **CONCLUSIONS:** After a sensible follow-up period exceeding the latency period, there is a lower rate of stroke/death for patients with treated, unruptured AVMs with SRS than for patients with untreated AVMs.

**[41] Surgical Management of Adverse Radiation Effects After Gamma Knife Radiosurgery for Cerebral Arteriovenous Malformations: A Population-Based Cohort Study.**

*World neurosurgery.* 2018;114:e840-e850

Meneghelli P, Pasqualin A, Zampieri P, Longhi M, Foroni R, Sini A, Tommasi N, Nicolato A

PMID: 29572169 DOI: 10.1016/j.wneu.2018.03.097

**OBJECTIVE:** The goal of this study is to report our experience in the surgical treatment of cerebral arteriovenous malformations (cAVMs) related permanent symptomatic adverse radiation effects (PSAREs), to clarify an appropriate surgical management and to identify the risk factors related to their development.

**METHODS:** We evaluated 549 patients treated with Gamma Knife radiosurgery (GKRS) for cAVMs with a follow-up of at least 8 years. Univariate and multivariate analyses were used to test different risk factors related to the development of PSARE. We retrospectively reviewed the records of these patients to analyze the clinical outcome. **RESULTS:** Fourteen patients (2.5%) developed PSARE and were submitted to surgery. Higher average treated volume represents a significant risk factors for the development of PSARE ( $P < 0.05$ ); on the other hand, older age and higher average dose reduce the risk of PSARE ( $P < 0.05$ ). A favorable clinical outcome was achieved in 13 patients (93%) after surgery; in 1 patient, the unfavorable outcome was due to hemorrhage that occurred months after GKRS. Serial MRI scans following either surgical removal of the nodule or Ommaya reservoir positioning showed progressive reduction of brain edema in all cases.

**CONCLUSIONS:** The management of PSARE is controversial, especially for cAVMs treated with SRS. Surgical removal is rarely needed, but-if unavoidable-it can be a valuable option in experienced hands. A careful preoperative planning is always necessary to detect pathologic blood flow through the PSARE.

**[42] Salvage Therapy for Brain Arteriovenous Malformations After Failure of Gamma Knife Stereotactic Radiosurgery.**

*World neurosurgery.* 2018;110:e942-e951

Quan K, Tang X, Song J, Chen X, Tian Y, Liu P, Shi Y, Yang Z, Liu Y, Zhou F, Pan L, Zhu W

PMID: 29198888 DOI: 10.1016/j.wneu.2017.11.143

**OBJECTIVE:** The aim of this study was to investigate delayed complications in patients with brain arteriovenous malformation (BAVM) after Gamma Knife stereotactic radiosurgery and to present the salvage therapy experiences of patients with BAVM with radiation-induced changes (RICs) or intracranial hemorrhage (ICH). **METHODS:** This cohort consisted of 44 patients with BAVM who underwent failed GKRS between 2000 and 2015. These patients were

further divided into an RIC group (23 patients) and an ICH group (21 patients) based on their post-GKRS complications. The patients' characteristics, treatment strategies, and long-term outcomes were analyzed. The modified Rankin Scale was used to assess the neurologic status of each patient. **RESULTS:** In our study, the marginal dose and radiosurgery-based arteriovenous malformation score were not significantly different between the 2 groups. Craniotomy was performed in 26 patients (9 patients with ICH and 17 patients with RICs), and histologic examination showed cavernous angioma changes in 6 patients. In addition, 6 patients underwent repeat radiosurgery in the ICH group, and 7 patients used bevacizumab in the RIC group. Thirty patients showed good outcomes at the last follow-up (modified Rankin Scale score <3). **CONCLUSIONS:** Salvage therapy for patients with BAVM should be performed based on the latency period and lesion characteristics of each individual. Prompt treatment and a longer follow-up are recommended to achieve good clinical outcomes.

#### [43] Does Advanced Age Affect the Outcomes of Stereotactic Radiosurgery for Cerebral Arteriovenous Malformation?

*World neurosurgery.* 2018;109:e715-e723

Hasegawa H, Hanakita S, Shin M, Sugiyama T, Kawashima M, Takahashi W, Nomoto AK, Shojima M, Nakatomi H, Saito N

PMID: 29066317 DOI: 10.1016/j.wneu.2017.10.071

**BACKGROUND:** Stereotactic radiosurgery (SRS) is generally considered a minimally invasive treatment modality. However, definitive evidence of the efficacy of SRS in the elderly population is still not available. **METHODS:** The outcomes of 561 elderly and nonelderly patients who underwent SRS for AVM at our institution between 1990 and 2013 were reviewed, analyzed, and compared. Elderly patients were defined as those age  $\geq 60$  years at the time of SRS. **RESULTS:** The elderly cohort comprised 55 patients; the nonelderly cohort, 506. In the elderly cohort, the median age was 65 years, and the duration of follow-up was 91 months. The actuarial obliteration rates were 47% at 3 years, 70% at 4 years, and 76% at 5 years in the elderly cohort, and 57% at 3 years, 76% at 4 years, and 83% at 5 years in the nonelderly cohort. In the elderly cohort, the hemorrhage rates during the post-SRS latent phase were 5.2%/year in patients with hemorrhagic onset and 0%/year in those with nonhemorrhagic onset, and event-free survival (EFS) was 93% at 6 years and 89% at 12 years. The obliteration rate, mortality, and EFS rate were not significantly different between the 2 cohorts, whereas the rate of perifocal edema was significantly lower ( $P = 0.021$ ) in the elderly cohort. The pre-SRS and post-SRS hemorrhage rates were slightly higher in the elderly cohort, albeit without statistical significance. **CONCLUSIONS:** Therapeutic effects and outcomes of SRS are similar in elderly and nonelderly patients. Treatment-related neurologic deficits are rare, and longer EFS can be expected.

#### [44] Effect of treatment period on outcomes after stereotactic radiosurgery for brain arteriovenous malformations: an international multicenter study.

*Journal of neurosurgery.* 2018;:1-10

Patibandla MR, Ding D, Kano H, Starke RM, Lee JYK, Mathieu D, Whitesell J, Pierce JT, Huang PP, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Almodovar L, Grills IS, Silva D, Abbassy M, Missios S, Barnett GH, Lunsford LD, Sheehan JP  
PMID: 29393755 DOI: 10.3171/2017.8.JNS171336

**OBJECTIVE:** The role of and technique for stereotactic radiosurgery (SRS) in the management of arteriovenous malformations (AVMs) have evolved over the past four decades. The aim of this multicenter, retrospective cohort study was to compare the SRS outcomes of AVMs treated during different time periods. **METHODS:** The authors selected patients with AVMs who underwent single-session SRS at 8 different centers from 1988 to 2014 with follow-up  $\geq 6$  months. The SRS eras were categorized as early (1988-2000) or modern (2001-2014). Statistical analyses were performed to compare the baseline characteristics and outcomes of the early versus modern SRS eras. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes (RICs). **RESULTS:** The study cohort comprised 2248 patients with AVMs, including 1584 in the early and 664 in the modern

SRS eras. AVMs in the early SRS era were significantly smaller ( $p < 0.001$  for maximum diameter and volume), and they were treated with a significantly higher radiosurgical margin dose ( $p < 0.001$ ). The obliteration rate was significantly higher in the early SRS era (65% vs 51%,  $p < 0.001$ ), and earlier SRS treatment period was an independent predictor of obliteration in the multivariate analysis ( $p < 0.001$ ). The rates of post-SRS hemorrhage and radiological, symptomatic, and permanent RICs were not significantly different between the two groups. Favorable outcome was achieved in a significantly higher proportion of patients in the early SRS era (61% vs 45%,  $p < 0.001$ ), but the earlier SRS era was not statistically significant in the multivariate analysis ( $p = 0.470$ ) with favorable outcome. **CONCLUSIONS:** Despite considerable advances in SRS technology, refinement of AVM selection, and contemporary multimodality AVM treatment, the study failed to observe substantial improvements in SRS favorable outcomes or obliteration for patients with AVMs over time. Differences in baseline AVM characteristics and SRS treatment parameters may partially account for the significantly lower obliteration rates in the modern SRS era. However, improvements in patient selection and dose planning are necessary to optimize the utility of SRS in the contemporary management of AVMs.

## 2017

#### [45] Incidence and Management of Late Adverse Radiation Effects After Arteriovenous Malformation Radiosurgery.

*Neurosurgery.* 2017;81(6):928-934

Pollock BE, Link MJ, Branda ME, Storlie CB

PMID: 28328005 DOI: 10.1093/neuros/nyx010

**BACKGROUND:** Late adverse radiation effects (ARE) typically occur many years after stereotactic radiosurgery (SRS) of intracranial arteriovenous malformations (AVM). They are characterized by perilesional edema or cyst formation and are distinct from radiation-induced changes (RIC) noted in the first 1 to 2 years after AVM SRS and radiation necrosis. **OBJECTIVE:** To determine the incidence of late ARE after AVM SRS. **METHODS:** Retrospective review of 233 AVM patients having SRS from 1990 to 2009. Patients had sporadic AVM, no prior radiation, and a minimum of 5 years of magnetic resonance imaging (MRI) follow-up. The median MRI follow-up after SRS was 9.8 years (range, 5-24.2). **RESULTS:** Late ARE were observed in 16 patients (6.9%) at a median of 8.7 years after SRS (range, 2.0-16.1). The 5-, 10-, and 15-year incidence of late ARE was 0.4%, 7.7%, and 12.5%, respectively. Eight patients (3.4%) were symptomatic at the time of ARE detection. Three of 8 patients who were initially asymptomatic had documented cyst progression (at 11, 40, and 42 months), for an overall symptomatic rate of 4.7%. Five patients with asymptomatic ARE have been observed for a median of 9.3 years (range, 2.0-14.1) without progression. Patients having early RIC (hazard ratio [HR] = 2.11,  $P < .001$ ), patients having obliteration (HR = 1.24,  $P = .02$ ), and patients having SRS before April 1997 (HR = 1.12,  $P = .02$ ) were more likely to develop late ARE. **CONCLUSION:** Late ARE are common in AVM patients who develop early RIC after SRS. Resection of the thrombosed AVM and the adjacent damaged tissue is effective at eliminating the mass effect and improving patients' neurological condition.

#### [46] Stereotactic Radiosurgery for Brainstem Arteriovenous Malformations: A Multicenter Study.

*Neurosurgery.* 2017;81(6):910-920

Cohen-Inbar O, Starke RM, Lee CC, Kano H, Huang P, Kondziolka D, Grills IS, Silva D, Abbassy M, Missios S, Barnett GH, Lunsford LD, Sheehan JP

PMID: 28645182 DOI: 10.1093/neuros/nyx189

**BACKGROUND:** The management of brainstem arteriovenous malformations (bAVMs) is a formidable challenge. bAVMs harbor higher morbidity and mortality compared to other locations. **OBJECTIVE:** To review the outcomes following

stereotactic radiosurgery (SRS) of bAVMs in a multicenter study. **METHODS:** Six medical centers contributed data from 205 patients through the International Gamma Knife Research Foundation. Median age was 32 yr (6-81). Median nidus volume was 1.4 mL (0.1-69 mL). Favorable outcome (FO) was defined as AVM obliteration and no post-treatment hemorrhage or permanent symptomatic radiation-induced complications. **RESULTS:** Overall obliteration was reported in 65.4% (n = 134) at a mean follow-up of 69 mo. Obliteration was angiographically proven in 53.2% (n = 109) and on MRA in 12.2% (n = 25). Actuarial rate of obliteration at 2, 3, 5, 7, and 10 yr after SRS was 24.5%, 43.3%, 62.3%, 73%, and 81.8% respectively. Patients treated with a margin dose >20 Gy were more likely to achieve obliteration (P = .001). Obliteration occurred earlier in patients who received a higher prescribed margin dose (P = .05) and maximum dose (P = .041). Post-SRS hemorrhage occurred in 8.8% (n = 18). Annual postgamma knife latency period hemorrhage was 1.5%. Radiation-induced complications were radiologically evident in 35.6% (n = 73), symptomatic in 14.6% (n = 30), and permanent in 14.6% (n = 30, which included long-tract signs and new cranial nerve deficits). FO was achieved in 64.4% (n = 132). Predictors of an FO were a higher Virginia radiosurgery AVM scale score (P = .003), prior hemorrhage (P = .045), and a lower prescribed maximum dose (P = .006). **CONCLUSION:** SRS for bAVMs results in obliteration and avoids permanent complications in the majority of patients.

**[47] Clinical outcomes and radiosurgical considerations for pediatric arteriovenous malformation: influence of clinical features on obliteration rate.**

*Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery.* 2017;33(12):2137-2145  
Park CK, Choi SK, Lee SH, Choi MK, Lim YJ  
PMID: 28871374 DOI: 10.1007/s00381-017-3579-7

**PURPOSE:** Gamma knife radiosurgery (GKRS) is an established treatment modality for brain arteriovenous malformation (AVM), but there have been few published studies examining the relationship between clinical features of AVM and successful obliteration with GKRS in pediatric patients. In the current study, we investigate the outcomes of GKRS for pediatric patients with brain AVM and analyze the variables that influence obliteration. **METHODS:** We analyzed 68 pediatric patients (<= 18 years) with a mean follow-up period of 61.9 months (range 6-215 months). The following parameters were analyzed to determine their influence on obliteration of AVM treated by GKRS: age, sex, target volume, irradiation dose, prior treatment, location of AVM, nidus structure, velocity of AVM, location of venous drainage, number of feeding arteries, and initial presenting symptoms. Also, we estimated clinical factors which should be considered during the follow-up period. **RESULTS:** Of the 68 patients, complete obliteration was confirmed in 26 (38.2%) by cerebral angiography. The response rate of AVM for GKRS was 92.6%. No significant association was observed between any of the parameters investigated and the obliteration of AVM, with the exception of number of feeding arteries, which exhibited a statistically significant difference by univariate analysis (p = 0.003). However, on multivariate analysis, nidus structure (p = 0.007), velocity of the main arterial phase (p = 0.013), velocity of the feeding artery phase (p = 0.004), and the number of feeding arteries (p = 0.018) showed statistical significance. **CONCLUSION:** GKRS yielded good long-term clinical outcomes in most pediatric patients. Multiple arterial feeding vessels, diffuse nidus structure, and fast flow of AVM were specific factors associated with a low rate of obliteration in pediatric AVMs.

**[48] Stereotactic radiosurgery for cerebellar arteriovenous malformations: an international multicenter study.**

*Journal of neurosurgery.* 2017;127(3):512-521  
Cohen-Inbar O, Starke RM, Kano H, Bowden G, Huang P, Rodriguez-Mercado R, Almodovar L, Grills IS, Mathieu D, Silva D, Abbassy M, Missios S, Lee JYK, Barnett GH, Kondziolka D, Lunsford LD, Sheehan JP  
PMID: 27689461 DOI: 10.3171/2016.7.JNS161208

**OBJECTIVE:** Cerebellar arteriovenous malformations (AVMs) represent the

majority of infratentorial AVMs and frequently have a hemorrhagic presentation. In this multicenter study, the authors review outcomes of cerebellar AVMs after stereotactic radiosurgery (SRS). **METHODS:** Eight medical centers contributed data from 162 patients with cerebellar AVMs managed with SRS. Of these patients, 65% presented with hemorrhage. The median maximal nidus diameter was 2 cm. Favorable outcome was defined as AVM obliteration and no posttreatment hemorrhage or permanent radiation-induced complications (RICs). Patients were followed clinically and radiographically, with a median follow-up of 60 months (range 7-325 months). **RESULTS:** The overall actuarial rates of obliteration at 3, 5, 7, and 10 years were 38.3%, 74.2%, 81.4%, and 86.1%, respectively, after single-session SRS. Obliteration and a favorable outcome were more likely to be achieved in patients treated with a margin dose greater than 18 Gy (p < 0.001 for both), demonstrating significantly better rates (83.3% and 79%, respectively). The rate of latency preobliteration hemorrhage was 0.85%/year. Symptomatic post-SRS RICs developed in 4.5% of patients (n = 7). Predictors of a favorable outcome were a smaller nidus (p = 0.0001), no pre-SRS embolization (p = 0.003), no prior hemorrhage (p = 0.0001), a higher margin dose (p = 0.0001), and a higher maximal dose (p = 0.009). The Spetzler-Martin grade was not found to be predictive of outcome. The Virginia Radiosurgery AVM Scale score (p = 0.0001) and the Radiosurgery-Based AVM Scale score (p = 0.0001) were predictive of a favorable outcome. **CONCLUSIONS:** SRS results in successful obliteration and a favorable outcome in the majority of patients with cerebellar AVMs. Most patients will require a nidus dose of higher than 18 Gy to achieve these goals. Radiosurgical and not microsurgical scales were predictive of clinical outcome after SRS.

**[49] Early versus late arteriovenous malformation responders after stereotactic radiosurgery: an international multicenter study.**

*Journal of neurosurgery.* 2017;127(3):503-511  
Cohen-Inbar O, Starke RM, Paisan G, Kano H, Huang PP, Rodriguez-Mercado R, Almodovar L, Grills IS, Mathieu D, Silva D, Abbassy M, Missios S, Lee JYK, Barnett GH, Kondziolka D, Lunsford LD, Sheehan JP  
PMID: 27662534 DOI: 10.3171/2016.7.JNS161194

**OBJECTIVE:** The goal of stereotactic radiosurgery (SRS) for arteriovenous malformation (AVM) is complete nidus obliteration, thereby eliminating the risk of future hemorrhage. This outcome can be observed within the first 18 months, although documentation of AVM obliteration can extend to as much as 5 years after SRS is performed. A shorter time to obliteration may impact the frequency and effect of post-SRS complications and latency hemorrhage. The authors' goal in the present study was to determine predictors of early obliteration (18 months or less) following SRS for cerebral AVM. **METHODS:** Eight centers participating in the International Gamma Knife Research Foundation (IGKRF) obtained institutional review board approval to supply de-identified patient data. From a cohort of 2231 patients, a total of 1398 patients had confirmed AVM obliteration. Patients were sorted into early responders (198 patients), defined as those with confirmed nidus obliteration at or prior to 18 months after SRS, and late responders (1200 patients), defined as those with confirmed nidus obliteration more than 18 months after SRS. The median clinical follow-up time was 63.7 months (range 7-324.7 months). **RESULTS:** Outcome parameters including latency interval hemorrhage, mortality, and favorable outcome were not significantly different between the 2 groups. Radiologically demonstrated radiation-induced changes were noted more often in the late responder group (376 patients [31.3%] vs 39 patients [19.7%] for early responders, p = 0.005). Multivariate independent predictors of early obliteration included a margin dose > 24 Gy (p = 0.031), prior surgery (p = 0.002), no prior radiotherapy (p = 0.025), smaller AVM nidus (p = 0.002), deep venous drainage (p = 0.039), and nidus location (p < 0.0001). Basal ganglia, cerebellum, and frontal lobe nidus locations favored early obliteration (p = 0.009). The Virginia Radiosurgery AVM Scale (VRAS) score was significantly different between the 2 responder groups (p = 0.039). The VRAS score was also shown to be predictive of early obliteration on univariate analysis (p = 0.009). For early obliteration, such prognostic ability was not shown for other SRS- and

AVM-related grading systems. **CONCLUSIONS:** Early obliteration ( $\leq 18$  months post-SRS) was more common in patients whose AVMs were smaller, located in the frontal lobe, basal ganglia, or cerebellum, had deep venous drainage, and had received a margin dose  $> 24$  Gy.

**[50] Effectiveness of Preradiosurgical Embolization with NBCA for Arteriovenous Malformations - Retrospective Outcome Analysis in a Japanese Registry of 73 Patients (J-REAL study).**

*Neurointervention.* 2017;12(2):100-109

Miyachi S, Izumi T, Satow T, Srivatanakul K, Matsumoto Y, Terada T, Matsumaru Y, Kiyosue H

PMID: 2895512 DOI: 10.5469/neuroint.2017.12.2.100

**PURPOSE:** Recent reports have posed doubts about the effect of preradiosurgical embolization in brain arteriovenous malformation (AVM) because it makes the planning of stereotactic radiosurgery (SRS) difficult and has the risk of recanalization out of the target. We investigated whether the performance and quality of embolization may influence the success of SRS based on a retrospective case cohort study. **MATERIALS AND METHODS:** Seventy-three patients who underwent embolization followed by SRS between 2003 and 2012 in eight institutes with neurointerventionists were considered. They were divided into the following two groups at 3 years of follow up after the final SRS: "successful occlusion group" (S group), with radiologically complete occlusion of AVM; and "non-successful occlusion group" (N group) with persistent remnant nidus or abnormal vascular networks. Patient background, AVM profile, embolization performance grade and complications were compared in each group. The quality of embolization was evaluated with the new grading system: embolization performance grade (E grade), specializing the achievement of nidus embolization. E grade A was defined as sufficient nidus embolization with more than half of the total number of feeders achieving nidus penetration. E grade B was defined as less than half achievement of nidus embolization, and E grade C was defined as failure to perform nidus embolization. **RESULTS:** Forty-three patients were included in the S group, and 29 patients were included in the N group. The size and Spetzler-Martin grade of AVM and the rate of diffuse type was higher in the N group without statistical significance. The embolization performance level according to E grade indicated a significantly higher rate of successful embolization with more than 50% of nidus penetration in the S group ( $P < 0.001$ ). This difference was also confirmed in the subanalysis for limited cases, excluding smaller AVMs with complete occlusion with SRS alone ( $P = 0.001$ ). **CONCLUSION:** The cause of the unsuccessful result of post-embolization SRS might be the large, diffuse angioarchitecture, but proper embolization with a high rate of nidus penetration to avoid recanalization is more important. Effective embolization is essential to contribute to and promote the effect of radiosurgery.

**[51] Gamma Knife Radiosurgery for Arteriovenous Malformations: Clinical Series of 199 Patients.**

*Turkish neurosurgery.* 2017;27(2):301-308

Arslan I, Tezcanli E, Yilmaz M, Cizmeli O, Sengoz M, Peker S

PMID: 27509452 DOI: 10.5137/1019-5149.JTN.15330-15.0

**AIM:** Cerebral arteriovenous malformations (AVM) are pathological connections between arteries and veins without capillaries. Stereotactic radiosurgery (RS) is a proven and accepted treatment method for cerebral AVMs. Our objective was to analyze the factors influencing the clinical outcome in patients suffering from AVMs. **MATERIAL AND METHODS:** We retrospectively reviewed 199 patients who were treated with Gamma-Knife RS for intracranial AVMs between 13 October 2005 and 31 October 2010. There were 89 male, 110 female patients with a median age of 32 years (range, 3-74 years). Obliteration was assessed with MRI angiography and DSA imaging. **RESULTS:** Complete obliteration rate after RS was 71 % (141 out of 199), including second RS treatments. In terms of obliteration rates, there was no significant difference between patients younger and older than 21 years old ( $p = 0.669$ ). After RS, 3 patients died due to intracranial hemorrhage and 1 died of heart disease. Death from AVM was determined

as 1.5 %. Intracranial hemorrhage was observed in 7 (3.5 %) patients post-RS.

**CONCLUSION:** Obliteration was found to be associated with Spetzler-Martin Grade, Pollock-Flickinger Grade, AVM volume, RS dose, bleeding history before RS and no previous embolization before RS. Gamma knife RS is an effective treatment method for the treatment of AVMs both for pediatric and adult patients. It provides high obliteration and low mortality rates.

**[52] Stereotactic Radiosurgery for ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations)-Eligible Spetzler-Martin Grade I and II Arteriovenous Malformations: A Multicenter Study.**

*World neurosurgery.* 2017;102:507-517

Ding D, Starke RM, Kano H, Mathieu D, Huang PP, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Almodovar L, Grills IS, Silva D, Abbassy M, Missios S, Barnett GH, Lunsford LD, Sheehan JP

PMID: 28344176 DOI: 10.1016/j.wneu.2017.03.061

**OBJECTIVE:** ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations) found better short-term outcomes after conservative management compared with intervention for unruptured arteriovenous malformations (AVMs). However, because Spetzler-Martin (SM) grade I-II AVMs have the lowest treatment morbidity, sufficient follow-up of these lesions may show a long-term benefit from intervention. The aim of this multicenter, retrospective cohort study is to assess the outcomes after stereotactic radiosurgery (SRS) for ARUBA-eligible SM grade I-II AVMs. **METHODS:** We pooled SRS data for patients with AVM from 7 institutes and selected ARUBA-eligible SM grade I-II AVMs with  $\geq 12$  months follow-up for analysis. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes. **RESULTS:** The ARUBA-eligible SM grade I-II AVM cohort comprised 232 patients (mean age, 42 years). The mean nidus volume, SRS margin dose, and follow-up duration were 2.1 cm(3), 22.5 Gy, and 90.5 months, respectively. The actuarial obliteration rates at 5 and 10 years were 72% and 87%, respectively; annual post-SRS hemorrhage rate was 1.0%; symptomatic and permanent radiation-induced changes occurred in 8% and 1%, respectively; and favorable outcome was achieved in 76%. Favorable outcome was significantly more likely in patients treated with a margin dose  $> 20$  Gy (83%) versus  $\leq 20$  Gy (62%;  $P < 0.001$ ). Stroke or death occurred in 10% after SRS. **CONCLUSIONS:** For ARUBA-eligible SM grade I-II AVMs, long-term SRS outcomes compare favorably with the natural history. SRS should be considered for adult patients harboring unruptured, previously untreated low-grade AVMs with a minimum life expectancy of a decade.

**[53] Radiosurgery for Arteriovenous Malformations and the Impact on Headaches.**

*Headache.* 2017;57(5):737-745

Bowden G, Cavaleri J, Kano H, Monaco E 3rd, Niranjana A, Flickinger J, Dade Lunsford L

PMID: 28217873 DOI: 10.1111/head.13055

**BACKGROUND:** Arteriovenous malformations (AVMs) can underlie many diverse neurological signs and symptoms. Headaches are a common presentation that can have a significant impact on quality of life. **OBJECTIVE:** The authors investigated Gamma Knife((R)) stereotactic radiosurgery (SRS) outcomes in patients with AVMs and associated headaches. **METHODS:** This retrospective study analyzed 102 patients with AVMs who underwent SRS between 1995 and 2013. The patient's headache symptoms led to their AVM diagnosis or developed post hemorrhage of their AVM. Information regarding headache characteristics was obtained from the patient's medical records and at follow-up using a scripted clinical interview. The median imaging follow-up was 61.7 months and clinical follow-up was 89.7 months. The median treatment volume at SRS was 4.1 cm(3) and the median marginal dose was 20 Gy. **RESULTS:** The actuarial AVM obliteration rate was 60% at 5 years and 78% at 10 years. Patients reported that their overall headache severity decreased by -43.6% and their headache frequency was reduced by -53.4%. Headache reduction was reported in 49.1% of

patients at 1 year and 69.5% at 5 years. The median time until improvement was 6.5 months. After SRS, headache medication usage decreased in 29% of patients. Permanent adverse radiation effects after SRS occurred in 3% of patients. Until obliteration was complete, the annual risk of a hemorrhage after SRS was 0.4% per year. **CONCLUSION:** Although recall bias related to a retrospective analysis can impact outcomes, headache symptoms associated with AVMs may potentially be decreased or eliminated in a subset of patients treated with Gamma Knife radiosurgery.

**[54] Radiosurgery in treatment of cerebral arteriovenous malformation: Mid-term results of 388 cases from a single center.**

*Asian journal of neurosurgery.* 2017;12(2):159-166

Bitaraf MA, Katoozpour R, Azar M, Nouri M, Mortazavi SA, Amirjamshidi A  
PMID: 28484523 DOI: 10.4103/1793-5482.145121

**BACKGROUND AND OBJECTIVES:** The purpose of this study is to evaluate the outcome and risks of radiosurgery for patients with arteriovenous malformations (AVM) of the brain all treated in a single center in the 3(rd) world with all its limitations. **MATERIALS AND METHODS:** We performed a retrospective analysis of 388 patients with AVM treated with radiosurgery during an 8-year period. Factors associated with increased chance of AVM obliteration or hemorrhages during the follow-up period were analyzed. **RESULTS:** Among 388 cases included in our series, 74 were Spetzler-Martin (SM) grade IV or V. Forty-four patients (11.3%) experienced post-radiosurgery hemorrhage in their follow-up period. The number of feeders (one/multiple) and deep location of the AVM did not alter the chance of bleeding ( $P < 0.05$ ). Higher SM grading of the AVM was associated with increased chance of hemorrhage and decreased obliteration rate ( $P > 0.05$ ) in the mid-term follow up. **CONCLUSIONS:** Our case series showed that radiosurgery can be considered a viable alternative in the treatment of even large AVMs which might not be considered good candidates for surgery or endovascular treatment. Further data including large size lesions are warranted to further support our findings.

**[55] Volume-Staged Stereotactic Radiosurgery for Intracranial Arteriovenous Malformations: Outcomes Based on an 18-Year Experience.**

*Neurosurgery.* 2017;80(4):543-550

Pollock BE, Link MJ, Stafford SL, Lanzino G, Garces YI, Foote RL  
PMID: 28362923 DOI: 10.1093/neuros/nyw107

**BACKGROUND:** Radiation-based treatment options of large intracranial arteriovenous malformations (AVM) must balance the likelihood of obliteration with the risk of adverse radiation effects (ARE). **OBJECTIVE:** To analyze the efficacy and risks of volume-staged stereotactic radiosurgery (VS-SRS) for AVM. **METHODS:** Retrospective study of 34 AVM patients having VS-SRS between 1997 and 2012. A median of 2 stages (range, 2-4) was used to treat a median AVM volume of 22.2 cm<sup>3</sup> (range, 7.4-56.7). The median AVM margin dose was 16 Gy (range, 14-18); the median radiosurgery-based AVM score was 2.81 (range, 1.54-6.45). The median follow-up after VS-SRS was 8.2 years (range, 3-13.3). **RESULTS:** Nidus obliteration was noted in 18 patients (53%) after VS-SRS. The rate of obliteration was 14% at 3 years, 54% at 5 years, and 75% at 7 years. Six patients (18%) had 11 bleeds after VS-SRS. Two patients (6%) remained neurologically stable, 2 (6%) patients had significant deficits, and 2 patients (6%) died. The actuarial risk of a first bleed after VS-SRS was 6% at 1 year, 12% at 3 years, and 19% at 7 years. Six patients (18%) underwent repeat SRS; all achieved nidus obliteration for an overall cure rate of 71%. Two patients (6%) had a permanent ARE after VS-SRS or repeat SRS. **CONCLUSION:** VS-SRS permitted large volume intracranial AVM to be treated with a low rate of ARE. Further study is needed on dose escalation and decreasing the treatment volume per stage to determine if this will increase the rate of obliteration with this technique.

**[56] Stereotactic radiosurgery for Spetzler-Martin Grade III arteriovenous malformations: an international multicenter study.**

*Journal of neurosurgery.* 2017;126(3):859-871

Ding D, Starke RM, Kano H, Lee JY, Mathieu D, Pierce J, Huang PP, Feliciano C, Rodriguez-Mercado R, Almodovar L, Grills IS, Silva D, Abbassy M, Missios S, Kondziolka D, Barnett GH, Lunsford LD, Sheehan JP  
PMID: 27081906 DOI: 10.3171/2016.1.JNS152564

**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 cm<sup>3</sup>, 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 AVMs. 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.

**[57] Seizure outcomes after stereotactic radiosurgery for the treatment of cerebral arteriovenous malformations.**

*Journal of neurosurgery.* 2017;126(3):845-851

Ditty BJ, Omar NB, Foreman PM, Miller JH, Kicieliński KP, Fisher WS 3rd, Harrigan MR  
PMID: 27058198 DOI: 10.3171/2015.12.JNS152461

**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.

**[58] International multicenter cohort study of pediatric brain arteriovenous malformations. Part 1: Predictors of hemorrhagic presentation.**

*Journal of neurosurgery. Pediatrics.* 2017;19(2):127-135

Ding D, Starke RM, Kano H, Mathieu D, Huang PP, Feliciano C, Rodriguez-Mercado R, Almodovar L, Grills IS, Silva D, Abbassy M, Missios S, Kondziolka D, Barnett GH, Dade Lunsford L, Sheehan JP

PMID: 27911248 DOI: 10.3171/2016.9.PEDS16283

**OBJECTIVE:** Brain arteriovenous malformations (AVMs) are the most common cause of spontaneous intracranial hemorrhage in pediatric patients (age < 18 years). Since the cumulative lifetime risk of AVM hemorrhage is considerable in children, an improved understanding of the risk factors influencing hemorrhagic presentation may aid in the management of pediatric AVMs. The aims of this first of a 2-part multicenter, retrospective cohort study are to evaluate the incidence and determine the predictors of hemorrhagic presentation in pediatric AVM patients. **METHODS:** The authors analyzed pooled AVM radiosurgery data from 7 institutions participating in the International Gamma Knife Research Foundation (IGKRF). Patients younger than 18 years at the time of radiosurgery and who had at least 12 months of follow-up were included in the study cohort. Patient and AVM characteristics were compared between unruptured and ruptured pediatric AVMs. **RESULTS:** A total of 357 pediatric patients were eligible for analysis, including 112 patients in the unruptured and 245 patients in the ruptured AVM cohorts (69% incidence of hemorrhagic presentation). The annual hemorrhage rate prior to radiosurgery was 6.3%. Hemorrhagic presentation was significantly more common in deep locations (basal ganglia, thalamus, and brainstem) than in cortical locations (frontal, temporal, parietal, and occipital lobes) (76% vs 62%,  $p = 0.006$ ). Among the factors found to be significantly associated with hemorrhagic presentation in the multivariate logistic regression analysis, deep venous drainage (OR 3.2,  $p < 0.001$ ) was the strongest independent predictor, followed by female sex (OR 1.7,  $p = 0.042$ ) and smaller AVM volume (OR 1.1,  $p < 0.001$ ). **CONCLUSIONS:** Unruptured and ruptured pediatric AVMs have significantly different patient and nidus features. Pediatric AVM patients who possess 1 or more of these high-risk features may be candidates for relatively more aggressive management strategies.

**[59] International multicenter cohort study of pediatric brain arteriovenous malformations. Part 2: Outcomes after stereotactic radiosurgery.**

*Journal of neurosurgery. Pediatrics.* 2017;19(2):136-148

Starke RM, Ding D, Kano H, Mathieu D, Huang PP, Feliciano C, Rodriguez-Mercado R, Almodovar L, Grills IS, Silva D, Abbassy M, Missios S, Kondziolka D, Barnett GH, Dade Lunsford L, Sheehan JP

PMID: 27911249 DOI: 10.3171/2016.9.PEDS16284

**OBJECTIVE:** Pediatric patients (age < 18 years) harboring brain arteriovenous malformations (AVMs) are burdened with a considerably higher cumulative lifetime risk of hemorrhage than adults. Additionally, the pediatric population was excluded from recent prospective comparisons of intervention versus conservative management for unruptured AVMs. The aims of this multicenter, retrospective cohort study are to analyze the outcomes after stereotactic radiosurgery for unruptured and ruptured pediatric AVMs. **METHODS:** We analyzed and pooled AVM radiosurgery data from 7 participating in the International Gamma Knife Research Foundation. Patients younger than 18 years of age who had at least 12 months of follow-up were included in the study cohort. Favorable outcome was defined as AVM obliteration, no post-radiosurgical hemorrhage, and no permanently symptomatic radiation-induced changes (RIC). The post-radiosurgery outcomes of unruptured versus ruptured pediatric AVMs were compared, and statistical analyses were performed to identify predictive factors. **RESULTS:** The

overall pediatric AVM cohort comprised 357 patients with a mean age of 12.6 years (range 2.8-17.9 years). AVMs were previously treated with embolization, resection, and fractionated external beam radiation therapy in 22%, 6%, and 13% of patients, respectively. The mean nidus volume was 3.5 cm<sup>3</sup>, 77% of AVMs were located in eloquent brain areas, and the Spetzler-Martin grade was III or higher in 59%. The mean radiosurgical margin dose was 21 Gy (range 5-35 Gy), and the mean follow-up was 92 months (range 12-266 months). AVM obliteration was achieved in 63%. During a cumulative latency period of 2748 years, the annual post-radiosurgery hemorrhage rate was 1.4%. Symptomatic and permanent radiation-induced changes occurred in 8% and 3%, respectively. Favorable outcome was achieved in 59%. In the multivariate logistic regression analysis, the absence of prior AVM embolization ( $p = 0.001$ ) and higher margin dose ( $p < 0.001$ ) were found to be independent predictors of a favorable outcome. The rates of favorable outcome for patients treated with a margin dose  $\geq 22$  Gy vs  $< 22$  Gy were 78% (110/141 patients) and 47% (101/216 patients), respectively. A margin dose  $\geq 22$  Gy yielded a significantly higher probability of a favorable outcome ( $p < 0.001$ ). The unruptured and ruptured pediatric AVM cohorts included 112 and 245 patients, respectively. Ruptured AVMs had significantly higher rates of obliteration (68% vs 53%,  $p = 0.005$ ) and favorable outcome (63% vs 51%,  $p = 0.033$ ), with a trend toward a higher incidence of post-radiosurgery hemorrhage (10% vs 4%,  $p = 0.07$ ). The annual post-radiosurgery hemorrhage rates were 0.8% for unruptured and 1.6% for ruptured AVMs. **CONCLUSIONS:** Radiosurgery is a reasonable treatment option for pediatric AVMs. Obliteration and favorable outcomes are achieved in the majority of patients. The annual rate of latency period hemorrhage after radiosurgery for both ruptured and unruptured pediatric AVM patients conveys a significant risk until the nidus is obliterated.

**[60] Long-Term Outcomes of Single-Session Stereotactic Radiosurgery for Cerebellar Arteriovenous Malformation, with a Median Follow-Up of 10 Years.**

*World neurosurgery.* 2017;98:314-322

Hasegawa H, Hanakita S, Shin M, Shojima M, Koga T, Takahashi W, Sakuramachi M, Nomoto AK, Saito N

PMID: 27826088 DOI: 10.1016/j.wneu.2016.10.137

**OBJECTIVE:** Cerebellar arteriovenous malformation (C-AVM) is poorly tolerated because of its aggressive natural history. The aim of this study was to delineate long-term outcomes of Gamma Knife stereotactic radiosurgery (GKRS) for C-AVM. **METHODS:** The outcomes of 45 patients who underwent GKRS for C-AVMs at our institution were retrospectively analyzed. Event-free survival was defined as free from any neurologic deficits caused by AVMs or adverse phenomena from the treatment. **RESULTS:** The median age and follow-up were 41 years (range, 6-77 years) and 120 months (range, 5-291 months), respectively. The median volume and Pollock-Flickinger radiosurgical AVM score were 1.3 cm<sup>3</sup> (range, 0.1-8.3 cm<sup>3</sup>) and 1.26 (range, 0.5-2.06), respectively. Actuarial obliteration rates were 46%, 75%, and 90% at 3, 5, and 6 years, respectively. Multivariate analysis showed that the maximal diameter  $\leq 15$  mm ( $P = 0.021$ ) and margin dose  $> 20$  Gy ( $P = 0.0008$ ) were significantly associated with better obliteration. Four patients experienced posttreatment hemorrhages, and annual hemorrhage rates were 1.9% and 0.30% before and after obliteration, respectively. One patient died because of hemorrhage, whereas the other 3 patients spontaneously recovered. Perifocal edema was confirmed in 8 (16%); however, no symptomatic edema was observed. Overall, neurologic deteriorations were noted in 4 patients; 3 were because of posttreatment hemorrhage, and 1 was because of pretreatment angiography. The event-free survival rates were 96%, 93%, and 93% at 4, 10, and 15 years, respectively. **CONCLUSIONS:** GKRS is a reasonable intervention for C-AVMs. Symptomatic complications are rare, and the long-term outcomes are favorable.

**[61] Estimating the Risks of Adverse Radiation Effects After Gamma Knife Radiosurgery for Arteriovenous Malformations.**

*Stroke.* 2017;48(1):84-90

Kano H, Flickinger JC, Tonetti D, Hsu A, Yang HC, Flannery TJ, Niranjana A,

Lunsford LD

PMID: 27899758 DOI: 10.1161/STROKEAHA.116.014825

**BACKGROUND AND PURPOSE:** We evaluated risk factors associated with the development of adverse radiation effects (ARE) after stereotactic radiosurgery (SRS) for cerebral arteriovenous malformations (AVMs). **METHODS:** We evaluated 755 patients with AVM who underwent a single Gamma Knife SRS procedure with at least a 2-year minimum follow-up. Eighty-seven patients (12%) underwent previous resection and 128 (17%) had previous embolization. The median target volume was 3.6 mL (range, 0.1-26.3 mL). The median margin dose was 20 Gy (range, 13-27 Gy). **RESULTS:** Fifty-five patients (7%) developed symptomatic ARE at a median follow-up of 75 months. The cumulative rates of symptomatic ARE were 3.2%, 5.8%, 6.7%, and 7.5% at 1, 2, 3, and 5 years, respectively. Factors associated with a higher rate of developing symptomatic ARE included larger AVM volume, higher margin dose, larger 12-Gy volume, higher Spetzler-Martin grade, and higher radiosurgery-based score. The rates of developing symptomatic ARE were higher in the brain stem (22%) or thalamus (16%), compared with AVMs located in other brain locations (4%-8%). Nineteen patients (3%) sustained irreversible new neurological deficits related to ARE, and 1 patient died. The rates of irreversible symptomatic ARE were 0.8%, 1.9%, 2.1%, and 2.8% at 1, 2, 3, and 5 years, respectively. The 5-year cumulative rates of irreversible symptomatic ARE were 9.1% in thalamus, 12.1% in brain stem, and 1.4% in other locations. **CONCLUSIONS:** The knowledge of ARE risk rates after AVM radiosurgery can assist informed consent for patients with AVM, their families, and healthcare providers.

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

*Journal of neurosurgery.* 2017;126(1):36-44

Starke RM, Kano H, Ding D, Lee JY, Mathieu D, Whitesell J, Pierce JT, Huang PP, Kondziolka D, Yen CP, Feliciano C, Rodriguez-Mercado R, Almodovar L, Pieper DR, Grills IS, Silva D, Abbassy M, Missios S, Barnett GH, Lunsford LD, Sheehan JP  
PMID: 26943847 DOI: 10.3171/2015.9.JNS151311

**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 cm<sup>3</sup>. 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 nidus 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.

## 2016

[63] Worse Outcomes After Repeat vs Initial Stereotactic Radiosurgery for Cerebral Arteriovenous Malformations: A Retrospective Matched-Cohort Study. *Neurosurgery.* 2016;79(5):690-700

Ding D, Xu Z, Shih HH, Starke RM, Yen CP, Cohen-Inbar O, Sheehan JP  
PMID: 27759676 DOI: 10.1227/NEU.0000000000001409

**BACKGROUND:** Incompletely obliterated cerebral 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 specified. **OBJECTIVE:** To retrospectively compare in matched cohorts the outcomes of repeat vs initial SRS for the treatment of matched cohorts with angioarchitecturally similar AVMs. **METHODS:** We studied a data set of patients with AVM treated with radiosurgery during the period spanning 1989 to 2013. Patients with AVM who underwent repeat SRS with radiologic follow-up of  $\geq 2$  years or nidus obliteration were identified for the study and matched, in a 1:1 fashion that was blinded to outcome, to patients with previously untreated AVMs who underwent initial SRS. Statistical analyses were performed to compare the outcomes after repeat vs initial SRS. **RESULTS:** The matching approach resulted in 84 patients for the repeat and the initial SRS cohort (mean margin doses, 20.7 and 20.9 Gy, respectively;  $P = .74$ ). In the repeat SRS cohort, obliteration was achieved in 67%; the radiologic, symptomatic, and permanent radiation-induced change rates were 35%, 10%, and 4%, respectively; and the post-SRS hemorrhage rate was 3.1%/y. Compared with the initial SRS cohort, the repeat SRS cohort had significantly lower obliteration rates ( $P = .04$ ) and higher post-SRS hemorrhage rates ( $P = .04$ ). The radiation-induced change 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. **ABBREVIATIONS:** AVM, arteriovenous malformation; RIC, radiation-induced change; RBAS, radiosurgery-based arteriovenous malformation score; SRS, stereotactic radiosurgery; VRAS, virginia radiosurgery AVM scale.

[64] Delayed cyst formations and/or expanding hematomas developing after Gamma Knife surgery for cerebral arteriovenous malformations.

*Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia.* 2016;33:96-99

Nakajima H, Yamanaka K, Ishibashi K, Iwai Y  
PMID: 27430414 DOI: 10.1016/j.jocn.2016.01.044

The authors retrospectively analyzed cyst formations and expanding haematomas (EHs) that developed after Gamma Knife surgery (GKS) for arteriovenous malformations (AVMs), and evaluated the treatment results of these lesions. Cyst formations and/or EHs which developed after GKS for AVMs were identified in 20 patients (5.0%) out of 404 patients who underwent this procedure. There were nine patients with cyst formations, two with EHs and nine with cyst formations with EHs. These lesions developed between 36 and 192 months (median 99 months) after GKS. The median nidus volume was 4.7 ml (range, 1.8-14.2 ml) and the median prescribed margin dose was 20 Gy (range, 15-23 Gy). The multivariate analysis showed no correlation between the appearance of cyst formations and/or EHs and the patients' age, sex, nidus volume, margin dose, repeated GKS, nidus obliteration, pre-GKS embolization and prior hemorrhage. Surgical treatment was required in nine patients. Eight patients had total removal of the angiomatous lesions (EHs or nodular lesions that were detected as enhancement part on MRI) via a craniotomy and one had a cyst aspiration. There was no recurrence of the lesions in all the patients that underwent a craniotomy. In the patient treated with a cyst aspiration, regrowth of the cyst formation occurred. Surgical treatment should be considered for symptomatic lesions and we recommend total removal of the angiomatous lesions to achieve a complete cure.

**[65] Late morphological changes after radiosurgery of brain arteriovenous malformations: an MRI study.**

*Acta neurochirurgica.* 2016;158(9):1683-90

Malikova H, Koubaska E, Vojtech Z, Weichet J, Syrucek M, Sroubek J, Rulseh A, Liscak R

PMID: 27368701 DOI: 10.1007/s00701-016-2876-3

**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.

**[66] Multimodality Management of Cerebral Arteriovenous Malformations with Special Reference to AVM-Related Hemorrhages During Ongoing Staged Treatment.**

*Acta neurochirurgica. Supplement.* 2016;123:153-8

Gruber A, Bavinzski G, Kitz K, Barthelmes S, Mayr M, Knosp E

PMID: 27637643 DOI: 10.1007/978-3-319-29887-0\_22

In this study we report and analyze the results of a multimodality management concept for intracranial arteriovenous malformations (AVMs), including microsurgery, embolization, and gamma knife radiosurgery. The study population consists of a consecutive series of 294 patients treated for 304 intracranial AVMs over a 10-year period.

**[67] Time-Staged Gamma Knife Stereotactic Radiosurgery for Large Cerebral Arteriovenous Malformations: A Preliminary Report.**

*PloS one.* 2016;11(11):e0165783

Park HR, Lee JM, Kim JW, Han JH, Chung HT, Han MH, Kim DG, Paek SH

PMID: 27806123 DOI: 10.1371/journal.pone.0165783

**OBJECTIVE:** We retrospectively analyzed our experience with time-staged gamma knife stereotactic radiosurgery (GKS) in treating large arteriovenous malformation (AVM);  $\geq 10$  cm<sup>3</sup>. **METHODS:** Forty-five patients who underwent time-staged GKS (2-stage,  $n = 37$ ; 3-stage,  $n = 8$ ) between March 1998 and December 2011 were included. The mean volume treated was 20.42 +/- 6.29 cm<sup>3</sup> (range, 10.20-38.50 cm<sup>3</sup>). Obliteration rates of AVMs and the associated complications after GKS were evaluated. **RESULTS:** Mean AVM volume (and median marginal dose) at each GKS session in the 37 patients who underwent 2-stage GKS was 19.67 +/- 6.08 cm<sup>3</sup> (13 Gy) at session 1 and 6.97 +/- 6.92 cm<sup>3</sup> (17 Gy) at session 2. The median interval period was 39 months. After follow-up period of 37 months, the complete obliteration rate was 64.9%. The mean AVM volume (and median marginal dose) at each GKS session in the 8 patients who

underwent 3-stage GKS was 23.90 +/- 6.50 cm<sup>3</sup> (12.25 Gy), 19.43 +/- 7.46 cm<sup>3</sup> (13.5 Gy), 7.48 +/- 6.86 cm<sup>3</sup> (15.5 Gy) at session 1, 2, and 3, respectively. The median interval duration between each GKS session was 37.5 and 38 months, respectively. After a median follow-up period of 47.5 months, 5 patients (62.5%) achieved complete obliteration. Postradiosurgical hemorrhage developed in 5 patients (11.1%) including one case of major bleeding and 4 cases of minor bleeding. No patient suffered from clinically symptomatic radiation necrosis following radiation.

**CONCLUSION:** Time-staged GKS could be an effective and safe treatment option in the management of large AVMs.

**[68] Risk Reduction of Cerebral Stroke After Stereotactic Radiosurgery for Small Unruptured Brain Arteriovenous Malformations.**

*Stroke.* 2016;47(5):1247-52

Hanakita S, Shin M, Koga T, Igaki H, Saito N

PMID: 27073242 DOI: 10.1161/STROKEAHA.116.013132

**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.

**[69] Stereotactic Radiosurgery for Arteriovenous Malformations: The Effect of Treatment Period on Patient Outcomes.**

*Neurosurgery.* 2016;78(4):499-509

Pollock BE, Link MJ, Stafford SL, Garces YI, Foote RL

PMID: 26990410 DOI: 10.1227/NEU.0000000000001085

**BACKGROUND:** Stereotactic radiosurgery (SRS) has been performed on patients with cerebral arteriovenous malformations (AVMs) for over 40 years.

**OBJECTIVE:** To evaluate the impact of treatment period on obliteration, intracranial hemorrhage (ICH), and radiation-induced complications (RICs).

**METHODS:** Retrospective comparison of 381 AVM patients having SRS during a 20-year period (group 1, January 1990 through March 1997,  $n = 160$ ; group 2, April 1997 through December 2009,  $n = 221$ ). The median radiological and clinical follow-up after initial SRS was 77 months and 93 months, respectively. **RESULTS:** Obliteration was 59.1% at 4 years and 85.1% at 8 years. Obliteration was more common in patients with hemispheric or cerebellar AVMs ( $P = .001$ ), smaller prescription isodose volume (PIV) ( $P < .001$ ), and group 1 patients ( $P < .001$ ). The ICH rate was 7.7% at 4 years and 10.6% at 8 years. ICH was more common in older patients ( $P = .02$ ), patients with deep AVM ( $P = .01$ ), and larger PIV ( $P < .001$ ). There was no difference in the ICH rate between the treatment groups ( $P = .18$ ). The rate of permanent RICs was 4.4% at 4 years and 8.6% at 8 years. RICs were more common with larger PIVs ( $P < .001$ ) and group 1 patients ( $P = .02$ ). There was no difference in the number of patients having obliteration without new deficits

between the 2 treatment periods (68.8% vs 73.3%,  $P = .33$ ). **CONCLUSION:** Advances in SRS procedures over the past 20 years have resulted in a lower risk of RIC, but fewer patients had AVM obliteration. Increasing the prescription dose for patients with medium- and large-volume AVMs by using current conformal dose-planning techniques may improve the obliteration rate while maintaining a low risk of RICs.

**[70] Microsurgical Resection for Persistent Arteriovenous Malformations Following Gamma Knife Radiosurgery: A Case-Control Study.**

*World neurosurgery.* 2016;88:277-288

Tong X, Wu J, Pan J, Lin F, Cao Y, Zhao Y, Wang S, Zhao J  
PMID: 26805683 DOI: 10.1016/j.wneu.2016.01.027

**OBJECTIVE:** To explore outcomes after microsurgery of brain arteriovenous malformations (AVMs) that failed to be obliterated by Gamma Knife radiosurgery (GKRS). **METHODS:** From January 2000 to January 2014, 42 consecutive patients underwent surgical resection of persistent AVMs after GKRS. These 42 patients with AVMs who underwent radiosurgery (radiosurgery group) were individually matched with 42 patients with AVMs who did not undergo radiosurgery (no radiosurgery group) based on patient and AVM characteristics. The modified Rankin Scale was used to assess neurologic status of patients. The effects of GKRS on AVM resection and surgical outcomes were analyzed. **RESULTS:** After GKRS, the mean AVM volume was significantly reduced by 76.8% ( $P < 0.01$ ), the size was reduced by 41% ( $P < 0.01$ ), and the Spetzler-Martin grade was reduced in 61.9% of the patients ( $P < 0.01$ ). During the time interval from radiosurgery to surgical resection, subsequent hemorrhages led to significant neurologic deterioration ( $P = 0.046$ ). Compared with the control group, the frequency of preoperative embolization, operative time, and blood loss were significantly lower in the radiosurgery group (all  $P < 0.05$ ). The no radiosurgery group had a significantly higher rate of worsening in mRS scores at 6 months after surgery (40.5% vs. 16.7%,  $P = 0.029$ ). Good neurologic status (mRS score  $< 3$ ) was achieved in 81% of the radiosurgery group and 83% of the no radiosurgery group at the final follow-up evaluation. **CONCLUSIONS:** GKRS performed several years before microsurgical resection can facilitate resectability of AVMs and decrease the rate of postoperative neurologic deterioration. For patients with persistent AVMs several years after GKRS, microsurgical resection is recommended to achieve good clinical outcomes.

**[71] Gamma Knife surgical treatment for partially embolized cerebral arteriovenous malformations.**

*Journal of neurosurgery.* 2016;124(3):767-76

Huo X, Jiang Y, Lv X, Yang H, Zhao Y, Li Y  
PMID: 26252461 DOI: 10.3171/2015.1.JNS142711

**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<sup>3</sup> and 10 cm<sup>3</sup>. **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<sup>3</sup>. The median volume and margin dose for GKS were 10.92 cm<sup>3</sup> 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<sup>3</sup>, 3-10 cm<sup>3</sup>, and more than 10 cm<sup>3</sup>. 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.

**[72] Radiosurgery for Cerebral Arteriovenous Malformations with Associated Arterial Aneurysms.**

*World neurosurgery.* 2016;87:77-90

Ding D, Xu Z, Starke RM, Yen CP, Shih HH, Buell TJ, Sheehan JP  
PMID: 26732956 DOI: 10.1016/j.wneu.2015.11.080

**OBJECTIVE:** The radiosurgical outcomes for cerebral arteriovenous malformations (AVM) with AVM-associated arterial aneurysms (AAA) are poorly understood, because many AAAs are embolized before nidus 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 prenidus (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 prenidus AAAs do not significantly affect AVM radiosurgical outcomes. Occlusion of distal prenidus AAAs commonly occurs after radiosurgery. These findings may support a more conservative stance for embolization before radiosurgery for AVMs with AAAs.

**[73] Angioarchitecture and Posttreatment Magnetic Resonance Imaging Characteristics of Brain Arteriovenous Malformations and Long-Term Seizure Control After Radiosurgery.**

*World neurosurgery.* 2016;87:277-82

Wu CC, Guo WY, Chung WY, Wu HM  
PMID: 26548816 DOI: 10.1016/j.wneu.2015.10.070

**OBJECTIVE:** To corroborate which pretreatment angioarchitectural characteristics and posttreatment magnetic resonance imaging (MRI) features were associated with better seizure and antiepileptic drug outcomes in patients with brain arteriovenous malformations (AVMs) treated by Gamma Knife radiosurgery. **METHODS:** During the period 2007-2010, 220 patients with intracranial AVMs undergoing radiosurgery at our hospital were evaluated. Imaging features on digital subtraction angiography and follow-up MRI, medical records, and direct patient interview were retrospectively assessed. Seizure outcome was assessed using the Engel classification and the status of antiepileptic drug use. **RESULTS:** At the last follow-up, 21 of 31 patients (68%) who met the recruitment criteria had

AVM obliteration on digital subtraction angiography or MRI. Seizure-free status (Engel class 1) was achieved in 20 patients (65%), and 13 of 20 (65%) seizure-free patients were medication-free. The presence of total obliteration at last imaging follow-up ( $P = 0.013$ ), absent retrograde cortical veins on digital subtraction angiography before GKRS ( $P = 0.013$ ), nidus  $<3.7$  cm ( $P = 0.006$ ), and lower modified radiosurgery-based AVM score ( $P = 0.026$ ) were significant predictors of seizure-free outcome. The strongest independent predictor of seizure-free status was absence of retrograde veins (odds ratio = 9.9). No angioarchitectural feature, post-radiosurgery imaging finding on MRI, or radiosurgical treatment parameter was a significant predictor of seizure control or cessation of medication in seizure-free patients. **CONCLUSIONS:** This study suggests that radiosurgery provides favorable outcomes in patients with AVM-related epilepsy. Patients with intracranial AVMs can benefit from seizure control after GKRS before undergoing AVM obliteration. Absence of retrograde veins is associated with better seizure-free outcomes, regardless of the parenchymal changes after radiosurgery.

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

*Stroke.* 2016;47(2):342-9

Ding D, Starke RM, Kano H, Mathieu D, Huang P, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Almodovar L, Grills IS, Silva D, Abbassy M, Missios S, Barnett GH, Lunsford LD, Sheehan JP  
PMID: 26658441 DOI: 10.1161/STROKEAHA.115.011400

**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  $\geq 12$  months of follow-up were screened for ARUBA eligibility criteria. Favorable outcome was defined as AVM obliteration, no post-radiosurgery 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 post-radiosurgery 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.

**[75] Volume-staged radiosurgery for large arteriovenous malformations: an evolving paradigm.**

*Journal of neurosurgery.* 2016;124(1):163-74

Seymour ZA, Sneed PK, Gupta N, Lawton MT, Molinaro AM, Young W, Dowd CF, Halbach VV, Higashida RT, McDermott MW  
PMID: 26140495 DOI: 10.3171/2014.12.JNS141308

**OBJECTIVE:** Large arteriovenous malformations (AVMs) remain difficult to treat, and ideal treatment parameters for volume-staged stereotactic radiosurgery (VS-SRS) are still unknown. The object of this study was to compare VS-SRS treatment outcomes for AVMs larger than 10 ml during 2 eras; Era 1 was 1992-March 2004, and Era 2 was May 2004-2008. In Era 2 the authors prospectively decreased the

AVM treatment volume, increased the radiation dose per stage, and shortened the interval between stages. **METHODS:** All cases of VS-SRS treatment for AVM performed at a single institution were retrospectively reviewed. **RESULTS:** Of 69 patients intended for VS-SRS, 63 completed all stages. The median patient age at the first stage of VS-SRS was 34 years (range 9-68 years). The median modified radiosurgery-based AVM score (mRBAS), total AVM volume, and volume per stage in Era 1 versus Era 2 were 3.6 versus 2.7, 27.3 ml versus 18.9 ml, and 15.0 ml versus 6.8 ml, respectively. The median radiation dose per stage was 15.5 Gy in Era 1 and 17.0 Gy in Era 2, and the median clinical follow-up period in living patients was 8.6 years in Era 1 and 4.8 years in Era 2. All outcomes were measured from the first stage of VS-SRS. Near or complete obliteration was more common in Era 2 (log-rank test,  $p = 0.0003$ ), with 3- and 5-year probabilities of 5% and 21%, respectively, in Era 1 compared with 24% and 68% in Era 2. Radiosurgical dose, AVM volume per stage, total AVM volume, era, compact nidus, Spetzler-Martin grade, and mRBAS were significantly associated with near or complete obliteration on univariate analysis. Dose was a strong predictor of response (Cox proportional hazards,  $p < 0.001$ , HR 6.99), with 3- and 5-year probabilities of near or complete obliteration of 5% and 16%, respectively, at a dose  $< 17$  Gy versus 23% and 74% at a dose  $\geq 17$  Gy. Dose per stage, compact nidus, and total AVM volume remained significant predictors of near or complete obliteration on multivariate analysis. Seventeen patients (25%) had salvage surgery, SRS, and/or embolization. Allowing for salvage therapy, the probability of cure was more common in Era 2 (log-rank test,  $p = 0.0007$ ) with 5-year probabilities of 0% in Era 1 versus 41% in Era 2. The strong trend toward improved cure in Era 2 persisted on multivariate analysis even when considering mRBAS (Cox proportional hazards,  $p = 0.055$ , HR 4.01, 95% CI 0.97-16.59). The complication rate was 29% in Era 1 compared with 13% in Era 2 (Cox proportional hazards, not significant). **CONCLUSIONS:** VS-SRS is an option to obliterate or downsize large AVMs. Decreasing the AVM treatment volume per stage to  $\leq 8$  ml with this technique allowed a higher dose per fraction and decreased time to response, as well as improved rates of near obliteration and cure without increasing complications. Reducing the volume of these very large lesions can facilitate a surgical approach for cure.

**[76] Stereotactic Radiosurgery for Partially Resected Cerebral Arteriovenous Malformations.**

*World neurosurgery.* 2016;85:263-72

Ding D, Xu Z, Shih HH, Starke RM, Yen CP, Sheehan JP  
PMID: 26459698 DOI: 10.1016/j.wneu.2015.10.001

**OBJECTIVE:** Incomplete microsurgical resection of cerebral arteriovenous malformations (AVM) occurs uncommonly. However, such patients harboring postoperative residual nidus 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  $\geq 2$  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 post-radiosurgery 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 post-radiosurgery 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.

## 2015

### [77] Leksell Gamma Knife for pediatric and adolescent cerebral arteriovenous malformations: results of 100 cases followed up for at least 36 months.

*Journal of neurosurgery. Pediatrics.* 2015;16(6):736-47

Nicolato A, Longhi M, Tommasi N, Ricciardi GK, Spinelli R, Foroni RI, Zivelonghi E, Zironi S, Dall'Oglio S, Beltramello A, Meglio M  
PMID: 26339954 DOI: 10.3171/2015.4.PEDS158

**OBJECTIVE:** The goal of this study was to evaluate advantages, risks, and failures of Gamma Knife radiosurgery (GKRS) in a large series of pediatric and adolescent patients with cerebral arteriovenous malformations (cAVMs) who were followed up for at least 36 months. **METHODS:** Since February 1993, 100 pediatric and adolescent patients ( $\leq 18$  years of age) with cAVMs have undergone GKRS at the authors' institution and were followed up for at least 36 months. Forty-six patients were boys and 54 were girls; the mean age was 12.8 years (range 3-18 years). Hemorrhage, either alone or combined with seizure, was the clinical onset in 70% of cases. The mean pre-GK cAVM volume was 2.8 ml; 92% of cAVMs were Spetzler-Martin (S-M) Grades I-III. Most lesions (94%) were in eloquent or deep-seated brain regions, according to S-M classification. The parameters for mean and range in treatment planning were prescription isodose 53.8% (40%-90%); prescription dose (PD) 20.2 Gy (9.0-26.4 Gy); maximal dose (MD) 37.8 Gy (18-50 Gy); and number of shots 4.7 (1-17). On the day of GKRS, stereotactic CT or stereotactic MRI and digital subtraction angiography were used. **RESULTS:** Obliteration rate (OR) was angiographically documented in 75 of 84 cases (89.3%) after single-session GKRS, with actuarial ORs at 3 and 5 years of 68.0% and 88.1%, respectively. A repeat treatment was performed in 7 patients (6 with obliteration), and 16 patients with cAVMs underwent staged treatment (9 of them were angiographically cured). Thus, the overall OR was 90%, with actuarial ORs at 3, 5, and 8 years of 59.0%, 76.0%, and 85.0%, respectively. Permanent symptomatic GK-related complications were observed in 11% of cases, with surgical removal of enlarged mass seen on post-RS imaging needed in 5 cases. Hemorrhage during the latency period occurred in 9% of patients, but surgical evacuation of the hematoma was required in only 1 patient. One patient died due to rebleeding of a brainstem cAVM. Radiosurgery outcomes varied according to cAVM sizes and doses: volumes  $\leq 10$  ml and PDs  $> 16$  Gy were significantly associated with higher ORs and lower rates of permanent complication and bleeding during the latency period. **CONCLUSIONS:** The data from this study reinforce the conclusion that GKRS is a safe and effective treatment for pediatric and adolescent cAVMs, yielding a high OR with minimal permanent severe morbidity and no mortality. The very low frequency of severe hemorrhages during the latency period further encourages a widespread application of RS in such patients. Univariate analysis found that modified RS-based cAVM score, nidus volume, PD, integral dose, S-M grade, and preplanned treatment (the last 2 parameters were also confirmed on multivariate analysis) significantly influenced OR. Lower S-M grades and single-session planned treatments correlated with shorter treatment obliteration interval on univariate analysis. This statistical analysis suggests that a staged radiosurgical treatment should be planned when nidus volume  $> 10$  ml and/or when the recommended PD is  $\leq 16$  Gy.

### [78] A quantitative analysis of adverse radiation effects following Gamma Knife radiosurgery for arteriovenous malformations.

*Journal of neurosurgery.* 2015;123(4):945-53

Cohen-Inbar O, Lee CC, Xu Z, Schlesinger D, Sheehan JP  
PMID: 25909572 DOI: 10.3171/2014.10.JNS142264

**OBJECTIVE:** 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  $\geq$  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.

### [79] Radiosurgery for temporal lobe arteriovenous malformations: effect of temporal location on seizure outcomes.

*Journal of neurosurgery.* 2015;123(4):924-34

Ding D, Quigg M, Starke RM, Xu Z, Yen CP, Przybylowski CJ, Dodson BK, Sheehan JP  
PMID: 25884262 DOI: 10.3171/2014.10.JNS141807

**OBJECTIVE:** 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 cm<sup>3</sup>, 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.

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

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

Oermann EK, Ding D, Yen CP, Starke RM, Bederson JB, Kondziolka D, Sheehan JP  
PMID: 25875580 DOI: 10.1227/NEU.0000000000000772

**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.

[81] Radiosurgery for Cerebral Arteriovenous Malformations in Elderly Patients: Effect of Advanced Age on Outcomes After Intervention.

*World neurosurgery.* 2015;84(3):795-804

Ding D, Xu Z, Yen CP, Starke RM, Sheehan JP  
PMID: 25997797 DOI: 10.1016/j.wneu.2015.05.012

**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,  $\geq 60$  years) with radiologic follow-up of  $\geq 2$  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.

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

*World neurosurgery.* 2015;84(3):653-62

Ding D, Quigg M, Starke RM, Yen CP, Przybylowski CJ, Dodson BK, Sheehan JP  
PMID: 26026628 DOI: 10.1016/j.wneu.2015.04.064

**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.

[83] Cerebral Arteriovenous Malformations and Epilepsy, Part 1: Predictors of Seizure Presentation.

*World neurosurgery.* 2015;84(3):645-52

Ding D, Starke RM, Quigg M, Yen CP, Przybylowski CJ, Dodson BK, Sheehan JP  
PMID: 25753234 DOI: 10.1016/j.wneu.2015.02.039

**OBJECTIVE:** Seizures are relatively common in patients harboring cerebral arteriovenous malformations (AVMs). Because 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 1989-2013, 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 1007 AVM patients included for analysis, 229 patients presented with seizures (22.7%). The incidence of seizure presentation was significantly higher in cortical than noncortical AVMs (33.1% vs. 6.6%,  $P < 0.0001$ ). Among 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.

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

*Journal of neurosurgery. Pediatrics.* 2015;16(2):222-31  
Hanakita S, Koga T, Shin M, Igaki H, Saito N  
PMID: 25955806 DOI: 10.3171/2015.1.PEDS14407

**OBJECTIVE:** 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  $\leq$  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.

[85] Stereotactic radiosurgery for arteriovenous malformations after Onyx embolization: a case-control study.

*Journal of neurosurgery.* 2015;123(1):126-35  
Lee CC, Chen CJ, Ball B, Schlesinger D, Xu Z, Yen CP, Sheehan J  
PMID: 25658780 DOI: 10.3171/2014.12.JNS141437

**OBJECTIVE:** Onyx, an ethylene-vinyl alcohol copolymer mixed in a dimethyl sulfoxide solvent, is currently one of the most widely used liquid materials for embolization of intracranial arteriovenous malformations (AVMs). The goal of this study was to define the risks and benefits of stereotactic radiosurgery (SRS) for patients who have previously undergone partial AVM embolization with Onyx. **METHODS:** Among a consecutive series of 199 patients who underwent SRS between January 2007 and December 2012 at the University of Virginia, 25 patients had Onyx embolization prior to SRS (the embolization group). To analyze the obliteration rates and complications, 50 patients who underwent SRS without prior embolization (the no-embolization group) were matched by propensity score method. The matched variables included age, sex, nidus volume before SRS, margin dose, Spetzler-Martin grade, Virginia Radiosurgery AVM Scale score, and median imaging follow-up period. **RESULTS:** After Onyx embolization, 18 AVMs were reduced in size. Total obliteration was achieved in 6 cases (24%) at a median of 27.5 months after SRS. In the no-embolization group, total obliteration was achieved in 20 patients (40%) at a median of 22.4 months after SRS. Kaplan-Meier analysis demonstrated obliteration rates of 17.7% and 34.1% in the embolization group at 2 and 4 years, respectively. In the no-embolization group, the corresponding obliteration rates were 27.0% and 55.9%. The between-groups difference in obliteration rates after SRS did not achieve statistical significance. The difference in complications, including adverse radiation effects, hemorrhage episodes, seizure control, and patient mortality also did not reach statistical significance. **CONCLUSIONS:** Onyx embolization can effectively reduce the size of many AVMs. This case-control study did not show any statistically significant difference in the rates of embolization or complications after SRS in patients who had previously undergone Onyx embolization and those who had not.

[86] Clinical outcome and complications of gamma knife radiosurgery for intracranial arteriovenous malformations.

*Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia.* 2015;22(7):1117-22  
Bir SC, Ambekar S, Maiti TK, Nanda A  
PMID: 25840878 DOI: 10.1016/j.jocn.2014.12.017

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.

[87] Combined treatment of brain AVMs by Onyx embolization and gamma knife radiosurgery decreased hemorrhage risk despite low obliteration rate.

*Turkish neurosurgery.* 2015;25(1):100-10  
Huo X, Li Y, Wu Z, Jiang Y, Yang H, Zhao Y  
PMID: 25640553 DOI: 10.5137/1019-5149.JTN.10708-14.1

**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.

[88] Effect of prior hemorrhage on intracranial arteriovenous malformation radiosurgery outcomes.

*Cerebrovascular diseases (Basel, Switzerland).* 2015;39(1):53-62  
Ding D, Yen CP, Starke RM, Xu Z, Sheehan JP  
PMID: 25547253 DOI: 10.1159/000369959

**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<sup>3</sup>) versus ruptured AVMs 3.5 cm<sup>3</sup>,  $p = 0.195$ ), 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.

#### [89] Radiosurgery for Large Arteriovenous Malformations as a Single-Session or Staged Treatment.

*Stereotactic and functional neurosurgery.* 2015;93(5):342-7

Chytka T, Liscak R, Kozubikova P, Vymazal J

PMID: 26355435 DOI: 10.1159/000439116

**BACKGROUND/OBJECTIVES:** The treatment of large arteriovenous malformations (AVMs) presents a challenge and the effectiveness of radiosurgery decreases with increasing treatment volume. Here, we analyzed and compared single-session treatment for AVMs >15 cm<sup>3</sup> with staged treatment, when the volume of a large AVM was divided into 2 or more compartments, which were subsequently treated at intervals of a few months. In the event that complete obliteration was not achieved within 3 years, repeat radiosurgery was considered. **METHODS/RESULTS:** Between 1993 and 2011, gamma-knife radiosurgery was performed on 50 patients with large AVMs. A total of 27 of them, with volumes ranging from 15.1 to 27 cm<sup>3</sup> (median = 17.8), were treated in a single session, with a marginal dose ranging from 10 to 17 Gy (median = 15). Complete obliteration was achieved in 7 (26%) of these; in 14 patients the treatment was repeated after a median of 38 months. The volume of AVMs subjected to repeat treatment regressed and ranged from 6.76 to 16.4 cm<sup>3</sup> (median = 7.7), with the marginal dose ranging from 13 to 18 Gy (median = 17); 10 patients later achieved complete obliteration at a median of 79 months after the initial treatment. Overall, 63% of patients achieved complete obliteration of AVM after treatment. Rebleeding in a latent period was recorded in 3 patients (11%) and symptomatic collateral edema in 2 (7%); 23 patients were treated using the staged method, with the interval between staged treatments usually being 6 months. Their overall AVM volume ranged from 13.2 to 46.6 cm<sup>3</sup> (median = 23.3), the volume for a single

stage ranged from 4.5 to 31.3 cm<sup>3</sup> (median 11.7), and the marginal dose ranged from 10 to 18 Gy (median = 17). Complete obliteration was achieved in 4 (17%) of them, in 8 patients the treatment was repeated at a median of 53 months after the first treatment, and a third retreatment was performed on 2 patients 98 and 102 months, respectively, after the first treatment. The volume for repeated treatment of AVMs ranged from 0.81 to 7.7 cm<sup>3</sup> (median = 3.3), with the marginal dose ranging from 14 to 20 Gy (median 17.5). Of all the retreated patients, 5 AVMs subsequently achieved complete obliteration. Overall, 9 patients (39%) were totally cured. Rebleeding in a latent period was observed in 1 of these patients (4.3%) and symptomatic edema in another 1 (4.3%). **CONCLUSIONS:** Radiosurgery of large AVMs is a valuable treatment either as a single-session or staged treatment, with a reasonable chance of cure and a low risk of complications.

#### [90] Seizure and anticonvulsant outcomes following stereotactic radiosurgery for intracranial arteriovenous malformations.

*Journal of neurosurgery.* 2015;122(6):1299-305

Przybylowski CJ, Ding D, Starke RM, Yen CP, Quigg M, Dodson B, Ball BZ, Sheehan JP

PMID: 25614948 DOI: 10.3171/2014.11.JNS141388

**OBJECTIVE:** 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.

#### [91] Draining vein shielding in intracranial arteriovenous malformations during gamma-knife: a new way of preventing post gamma-knife edema and hemorrhage.

*Neurosurgery.* 2015;76(5):623-31; discussion 631-2

Bose R, Agrawal D, Singh M, Kale SS, Gopishankar N, Bisht RK, Sharma BS

PMID: 25635888 DOI: 10.1227/NEU.0000000000000660

**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.

**[92] Radiosurgery for unruptured cerebral arteriovenous malformations in pediatric patients.**

*Acta neurochirurgica.* 2015;157(2):281-91

Ding D, Xu Z, Yen CP, Starke RM, Sheehan JP

PMID: 25514868 DOI: 10.1007/s00701-014-2305-4

**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 cm<sup>3</sup> 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.

**[93] Stereotactic radiosurgery for arteriovenous malformations of the postgeniculate visual pathway.**

*Journal of neurosurgery.* 2015;122(2):433-40

Bowden G, Kano H, Caparosa E, Tonetti D, Niranjana A, Monaco EA 3rd, Flickinger J, Arai Y, Lunsford LD

PMID: 25423270 DOI: 10.3171/2014.10.JNS1453

**OBJECTIVE:** 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 cm<sup>3</sup> (range 0.4-22 cm<sup>3</sup>), 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 cm<sup>3</sup> 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  $\geq 22$  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.

**[94] Targeted embolization reduces hemorrhage complications in partially embolized cerebral AVM combined with gamma knife surgery.**

*Interventional neuroradiology : journal of peritherapeutic neuroradiology, surgical procedures and related neurosciences.* 2015;21(1):80-7

Xiaochuan H, Yuhua J, Xianli L, Hongchao Y, Yang Z, Youxiang L

PMID: 25934780 DOI: 10.15274/inr-2014-10090

This study investigated the effect and safety of targeted embolization in partially embolized cerebral arteriovenous malformation (AVM) followed by gamma knife surgery (GKS). We retrospectively analyzed 86 AVM patients who were targeted embolized by Onyx followed by GKS for residual nidus. Embolization-related complications were collected and the clinical effect was evaluated. During targeted embolization, intranidus or hemodynamic aneurysms and AVM-related fistula were evaluated and targeted embolized. Patients with AVM-related aneurysms and fistula were divided into a targeted embolization group and non-targeted embolization group based on the retrospectively determined treatment strategy. The effect of targeted embolization on hemorrhage risk was evaluated. The overall annual hemorrhage rate was 1.66% with 2.26% for ruptured AVMs and 1.08% for unruptured lesions. The annual mortality rate was 0.4%. Only one in 16 patients with embolization-related complications had permanent neurologic deficit. Twenty-four of 29 cases with intranidus aneurysms were targeted embolized, four of five cases with hemodynamic aneurysms were targeted embolized and eight of nine cases with arteriovenous fistula were targeted embolized. Chi square results showed the hemorrhage complications in the target embolization group were significantly lower than those in the non-target embolization group ( $p < 0.01$ ). Targeted embolization combined with GKS treatment decreased the annual hemorrhage rate and improved clinical outcome with low permanent complications in partially embolized AVMs. This method could be proposed for the treatment of large brain AVMs when a single-technique treatment is not feasible.

## 2014

**[95] Application of single-stage stereotactic radiosurgery for cerebral arteriovenous malformations >10 cm<sup>3</sup>.**

*Stroke.* 2014;45(12):3543-8

Hanakita S, Koga T, Shin M, Igaki H, Saito N

PMID: 25293662 DOI: 10.1161/STROKEAHA.114.007162

**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 cm(3) 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 cm(3) (+/-3.8 cm(3)), 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 cm(3), 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.

[96] [Gamma Knife surgery for arteriovenous malformations within or adjacent to the ventricles.](#)

*Journal of neurosurgery.* 2014;121(6):1416-23

Bowden G, Kano H, Yang HC, Niranjana A, Flickinger J, Lunsford LD

PMID: 24878292 DOI: 10.3171/2014.4.JNS131943

**OBJECTIVE:** 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 cm(3) (range 0.1-22 cm(3)), 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 periventricular AVMs.

[97] [Hemorrhage during pregnancy in the latency interval after stereotactic radiosurgery for arteriovenous malformations.](#)

*Journal of neurosurgery.* 2014;121 Suppl:226-31

Tonetti D, Kano H, Bowden G, Flickinger JC, Lunsford LD

PMID: 25434957 DOI: 10.3171/2014.7.GKS141297

**OBJECTIVE:** 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.

[98] [Is stereotactic radiosurgery the best treatment option for patients with a radiosurgery-based arteriovenous malformation score <math>\leq 1</math>?](#)

*World neurosurgery.* 2014;82(6):1144-7

Burrow AM, Link MJ, Pollock BE

PMID: 25014752 DOI: 10.1016/j.wneu.2014.07.009

**OBJECTIVE:** The best management of patients with brain arteriovenous malformations (BAVM) is controversial. The radiosurgery-based arteriovenous malformation (AVM) score (RBAS) was developed to predict outcomes for patients with BAVM having stereotactic radiosurgery (SRS). **METHODS:** The RBAS is calculated for patients with BAVM having SRS at our center as part of our prospectively maintained SRS database (RBAS = [0.1] [AVM volume; cm(3)] + [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 to 2009 identified 80 patients with a RBAS <math>\leq 1</math> and at least 1 year of follow-up. The primary end point of the study was a decline in modified Rankin Score. 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 cm(3) (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% confidence interval 84%-97%). No patient had a hemorrhage or a radiation-related complication after SRS. The observed rate of modified Rankin Score decrease after SRS was 0% (0/80; 95% confidence interval 0%-6%). **CONCLUSIONS:** SRS provided a high rate of obliteration at very low risk for patients with BAVM with a RBAS <math>\leq 1</math>. 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.

[99] Results for a series of 697 arteriovenous malformations treated by gamma knife: influence of angiographic features on the obliteration rate.

*Neurosurgery.* 2014;75(5):568-83; discussion 582-3; quiz 583  
Paul L, Casasco A, Kusak ME, Martinez N, Rey G, Martinez R  
PMID: 25050575 DOI: 10.1227/NEU.0000000000000506

**BACKGROUND:** Stereotactic radiosurgery (RS) is an effective tool in treating brain arteriovenous malformations (AVMs). Careful study of AVM angiographic characteristics may improve results. **OBJECTIVE:** To report the long-term outcomes of Gamma Knife RS (GKRS) in brain AVMs, focusing on how the angioarchitectural and hemodynamic parameters of AVMs affect the post-RS results. **METHODS:** This was a retrospective, longitudinal study of 697 consecutive GKRS treatments of brain AVMs in 662 patients performed at a single center between 1993 and 2005. The mean age of the patients was 37 years; the median AVM volume was 3.6 cm<sup>3</sup>; and the mean follow-up was 11 years. Forty-five percent of patients presented with intracranial hemorrhage; 44% underwent embolization; and 7% had multiple RSs. AVM characteristics in the RS-planning angiograms were analyzed, and their relationship to the post-RS obliteration rate was determined by univariate and multivariate analyses. **RESULTS:** The obliteration rate after a single RS was 69.3%; after multiple RS, it was 75%. Positive predictors of obliteration included compact nidus (odds ratio = 3.16; 95% confidence interval, 1.92-5.22), undilated feeders (odds ratio = 0.36; 95% confidence interval, 0.23-0.57), smaller AVM volume (odds ratio = 0.95; 95% confidence interval, 0.92-0.99), and higher marginal dose (odds ratio = 1.16; 95% confidence interval, 1.06-1.27). Improvement or clinical stability was observed in 89.3% of patients; postprocedural bleeding was noted in 6.1%; and clinical worsening attributable to RS was seen in 3.8%. The annual risk of hemorrhage in the 4 years after 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 undilated feeder arteries contribute to AVM occlusion by RS. GKRS can be regarded as the treatment of choice for AVMs <6 cm<sup>3</sup>, even after bleeding.

[100] Gamma Knife surgery for incidental cerebral arteriovenous malformations.

*Journal of neurosurgery.* 2014;121(5):1015-21  
Yen CP, Ding D, Cheng CH, Starke RM, Shaffrey M, Sheehan J  
PMID: 25148009 DOI: 10.3171/2014.7.JNS131397

**OBJECTIVE:** 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 cm<sup>3</sup> (median 3.2 cm<sup>3</sup>). 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.

[101] Outcomes following single-session radiosurgery for high-grade intracranial arteriovenous malformations.

*British journal of neurosurgery.* 2014;28(5):666-74  
Ding D, Yen CP, Starke RM, Xu Z, Sun X, Sheehan JP  
PMID: 24372542 DOI: 10.3109/02688697.2013.872227

**INTRODUCTION:** The management of Spetzler-Martin Grade-IV and -V arteriovenous malformations (AVMs) is controversial due to their uncertain natural history, the high rate of morbidity and mortality associated with microsurgical resection, and the relatively low rate of successful obliteration from less invasive approaches such as radiosurgery and embolization. We present our radiosurgical results for high-grade AVMs. **METHODS:** We identified all patients with Spetzler-Martin Grade-IV and -V AVMs treated with single-session radiosurgery at the University of Virginia between 1989 and 2009. Patients with less than 2 years of follow-up without obliteration were excluded. This yielded 110 patients with a median age 27.6 years. The median AVM volume was 5.7 cc and prescription dose was 19 Gy. The median radiographic and clinical follow-up intervals were 88 and 97 months, respectively. **RESULTS:** Complete AVM obliteration was identified on MRI only in 11 patients (10%) and confirmed by DSA in 38 patients (34%) for a cumulative obliteration rate of 44%. The actuarial rates of obliteration at 3 and 5 years were 10% and 23%, respectively. The mean and median times to obliteration were 60 months and 43 months, respectively. Significant independent predictors of obliteration were no pre-radiosurgery embolization (P = 0.008), superficial location (P = 0.001), and higher prescription dose (P = 0.028). The annual rate of post-radiosurgery hemorrhage was 3.0%, and symptomatic RIC was observed in 12% of patients. Unruptured AVMs were more likely to have RIC (P = 0.005). The rates of temporary and permanent post-radiosurgery clinical deterioration were 9% and 10%, respectively. **CONCLUSION:** Single-session radiosurgery is an acceptable treatment option for select patients harboring high-grade AVMs for which microsurgery or conservative management are associated with an unacceptably high risk of adverse outcomes.

[102] An updated assessment of the risk of radiation-induced neoplasia after radiosurgery of arteriovenous malformations.

*World neurosurgery.* 2014;82(3-4):395-401  
Starke RM, Yen CP, Chen CJ, Ding D, Mohila CA, Jensen ME, Kassell NF, Sheehan JP  
PMID: 23403354 DOI: 10.1016/j.wneu.2013.02.008

**OBJECTIVE:** Gamma Knife radiosurgery (GKRS) is a minimally invasive technique employed in the treatment of intracranial arteriovenous malformations (AVMs). Patients experience a low incidence of complications following treatment. As 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 University of Virginia, imaging and clinical outcomes of 1309 patients with intracranial AVMs treated with GKRS have been reviewed. AVM patients underwent magnetic resonance imaging (MRI) every 6 months for 2 years and then annually following GKRS. When the nidus were no longer visible on magnetic resonance imaging, angiography was performed to verify the obliteration of AVMs. Patients were thereafter recommended to continue MRIs every 3-5 years to detect any long-term complications. A subset of 812, 358, and 78 patients had neuroimaging 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 radiologic characteristics of a meningioma. As the lesions have shown no evidence of mass effect, they are being followed with serial neuroimaging. A third patient was found to have neurologic 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  $\geq 10$  years following GKRS. If we calculate rates based on a subset of 78 patients with neuroimaging and clinical follow-up of  $\leq 15$  years, the cumulative rate was 3.4%. These are the second, third, and fifth reported cases of radiation-induced tumors following GKRS for an AVM. **CONCLUSIONS:** Although radiosurgery is generally considered a safe modality in the treatment of AVMs, 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.

**[103] Deep arteriovenous malformations in the basal ganglia, thalamus, and insula: multimodality management, patient selection, and results.**

*World neurosurgery.* 2014;82(3-4):386-94

Potts MB, Jahangiri A, Jen M, Sneed PK, McDermott MW, Gupta N, Hetts SW, Young WL, Lawton MT

PMID: 24657255 DOI: 10.1016/j.wneu.2014.03.033

**OBJECTIVE:** This study sought to describe a single institution's experience treating arteriovenous malformations (AVMs) of the basal ganglia, thalamus, and insula in a multimodal fashion. **METHODS:** We conducted a retrospective review of all deep AVMs treated at our institution between 1997 and 2011 with attention to patient selection, treatment strategies, and radiographic and functional outcomes. **RESULTS:** A total of 97 patients underwent initial treatment at our institution. 64% presented with hemorrhage with 29% 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, whereas Spetzler-Martin score and time to follow-up were significantly associated with improved/unchanged functional status at time of last follow-up. Posttreatment 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 with SRS, and is associated with satisfactory results in carefully selected patients.

**[104] Smoking is a negative predictor of arteriovenous malformation posttreatment obliteration: analysis of vascular risk factors in 774 patients.**

*Neurosurgical focus.* 2014;37(3):E3

Dalyai R, Starke RM, Chalouhi N, Theofanis T, Busack C, Jabbour P, Gonzalez LF, Rosenwasser R, Tjoumakaris S

PMID: 25175441 DOI: 10.3171/20145.FOCUS14121

**OBJECTIVE:** 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.

**[105] Treatment and outcomes of ARUBA-eligible patients with unruptured brain arteriovenous malformations at a single institution.**

*Neurosurgical focus.* 2014;37(3):E8

Rutledge WC, Abila AA, Nelson J, Halbach VV, Kim H, Lawton MT

PMID: 25175446 DOI: 10.3171/2014.7.FOCUS14242

**OBJECTIVE:** Management of unruptured arteriovenous malformations (AVMs) is controversial. In the first randomized trial of unruptured AVMs (A Randomized Trial of Unruptured Brain Arteriovenous Malformations [ARUBA]), medically managed patients had a significantly lower risk of death or stroke and had better outcomes. The University of California, San Francisco (UCSF) was one of the participating ARUBA sites. While 473 patients were screened for eligibility, only 4 patients were enrolled in ARUBA. The purpose of this study is to report the treatment and outcomes of all ARUBA-eligible patients at UCSF. **METHODS:** The authors compared the treatment and outcomes of ARUBA-eligible patients using prospectively collected data from the UCSF brain AVM registry. Similar to ARUBA, they compared the rate of stroke or death in observed and treated patients and used the modified Rankin Scale to grade outcomes. **RESULTS:** Of 74 patients, 61 received an intervention and 13 were observed. Most treated patients had resection with or without preoperative embolization (43 [70.5%] of 61 patients). One of the 13 observed patients died after AVM hemorrhage. Nine of the 61 treated patients had a stroke or died. There was no significant difference in the rate of stroke or death (HR 1.34, 95% CI 0.12-14.53,  $p = 0.81$ ) or clinical impairment (Fisher's exact test,  $p > 0.99$ ) between observed and treated patients. **CONCLUSIONS:** The risk of stroke or death and degree of clinical impairment among treated patients was lower than reported in ARUBA. The authors found no significant difference in outcomes between observed and treated ARUBA-eligible patients at UCSF. Results in ARUBA-eligible patients managed outside that trial led to an entirely different conclusion about AVM intervention, due to the primary role of surgery, judicious surgical selection with established outcome predictors, and technical expertise developed at high-volume AVM centers.

**[106] Stereotactic radiosurgery for sylvian fissure arteriovenous malformations with emphasis on hemorrhage risks and seizure outcomes.**

*Journal of neurosurgery.* 2014;121(3):637-44

Bowden G, Kano H, Tonetti D, Niranjana A, Flickinger J, Arai Y, Lunsford LD

PMID: 24926653 DOI: 10.3171/2014.5.JNS132244

**OBJECTIVE:** 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 cm<sup>3</sup> (range 0.1-17.7 cm<sup>3</sup>), 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.

**[107] Stereotactic radiosurgery of intracranial arteriovenous malformations and the use of the K index in determining treatment dose.**

*Neurosurgical focus.* 2014;37(3):E15

Missios S, Bekelis K, Al-Shyal G, Rasmussen PA, Barnett GH  
PMID: 25175434 DOI: 10.3171/2014.7.FOCUS14157

**OBJECTIVE:** 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.

**[108] Gamma Knife radiosurgery for arteriovenous malformations in pediatric patients.**

*Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery.* 2014;30(9):1485-92

Borcek AO, Emmez H, Akkan KM, Ocal O, Kurt G, Aykol S, Karahacioglu E, Baykaner KM

PMID: 24972531 DOI: 10.1007/s00381-014-2469-5

**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<sup>3</sup>. 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.

**[109] Radiosurgery for low-grade intracranial arteriovenous malformations.**

*Journal of neurosurgery.* 2014;121(2):457-67

Ding D, Yen CP, Xu Z, Starke RM, Sheehan JP

PMID: 24605839 DOI: 10.3171/2014.1.JNS131713

**OBJECTIVE:** 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 cm<sup>3</sup> 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.

**[110] Radiosurgery for ruptured intracranial arteriovenous malformations.**

*Journal of neurosurgery.* 2014;121(2):470-81

Ding D, Yen CP, Starke RM, Xu Z, Sheehan JP

PMID: 24655098 DOI: 10.3171/2014.2.JNS131605

**OBJECTIVE:** 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 AVM 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 cm<sup>3</sup> 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.

#### [111] Radiosurgery for cerebellar arteriovenous malformations: does infratentorial location affect outcome?

*World neurosurgery.* 2014;82(1-2):e209-17

Ding D, Starke RM, Yen CP, Sheehan JP

PMID: 24530455 DOI: 10.1016/j.wneu.2014.02.007

**OBJECTIVE:** 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 mL 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 < .001). Obliteration was achieved in 72% of cerebellar AVMs. Younger age (P = .019), no preradiosurgery embolization (P < .001), and decreased volume (P = .034)

were independent predictors of obliteration. The annual risk of postradiosurgery hemorrhage in cerebellar AVMs was 1.3%. The rates of symptomatic and permanent radiation-induced changes were 7% and 3%, respectively. Compared with the matched supratentorial AVM cohort, there was no difference in the rates of obliteration, postradiosurgery hemorrhage, or symptomatic radiation-induced changes. **CONCLUSIONS:** Radiosurgery is an effective treatment modality for cerebellar AVMs with relatively limited adverse events. Infratentorial location did not affect radiosurgery outcomes.

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

*Journal of neurosurgery. Pediatrics.* 2014;14(1):1-11

Potts MB, Sheth SA, Louie J, Smyth MD, Sneed PK, McDermott MW, Lawton MT, Young WL, Hetts SW, Fullerton HJ, Gupta N

PMID: 24766309 DOI: 10.3171/2014.3.PEDS13381

**UNLABELLED: OBJECTIVE:** 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 cm<sup>3</sup> (range 0.09-62.3 cm<sup>3</sup>), 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.

#### [113] Long-term outcomes of gamma knife surgery for posterior fossa arteriovenous malformations.

*Neurologia medico-chirurgica.* 2014;54(10):799-805

Matsunaga S, Shuto T

PMID: 24418791 DOI: 10.2176/nmc.0a.2013-0090

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 cm<sup>3</sup>. 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 radiation-induced 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.

**[114] Radiosurgery for Spetzler-Martin Grade III arteriovenous malformations.**

*Journal of neurosurgery.* 2014;120(4):959-69

Ding D, Yen CP, Starke RM, Xu Z, Sun X, Sheehan JP

PMID: 24460487 DOI: 10.3171/2013.12.JNS131041

**OBJECTIVE:** 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 cm<sup>3</sup>, 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.

**[115] Stereotactic radiosurgery for Spetzler-Martin Grade III arteriovenous malformations.**

*Journal of neurosurgery.* 2014;120(4):973-81

Kano H, Flickinger JC, Yang HC, Flannery TJ, Tonetti D, Niranjan A, Lunsford LD

PMID: 24484227 DOI: 10.3171/2013.12.JNS131600

**OBJECTIVE:** 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.

**[116] Stereotactic radiosurgery for arteriovenous malformations of the cerebellum.**

*Journal of neurosurgery.* 2014;120(3):583-90

Bowden G, Kano H, Tonetti D, Niranjan A, Flickinger J, Lunsford LD

PMID: 24160482 DOI: 10.3171/2013.9.JNS131022

**OBJECTIVE:** Arteriovenous malformations (AVMs) of the posterior fossa have an aggressive natural history and propensity for hemorrhage. Although the cerebellum accounts for the majority of the posterior fossa volume, there is a paucity of stereotactic radiosurgery (SRS) outcome data for AVMs of this region. The authors sought to evaluate the long-term outcomes and risks of cerebellar AVM radiosurgery. **METHODS:** This single-institution retrospective analysis reviewed the authors' experience with Gamma Knife surgery during the period 1987-2007. During this time 64 patients (median age 47 years, range 8-75 years) underwent SRS for a cerebellar AVM. Forty-seven patients (73%) presented with an intracranial hemorrhage. The median target volume was 3.85 cm<sup>3</sup> (range 0.2-12.5 cm<sup>3</sup>), and the median marginal dose was 21 Gy (range 15-25 Gy). **RESULTS:** Arteriovenous malformation obliteration was confirmed by MRI or angiography in 40 patients at a median follow-up of 73 months (range 4-255 months). The actuarial rates of total obliteration were 53% at 3 years, 69% at 4 years, and 76% at 5 and 10 years. Elevated obliteration rates were statistically higher in patients who underwent AVM SRS without prior embolization ( $p = 0.005$ ). A smaller AVM volume was also associated with a higher rate of obliteration ( $p = 0.03$ ). Four patients (6%) sustained a hemorrhage during the latency period and 3 died. The cumulative rates of AVM hemorrhage after SRS were 6% at 1, 5, and 10 years. This correlated with an overall annual hemorrhage rate of 2.0% during the latency interval. One patient experienced a hemorrhage 9 years after confirmed MRI and angiographic obliteration. A permanent neurological deficit due to adverse radiation effects developed in 1 patient (1.6%) and temporary complications were seen in 2 additional patients (3.1%). **CONCLUSIONS:** Stereotactic radiosurgery proved to be most effective for patients with smaller and previously nonembolized cerebellar malformations. Hemorrhage during the latency period occurred at a rate of 2.0% per year until obliteration occurred.

## 2013

**[117] Radiosurgery for primary motor and sensory cortex arteriovenous malformations: outcomes and the effect of eloquent location.**

*Neurosurgery.* 2013;73(5):816-24; discussion 824

Ding D, Yen CP, Xu Z, Starke RM, Sheehan JP

PMID: 23867301 DOI: 10.1227/NEU.0000000000000106

**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 with radiosurgery outcomes in a matched cohort of noneloquent lobar AVMs. **METHODS:** Between 1989 and 2009, 134 patients with PMSC AVMs underwent Gamma Knife radiosurgery with a 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 mL (range, 0.1-22.6 mL), and prescription dose was 20 Gy (range, 7-30 Gy). Cox regression analysis was performed to identify factors associated with obliteration. **RESULTS:** The overall obliteration rate, including magnetic resonance imaging and angiography, after radiosurgery was 63%. Obliteration was achieved in 80% of AVMs with a volume less than 3 mL compared with 55% for AVMs larger than 3 mL. No previous embolization ( $P = .002$ ) and a single draining vein ( $P = .001$ ) 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. Comparing PMSC AVMs with matched noneloquent lobar AVMs, the obliteration rates and clinical outcomes after 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.

[118] Factors Determining the Clinical Complications of Radiosurgery for AVM.

*The Canadian journal of neurological sciences. Le journal canadien des sciences neurologiques.* 2013;40(6):807-13

Machnowska M, Taeshineetanakul P, Geibprasert S, Menezes R, Agid R, Terbrugge KG, Andrade-Souza Y, Schwartz ML, Krings T  
PMID: 24257221 DOI: 10.1017/s0317167100015936

**PURPOSE:** To identify the predictors of symptomatic post-radiation T2 signal change in patients with arteriovenous malformations (AVM) treated with radiosurgery. **MATERIALS AND METHODS:** The charts of 211 consecutive patients with arteriovenous malformations treated with either gamma knife radiosurgery or linear accelerator radiosurgery between 2000-2009 were retrospectively reviewed. 168 patients had a minimum of 12 months of clinical and radiologic follow-up following the procedure and complete dosage data. Pretreatment characteristics and dosimetric variables were analyzed to identify predictors of adverse radiation effects. **RESULTS:** 141 patients had no clinical symptomatic complications. 21 patients had global or focal neurological deficits attributed to symptomatic edema. Variables associated with development of symptomatic edema included a non-hemorrhagic symptomatic presentation compared to presentation with hemorrhage,  $p=0.001$ ; OR (95%CI) = 6.26 (1.99, 19.69); the presence of venous rerouting compared to the lack of venous rerouting,  $p=0.031$ ; OR (95% CI) = 3.25 (1.20, 8.80); radiosurgery with GKS compared to linear accelerator radiosurgery  $p = 0.012$ ; OR (95% CI) = 4.58 (1.28, 16.32); and the presence of more than one draining vein compared to a single draining vein  $p = 0.032$ ; OR (95% CI) = 2.82 (1.06, 7.50). **CONCLUSIONS:** We postulated that the higher maximal doses used with gamma knife radiosurgery may be responsible for the greater number of adverse radiation effects with this modality compared to linear accelerator radiosurgery. We found that AVMs with greater venous complexity and therefore instability resulted in more adverse treatment outcomes, suggesting that AVM angioarchitecture should be considered when making treatment decisions. Facteurs en cause dans les complications cliniques de la radiochirurgie pour une malformation artériovéineuse.

[119] Impact on seizure control of surgical resection or radiosurgery for cerebral arteriovenous malformations.

*Neurosurgery.* 2013;73(4):648-55; discussion 655-6

Wang JY, Yang W, Ye X, Rigamonti D, Coon AL, Tamargo RJ, Huang J

PMID: 23842554 DOI: 10.1227/NEU.0000000000000071

**BACKGROUND:** Seizures are a common presenting symptom of arteriovenous malformations (AVMs). However, the impact of treatment modality on seizure control remains unclear. **OBJECTIVE:** To compare seizure control after surgical resection or radiosurgery for AVMs. **METHODS:** We analyzed retrospectively collected information for 378 patients with cerebral AVMs treated at our institution from 1990 to 2010. The application of strict inclusion criteria resulted in a study population of 164 patients. **RESULTS:** In our cohort, 31 patients (20.7%) had Spetzler-Martin grade I AVMs, 51 (34.0%) grade II, 47 (31.3%) grade III, 20 (13.3%) grade IV, and 1 (0.7%) grade V. Of the 49 patients (30%) presenting with seizures, 60.4% experienced seizure persistence after treatment. For these patients, radiosurgery was associated with seizure recurrence (odds ratio: 4.32, 95% confidence interval: 1.24-15.02,  $P = .021$ ). AVM obliteration was predictive of seizure freedom at last follow-up ( $P = .002$ ). In contrast, for patients presenting without seizures, 18.4% experienced de novo seizures after treatment, for which surgical resection was identified as an independent risk factor (hazard ratio: 8.65, 95% confidence interval: 3.05-24.5,  $P < .001$ ). **CONCLUSION:** Although our data suggest that achieving seizure freedom should not be the primary goal of AVM treatment, surgical resection may result in improved seizure control compared with radiosurgery for patients who present with seizures. Conversely, in patients without presenting seizures, surgical resection increases the risk of new-onset seizures compared with radiosurgery, but primarily within the early posttreatment period. Surgical resection and radiosurgery result in divergent seizure control rates depending on seizure presentation.

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

*Journal of neurosurgery.* 2013;119(4):981-7

Starke RM, Yen CP, Ding D, Sheehan JP  
PMID: 23829820 DOI: 10.3171/2013.5.JNS1311

**OBJECTIVE:** 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 cm<sup>3</sup>, eloquent AVM location, or a history of hemorrhage, and 2 points for having an AVM volume greater than 4 cm<sup>3</sup>. 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.

**[121] Natural history of cerebral arteriovenous malformations and the risk of hemorrhage after radiosurgery.**

*Progress in neurological surgery.* 2013;27:5-21

Yen CP, Schlesinger D, Sheehan JP

PMID: 23258505 DOI: 10.1159/000341616

The annual hemorrhage rate of intracranial arteriovenous malformations (AVMs) varies from 2 to 4%. In a patient with decades of life ahead, the cumulative risk of hemorrhage is significant. AVMs exhibiting characteristics such as deep venous drainage, venous stenosis, associated aneurysms and feeders from perforators are associated with an elevated risk of hemorrhage. We reviewed 1,400 AVM patients who underwent Gamma Knife surgery (GKS) at the University of Virginia between 1989 and 2009. The dose selection was based on the size and location of the nidus. The mean prescription dose was 21.2 Gy (range 5-36 Gy), and the mean maximum dose was 39.4 Gy (range 10-60 Gy). A total of 657 patients suffered 803 hemorrhagic events over 42,495 risk years before GKS. Assuming that these patients were at risk for hemorrhage since birth, the annual hemorrhage rate was 2.0%. If we calculate the hemorrhage rate after the diagnosis of the AVMs, the hemorrhage rate was 6.6%. Following GKS and prior to a radiographic documented obliteration, the annual hemorrhage rate was 2.5%; this rate is very similar to the 2.0% one computed prior to radiosurgery by assuming AVMs to be congenital. Once angiographic obliteration was confirmed after GKS, the hemorrhage rate dropped to zero.

**[122] Stereotactic radiosurgery after embolization for arteriovenous malformations.**

*Progress in neurological surgery.* 2013;27:89-96

Kano H, Kondziolka D, Flickinger JC, Park KJ, Iyer A, Yang HC, Liu X, Monaco EA 3rd, Niranjan A, Lunsford LD

PMID: 23258513 DOI: 10.1159/000341646

We sought to define the long-term benefits and risks of stereotactic radiosurgery (SRS) for arteriovenous malformation (AVM) patients who underwent prior embolization. Between 1987 and 2006, we performed Gamma Knife(R) SRS on 120 patients with AVM who underwent embolization followed by SRS. Sixty-four patients (53%) had at least 1 prior hemorrhage. The median number of embolizations varied from 1 to 5. The median target volume was 6.6 cm<sup>3</sup> (range, 0.2-26.3 cm<sup>3</sup>). The median margin dose was 18 Gy (range, 13.5-25 Gy). After embolization, 25 patients (21%) developed symptomatic neurological deficits. The overall rates of total obliteration documented by either angiography or magnetic resonance imaging were 35, 53, 55 and 59% at 3, 4, 5 and 10 years, respectively. Nine patients (8%) had a hemorrhage during the latency interval and 7 patients died due to hemorrhage. The actuarial rates of AVM hemorrhage after SRS were 0.8, 3.5, 5.4, 7.7 and 7.7% at 1, 2, 3, 5 and 10 years, respectively. Permanent neurological deficits due to adverse radiation effects developed in 3 patients (2.5%) after SRS. Using a case-match control technique, we found that embolization prior to SRS was associated with a lower rate of total obliteration (p=0.028) in comparison to radiosurgery alone. In this 20-year experience, we found that prior embolization reduced the rate of total obliteration after SRS and latency interval hemorrhage risks were not affected by prior embolization. In the future, the role of embolization after SRS should be explored.

**[123] Multistaged volumetric management of large arteriovenous malformations.**

*Progress in neurological surgery.* 2013;27:73-80

Kano H, Kondziolka D, Flickinger JC, Park KJ, Parry PV, Yang HC, Sirin S, Niranjan A, Novotny J Jr, Lunsford LD

PMID: 23258511 DOI: 10.1159/000341629

We sought to define the long-term outcomes and risks of arteriovenous malformation (AVM) management using 2 or more stages of stereotactic radiosurgery (SRS) for symptomatic large-volume AVMs unsuitable for surgery. Two decades ago, we prospectively began to stage anatomical components in order to deliver higher single doses to AVMs >10 cm<sup>3</sup> in volume. Forty-seven patients

with large AVMs underwent volume-staged SRS. The median interval between the two SRS procedures was 4.9 months (range, 3-14 months). The median nidus volume was 11.5 cm<sup>3</sup> (range, 4.0-26 cm<sup>3</sup>) in the first stage of SRS and 9.5 cm<sup>3</sup> in the second. The median margin dose was 16 Gy (range, 13-18 Gy) for both SRS stages. The actuarial rates of total obliteration after 2-staged SRS were 7, 20, 28 and 36% at 3, 4, 5 and 10 years, respectively. Sixteen patients needed additional SRS at a median interval of 61 months (range, 33-113 months) after the 2-staged SRS. After repeat procedure(s), the eventual obliteration rate was 66% at 10 years. The cumulative rates of AVM hemorrhage after SRS were 4.3, 8.6, 13.5 and 36.0% at 1, 2, 5 and 10 years, respectively. Symptomatic adverse radiation effects were detected in 13% of patients. Successful prospective volume-staged SRS for large AVMs unsuitable for surgery requires 2 or more procedures to complete the obliteration process. Patients remain at risk for hemorrhage if the AVM persists.

**[124] Radiosurgery for patients with unruptured intracranial arteriovenous malformations.**

*Journal of neurosurgery.* 2013;118(5):958-66

Ding D, Yen CP, Xu Z, Starke RM, Sheehan JP

PMID: 23530863 DOI: 10.3171/2013.2.JNS121239

**OBJECTIVE:** The appropriate management of unruptured intracranial arteriovenous malformations (AVMs) remains controversial. In the present study, the authors evaluate the radiographic and clinical outcomes of radiosurgery for a large cohort of patients with unruptured AVMs. **METHODS:** From a prospective database of 1204 cases of AVMs involving patients treated with radiosurgery at their institution, the authors identified 444 patients without evidence of rupture prior to radiosurgery. The patients' mean age was 36.9 years, and 50% were male. The mean AVM nidus volume was 4.2 cm<sup>3</sup>, 13.5% of the AVMs were in a deep location, and 44.4% were at least Spetzler-Martin Grade III. The median radiosurgical prescription dose was 20 Gy. Univariate and multivariate Cox regression analyses were used to determine risk factors associated with obliteration, postradiosurgery hemorrhage, radiation-induced changes, and postradiosurgery cyst formation. The mean duration of radiological and clinical follow-up was 76 months and 86 months, respectively. **RESULTS:** The cumulative AVM obliteration rate was 62%, and the postradiosurgery annual hemorrhage rate was 1.6%. Radiation-induced changes were symptomatic in 13.7% and permanent in 2.0% of patients. The statistically significant independent positive predictors of obliteration were no preradiosurgery embolization (p < 0.001), increased prescription dose (p < 0.001), single draining vein (p < 0.001), radiological presence of radiation-induced changes (p = 0.004), and lower Spetzler-Martin grade (p = 0.016). Increased volume and higher Pittsburgh radiosurgery-based AVM score were predictors of postradiosurgery hemorrhage in the univariate analysis only. Clinical deterioration occurred in 30 patients (6.8%), more commonly in patients with postradiosurgery hemorrhage (p = 0.018). **CONCLUSIONS:** Radiosurgery afforded a reasonable chance of obliteration of unruptured AVMs with relatively low rates of clinical and radiological complications.

**[125] Evaluation of prognostic factors as predictor of AVMs obliteration after Gamma Knife radiosurgery.**

*Acta neurochirurgica.* 2013;155(4):619-26

Franzin A, Snider S, Boari N, Scomazzoni F, Picozzi P, Spatola G, Gagliardi F, Mortini P

PMID: 23420116 DOI: 10.1007/s00701-013-1631-2

**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.

**[126] The risk of stroke or clinical impairment after stereotactic radiosurgery for ARUBA-eligible patients.**

*Stroke.* 2013;44(2):437-41

Pollock BE, Link MJ, Brown RD

PMID: 23287780 DOI: 10.1161/STROKEAHA.112.670232

**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  $\geq 2$ ) 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  $\leq 5.6$  cm<sup>3</sup> 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).

**[127] Treatment for brain arteriovenous malformation in the 1998-2011 period and review of the literature.**

*Acta neurochirurgica.* 2013;155(2):199-209

Bradac O, Charvat F, Benes V

PMID: 23238943 DOI: 10.1007/s00701-012-1572-1

**PURPOSE:** The results of the treatment of pial AVM provided at our neurosurgical centre are presented. Based on these results and on an overview of literary data on the efficacy and complications of each therapeutic modality, the algorithm of indications, as used at our institution, is presented. **COHORT OF PATIENTS:** The series comprises 195 patients, aged 9 to 87 years and treated in the years 1998-2011. The surgical group consists of 76 patients; of these, 49 patients solely received endovascular treatment, 25 were consulted and referred directly to the radiosurgical unit, and the remaining 45 were recommended to abide by the strategy of "watch and wait". **RESULTS:** In the surgical group, serious complications were 3.9%, at a 96.1% therapeutic efficacy. As for AVM treated with purely endovascular methods, serious procedural complications were seen in 4.1% of patients, with efficacy totalling 32.7%. One observed patient suffered bleeding, resulting in death. For comparison with literary data for each modality, a survival analysis without haemorrhage following monotherapy for AVM with each particular modality was carried out. **CONCLUSIONS:** Based on

our analysis, we have devised the following algorithm of treatment: 1. We regard surgical treatment as the treatment of choice for AVM of Spetzler-Martin (S-M) grades I and II, and only for those grade III cases that are surgically accessible. 2. Endovascular intervention should mainly be used for preoperative embolisation, as a curative procedure for lower-grade AVM in patients with comorbidities, and as palliation only for higher-grade cases. 3. Stereotactic irradiation with Leksell Gamma Knife (LGK) is advisable, mainly for poorly accessible, deep-seated grade-III AV malformations. In the case of lower grades, the final decision is left to the properly informed patient. 4. Observation should be used as the method of choice in AVM of grades IV and V, where active therapy carries greater risk than the natural course of the disease.

**[128] Long-term outcome of Gamma Knife stereotactic radiosurgery for arteriovenous malformations graded by the Spetzler-Martin classification.**

*Journal of neurosurgery.* 2013;118(1):74-83

Koltz MT, Polifka AJ, Saltos A, Slawson RG, Kwok Y, Aldrich EF, Simard JM

PMID: 23082882 DOI: 10.3171/2012.9.JNS112329

**OBJECTIVE:** The object of this study was to assess outcomes in patients with arteriovenous malformations (AVMs) treated by Gamma Knife stereotactic radiosurgery (SRS); lesions were stratified by size, symptomatology, and Spetzler-Martin (S-M) grade. **METHODS:** The authors performed a retrospective analysis of 102 patients treated for an AVM with single-dose or staged-dose SRS between 1993 and 2004. Lesions were grouped by S-M grade, as hemorrhagic or nonhemorrhagic, and as small ( $< 3$  cm) or large ( $\geq 3$  cm). Outcomes included death, morbidity (new neurological deficit, new-onset seizure, or hemorrhage/rehemorrhage), nidus obliteration, and Karnofsky Performance Scale score. **RESULTS:** The mean follow-up was 8.5 years (range 5-16 years). Overall nidus obliteration (achieved in 75% of patients) and morbidity (19%) correlated with lesion size and S-M grade. For S-M Grade I-III AVMs, nonhemorrhagic and hemorrhagic combined, treatment yielded obliteration rates of 100%, 89%, and 86%, respectively; high functional status (Karnofsky Performance Scale Score  $\geq 80$ ); and 1% mortality. For S-M Grade IV and V AVMs, outcomes were less favorable, with obliteration rates of 54% and 0%, respectively. The AVMs that were not obliterated had a mean reduction in nidus volume of 69% (range 35%-96%). On long-term follow-up, 10% of patients experienced hemorrhage/rehemorrhage (6% mortality rate), which correlated with lesion size and S-M grade; the mean interval to hemorrhage was 81 months. **CONCLUSIONS:** For patients with S-M Grade I-III AVMs, SRS offers outcomes that are favorable and that, except for the timing of obliteration, appear to be comparable to surgical outcomes reported for the same S-M grades. Staged-dose SRS results in lesion obliteration in half of patients with S-M Grade IV lesions.

**[129] Radiation-induced imaging changes following Gamma Knife surgery for cerebral arteriovenous malformations.**

*Journal of neurosurgery.* 2013;118(1):63-73

Yen CP, Matsumoto JA, Wintermark M, Schwyzler L, Evans AJ, Jensen ME, Shaffrey ME, Sheehan JP

PMID: 23140155 DOI: 10.3171/2012.10.JNS12402

**OBJECTIVE:** The objective of this study was to evaluate the incidence, severity, clinical manifestations, and risk factors of radiation-induced imaging changes (RIICs) following Gamma Knife surgery (GKS) for cerebral arteriovenous malformations (AVMs). **METHODS:** A total of 1426 GKS procedures performed for AVMs with imaging follow-up available were analyzed. Radiation-induced imaging changes were defined as newly developed increased T2 signal surrounding the treated AVM nidi. A grading system was developed to categorize the severity of RIICs. Grade I RIICs were mild imaging changes imposing no mass effect on the surrounding brain. Grade II RIICs were moderate changes causing effacement of the sulci or compression of the ventricles. Grade III RIICs were severe changes causing midline shift of the brain. Univariate and multivariate logistic regression analyses were applied to test factors potentially affecting the occurrence, severity, and associated symptoms of RIICs. **RESULTS:** A total of 482 nidi (33.8%)

developed RIIcs following GKS, with 281 classified as Grade I, 164 as Grade II, and 37 as Grade III. The median duration from GKS to the development of RIIcs was 13 months (range 2-124 months). The imaging changes disappeared completely within 2-128 months (median 22 months) following the development of RIIcs. The RIIcs were symptomatic in 122 patients, yielding an overall incidence of symptomatic RIIcs of 8.6%. Twenty-six patients (1.8%) with RIIcs had permanent deficits. A negative history of prior surgery, no prior hemorrhage, large nidus, and a single draining vein were associated with a higher risk of RIIcs. **CONCLUSIONS:** Radiation-induced imaging changes are the most common adverse effects following GKS. Fortunately, few of the RIIcs are symptomatic and most of the symptoms are reversible. Patients with a relatively healthy brain and nidi that are large, or with a single draining vein, are more likely to develop RIIcs.

## 2012

### [130] Long-term results of gamma knife surgery for partially embolized arteriovenous malformations.

*Neurosurgery.* 2012;71(6):1139-47; discussion 1147-8

Schwytzer L, Yen CP, Evans A, Zavoian S, Steiner L

PMID: 22986603 DOI: 10.1227/NEU.0b013e3182720280

**BACKGROUND:** The effectiveness and risk of gamma knife surgery (GKS) in the management of partially embolized cerebral arteriovenous malformations (AVMs) remain to be elucidated. **OBJECTIVE:** To evaluate the long-term imaging and clinical outcomes of GKS in AVM patients who had undergone previous partial embolization and compare the results with patients treated with GKS alone.

**METHODS:** A total of 215 embolized AVMs were analyzed. The mean patient age was 32.9 years. The mean volume of the nidus was 4.6 mL (range, 0.1-29.4 mL), and the mean prescription dose was 19.6 Gy (range, 4-28 Gy). This group was compared with 729 nonembolized AVMs. **RESULTS:** After embolization and GKS, angiographically confirmed total obliteration of the AVMs was significantly lower (33%) compared with patients in whom GKS was used alone (60.9%;  $P < .001$ ). However, the mean nidus size was larger and the Spetzler-Martin grade was higher for the embolized AVMs compared with the nonembolized AVMs. Radiation-induced changes occurred more often in the embolized (43.4%) than the nonembolized (33.4%) AVMs ( $P = .028$ ). Permanent neurological deficits associated with radiation-induced changes occurred in 2.7% of the embolized compared with 1.3% of the nonembolized patients ( $P = .14$ ). **CONCLUSION:** In our retrospective and historical series, the long-term results suggest that the obliteration rate is significantly lower in embolized AVMs compared with nonembolized AVMs, also because of the fact that the combined treatment is applied to higher grade AVMs; the percentage of grade III-V AVMs was 58.6% and 48.8% for nonembolized AVMs.

### [131] Risks of history of diabetes mellitus, hypertension, and other factors related to radiation-induced changes following Gamma Knife surgery for cerebral arteriovenous malformations.

*Journal of neurosurgery.* 2012;117 Suppl:144-9

Quigg M, Yen CP, Chatman M, Quigg AH, McNeill IT, Przybylowski CJ, Yan G, Sheehan JP

PMID: 23205802 DOI: 10.3171/2012.6.GKS1245

**OBJECTIVE:** Diabetes mellitus (DM) and hypertension may be associated with complications following fractionated radiotherapy. To date no studies have determined the risk of radiation toxicity in patients with DM or hypertension who have undergone Gamma Knife surgery (GKS) for brain arteriovenous malformations (AVMs). The goal of the present study was to determine associations between DM or hypertension and other factors in the development of radiotoxicity, as measured by radiation-induced changes (RICs) on MR images following radiosurgery for AVM. **METHODS:** Using univariate methods and

multivariate logistic regression, the authors compared the RIC status in patients 18 years of age and older with these patients' history of, or medication use for, DM or hypertension; tobacco use; patient age and sex; AVM volume; Spetzler-Martin AVM severity scale (Grades I and II vs Grades III-V); AVM surgery, AVM embolization, or hemorrhage prior to radiosurgery; AVM location; number of draining veins; and radiosurgery margin dose. **RESULTS:** Radiation-induced changes occurred in 38% of 539 adults within a mean (+/- standard deviation) of 12 +/- 10 months after radiosurgery, as observed during a median follow-up time of 55 months. Among patients in whom RICs occurred, 34% had headaches, neurological deficits, or new-onset seizures. Larger RICs were associated with worse symptoms. According to a univariate analysis, DM (3% of patients), larger AVM volume, worse Spetzler-Martin grade, lack of AVM surgery prior to radiosurgery, lack of hemorrhage prior to radiosurgery, and smaller margin dose of radiation had significant associations with the presence of RICs. Hypertension (20%), patient sex, tobacco use, number of draining veins, superficial or deep location of the lesion, and AVM embolization prior to radiosurgery had no association with the presence of RICs. According to a multivariate analysis, larger AVM volume, worse Spetzler-Martin grade, and no AVM surgery prior to radiosurgery predicted the occurrence of an RIC. Diabetes mellitus had borderline significance. **CONCLUSIONS:** Vascular factors such as hypertension, patient sex, and tobacco use did not convey additional risks of radiotoxicity, but DM remained a possible cardiovascular risk factor in the development of RICs.

### [132] Long-term follow-up results of intentional 2-stage Gamma Knife surgery with an interval of at least 3 years for arteriovenous malformations larger than 10 cm(3).

*Journal of neurosurgery.* 2012;117 Suppl:126-34

Yamamoto M, Akabane A, Matsumaru Y, Higuchi Y, Kasuya H, Urakawa Y

PMID: 23205800 DOI: 10.3171/2012.6.GKS12757

**OBJECTIVE:** Little information is available on staged Gamma Knife surgery (GKS) with an interval of 3 years or more when used to treat arteriovenous malformations (AVMs) with volumes larger than 10 cm(3). The goal of this study was to increase knowledge in this area by reporting the authors' experience. **METHODS:** The authors describe an institutional review board-approved retrospective study in which they examined databases including information on 250 patients who consecutively underwent GKS for cerebral AVMs during a 16-year period (1988-2004). Among the 250 patients the authors identified 31 patients (12.4%, 15 female and 16 male patients with a mean age of 29 years [range 10-63 years]) in whom 2-stage GKS was intentionally planned at the time of initial treatment because the volume of the AVM nidus was larger than 10 cm(3). The most common presentation was bleeding (14 patients), followed by seizures (9 patients), incidental findings (7 patients), and headache with scintillation (1 patient). One patient underwent GKS for the treatment of 2 AVMs simultaneously, and thus 32 AVMs are included in this study. The mean nidus volume was 16.2 cm(3) (maximum 55.8 cm(3)). In all 31 patients, relatively low radiation doses (12-16 Gy directed at the periphery of the lesion) were intentionally used for the first GKS. The second GKS was scheduled for at least 36 months after the first. **RESULTS:** Complete nidus obliteration was obtained after the first GKS in 1 patient. To date, 26 patients have undergone a second procedure with a post-GKS mean interval of 41 months (range 24-83 months); 2 other patients refused to undergo the second GKS, and no further treatment was given because of severe morbidity in 1 case and death due to bleeding in the other case. Among the 26 patients who did undergo a second procedure, 3 patients refused follow-up digital subtraction (DS) angiography, another is scheduled for follow-up DS angiography, and 2 patients died, one of bleeding and the other of an unknown cause. The remaining 20 patients underwent follow-up DS angiography. Complete nidus obliteration was confirmed in 13 patients (65.0%) and remarkable nidus shrinkage in the other 7 patients (35.0%). In 2 of these 7 patients, a third GKS achieved complete nidus obliteration. Therefore, the cumulative complete obliteration rate in this series was 76.2% (16 of 21 eligible patients). Seven patients (22.6%) experienced bleeding. The bleeding rates were 9.7%, 16.1%, 16.1%, and 26.1%, respectively,

at 1, 2, 5, and 10 years post-GKS. There were 2 deaths and 3 cases of morbidity (persistent coma, mild hemimotor weakness, and hemianopsia in 1 patient each). Hemorrhage did not produce neurological deficits in the other 2 patients. During the mean post-GKS follow-up period of 105 months (range 42-229 months) to date, mild symptomatic GKS-related complications occurred in 2 patients (6.5%); these were classified as Radiation Oncology Group Neurotoxicity Grade 1 in 1 patient and Grade 2 in the other. Among various pre-GKS clinical factors, univariate analysis showed only patient age to impact complications (hazard ratio 0.675, 95% CI 0.306-0.942,  $p = 0.0085$ ). The rate of complications in the pediatric cases was 33.3%, whereas that in the adolescent and adult cases was 0% ( $p = 0.0323$ ). **CONCLUSIONS:** Although a final conclusion awaits further studies and patient follow-up, these results suggest 2-stage GKS to be beneficial even for relatively large AVMs.

**[133] Gamma knife surgery for pediatric arteriovenous malformations: a 25-year retrospective study.**

*Journal of neurosurgery. Pediatrics.* 2012;10(5):445-50

Dinca EB, de Lacy P, Yianni J, Rowe J, Radatz MW, Preotiu-Pietro D, Kemeny AA  
PMID: 22938080 DOI: 10.3171/2012.8.PEDS1241

**OBJECTIVE:** The authors present their 25-year experience in treating pediatric arteriovenous malformations (AVMs) to allow comparisons with other historic studies and data in adults. **METHODS:** Data were collected from a prospectively maintained departmental database selected for age and supplemented by case note review and telephone interviews as appropriate. **RESULTS:** Three hundred sixty-three patients, ages 1-16 years (mean +/- SD, 12 +/- 3.2 years), underwent 410 treatments; 4 had planned 2-stage treatments and 43 were retreated subsequent to an initial partial response. Fifty-eight percent received general anesthesia for the procedure. Sixteen percent had previously undergone embolization. The most common presenting symptoms were as follows: hemorrhage (80.2%), epilepsy (8.3%; overall seizure prevalence 19.9%), and migrainous headaches (6.3%). Only 0.28% of the AVMs were incidental findings. The mean lesion volume was 3.75 +/- 5.3 cm<sup>3</sup> (range 0.01-32.8 cm<sup>3</sup>), with a median Spetzler-Martin grade of III (range I-V). The mean peripheral (therapeutic) dose was 22.7 +/- 2.3 Gy (range 15-25 Gy), corresponding to a mean maximum dose of 43.6 +/- 6 Gy (range 25-51.4 Gy). The obliteration rate was 71.3% in patients who received one treatment and 62.5% for retreated patients, with a mean obliteration time of 32.4 and 79.6 months, respectively. The overall obliteration rate was 82.7%. No follow-up data are as yet available for the 4 patients who underwent the staged treatments. Only 4 patients received peripheral doses below 20 Gy, and the AVM was obliterated in 3 of these patients. The other patients received 20, 22.5, or 25 Gy and had obliteration rates of 82.6%, 77.7%, and 86.3%, respectively. The bleeding rate post radiosurgery was 2.2%, and the cumulative complication rate was 3.6%, with radionecrosis being the most common complication (1.1%). **CONCLUSIONS:** Surprisingly, there was no correlation ( $p = 0.43$ ) between outcome and radiosurgical dose when that dose was between 20 and 25 Gy, thus suggesting that the lower of these 2 doses may be effective. Radiosurgery for pediatric AVM is safe and effective.

**[134] Aneurysms increase the risk of rebleeding after stereotactic radiosurgery for hemorrhagic arteriovenous malformations.**

*Stroke.* 2012;43(10):2586-91

Kano H, Kondziolka D, Flickinger JC, Yang HC, Park KJ, Flannery TJ, Liu X, Niranjan A, Lunsford LD

PMID: 22879101 DOI: 10.1161/STROKEAHA.112.664045

**BACKGROUND AND PURPOSE:** The purpose of this study was to define the risk of rebleeding after stereotactic radiosurgery (SRS) for hemorrhagic arteriovenous malformations with or without associated intracranial aneurysms. **METHODS:** Between 1987 and 2006, we performed Gamma Knife SRS on 996 patients with brain arteriovenous malformations; 407 patients had sustained an arteriovenous malformation hemorrhage. Sixty-four patients (16%) underwent prior embolization and 84 (21%) underwent prior surgical resection. The median target volume was

2.3 mL (range, 0.1-20.7 mL). The median margin dose was 20 Gy (range, 13.5-27 Gy). **RESULTS:** The overall rate of total obliteration defined by angiography or MRI was 56%, 77%, 80%, and 82% at 3, 4, 5, and 10 years, respectively. Before obliteration, 33 patients (8%) sustained an additional hemorrhage after SRS. The overall annual hemorrhage rate until obliteration after SRS was 1.3%. The presence of a patent aneurysm was significantly associated with an increased rehemorrhage risk after SRS (annual hemorrhage rate, 6.4%) compared with patients with a clipped or embolized aneurysm (annual hemorrhage rate, 0.8%;  $P=0.033$ ). **CONCLUSIONS:** When an aneurysm is identified in patients with arteriovenous malformations selected for SRS, additional endovascular or surgical strategies should be considered to reduce the risk of bleeding during the latency interval.

**[135] Retrospective analysis of imaging techniques for treatment planning and monitoring of obliteration for gamma knife treatment of cerebral arteriovenous malformation.**

*Neurosurgery.* 2012;71(4):893-9

Amponsah K, Ellis TL, Chan MD, Lovato JF, Bourland JD, deGuzman AF, Ekstrand KE, Munley MT, McMullen KP, Shaw EG, Tatter SB

PMID: 22791027 DOI: 10.1227/NEU.0b013e3182672a83

**BACKGROUND:** It has been well established that Gamma Knife radiosurgery (GKS) is an effective treatment for brain arteriovenous malformations (AVMs). **OBJECTIVE:** To evaluate complete obliteration rates for magnetic resonance imaging (MRI)-based GKS treatment planning performed with and without angiography and to conduct a preliminary assessment of the utility of using pulsed arterial spin labeling (PASL) magnetic resonance (MR) perfusion imaging to confirm complete obliteration. **METHODS:** Forty-six patients were identified who had undergone GKS without embolization with a minimum follow-up of 2 years. One group was planned with integrated stereotactic angiography and MR (spoiled gradient recalled) images obtained on the day of GKS. A second technique avoided the risk of arteriography by using only axial MR images. Beginning in 2007, PASL MR perfusion imaging was routinely performed as a portion of the follow-up MRI to assess the restoration of normal blood flow of the nidus and surrounding area. **RESULTS:** The overall obliteration rate for the angiography/MRI group was 88.0% (29 of 33). Patients in the MRI-only group had an obliteration rate of 61.5% (8 of 13), with  $P=.092$  with the Fisher exact test, which is not statistically significant. A Kaplan-Meier analysis was also not statistically significant (log rank test,  $P=.474$ ). Four of 9 patients with incomplete obliteration on angiography also had shown residual abnormal blood flow on PASL imaging. **CONCLUSION:** This retrospective analysis shows that treatment planning technique used in GKS does not play a role in the eventual obliteration of treated AVMs. PASL may have potential in the evaluation of AVM obliteration.

**[136] Stereotactic radiosurgery for arteriovenous malformations after embolization: a case-control study.**

*Journal of neurosurgery.* 2012;117(2):265-75

Kano H, Kondziolka D, Flickinger JC, Park KJ, Iyer A, Yang HC, Liu X, Monaco EA 3rd, Niranjan A, Lunsford LD

PMID: 22631689 DOI: 10.3171/2012.4.JNS111935

**OBJECTIVE:** In this paper the authors' goal was to define the long-term benefits and risks of stereotactic radiosurgery (SRS) for patients with arteriovenous malformations (AVMs) who underwent prior embolization. **METHODS:** Between 1987 and 2006, the authors performed Gamma Knife surgery in 996 patients with brain AVMs; 120 patients underwent embolization followed by SRS. In this series, 64 patients (53%) had at least one prior hemorrhage. The median number of embolizations varied from 1 to 5. The median target volume was 6.6 cm<sup>3</sup> (range 0.2-26.3 cm<sup>3</sup>). The median margin dose was 18 Gy (range 13.5-25 Gy). **RESULTS:** After embolization, 25 patients (21%) developed symptomatic neurological deficits. The overall rates of total obliteration documented by either angiography or MRI were 35%, 53%, 55%, and 59% at 3, 4, 5, and 10 years, respectively. Factors associated with a higher rate of AVM obliteration were smaller target volume,

smaller maximum diameter, higher margin dose, timing of embolization during the most recent 10-year period (1997-2006), and lower Pollock-Flickinger score. Nine patients (8%) had a hemorrhage during the latency period, and 7 patients died of hemorrhage. The actuarial rates of AVM hemorrhage after SRS were 0.8%, 3.5%, 5.4%, 7.7%, and 7.7% at 1, 2, 3, 5, and 10 years, respectively. The overall annual hemorrhage rate was 2.7%. Factors associated with a higher risk of hemorrhage after SRS were a larger target volume and a larger number of prior hemorrhages. Permanent neurological deficits due to adverse radiation effects (AREs) developed in 3 patients (2.5%) after SRS, and 1 patient had delayed cyst formation 210 months after SRS. No patient died of AREs. A larger 12-Gy volume was associated with higher risk of symptomatic AREs. Using a case-control matched approach, the authors found that patients who underwent embolization prior to SRS had a lower rate of total obliteration ( $p = 0.028$ ) than patients who had not undergone embolization. **CONCLUSIONS:** In this 20-year experience, the authors found that prior embolization reduced the rate of total obliteration after SRS, and that the risks of hemorrhage during the latency period were not affected by prior embolization. For patients who underwent embolization to volumes smaller than 8 cm(3), success was significantly improved. A margin dose of 18 Gy or more also improved success. In the future, the role of embolization after SRS should be explored.

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

*The British journal of radiology.* 2012;85(1016):1064-9

Lim HK, Choi CG, Kim SM, Kim JL, Lee DH, Kim SJ, Suh DC

PMID: 22294705 DOI: 10.1259/bjr/30618275

**OBJECTIVE:** To evaluate the diagnostic accuracy of four-dimensional MR angiography (4D-MRA) at 3.0 T for detecting residual arteriovenous malformations (AVMs) after Gamma Knife (Elekta Instrument AB, Stockholm, Sweden) 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 1 x 1 x 1 mm and a temporal resolution of 1.1 s (13 patients) or a voxel size of 1 x 1 x 2 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.

**[138] Quality of life after radiosurgery for cerebral arteriovenous malformation patients who present with seizure.**

*European journal of neurology.* 2012;19(7):984-91

Yang SY, Paek SH, Kim DG, Chung HT

PMID: 22340506 DOI: 10.1111/j.1468-1331.2012.03664.x

**BACKGROUND AND PURPOSE:** This study assessed the quality of life (QOL) and employment status after radiosurgery for arteriovenous malformation (AVM) patients who presented with seizure. **METHODS:** Between 1997 and 2006, 78 AVM patients who presented with seizure and received radiosurgery were assessed using serial imaging tests, clinical evaluations that included employment status, and a QOL survey. The QOL questionnaire was developed

as a retrospective screening tool to estimate the present QOL and the patient's self-rated relative changes (trend values) in QOL after radiosurgery. These results were correlated to one another using the Engel seizure frequency scoring system. **RESULTS:** The follow-up periods ranged from 48.0 to 151.0 months (mean, 92.5). The mean trend values and mean QOL scores in patients with seizure freedom or AVM obliteration were significantly greater than in patients without these outcomes (all P values < 0.05). Good radiosurgical outcomes were associated with attaining employment (all P values < 0.05). However, differences in employment status were not significant ( $P = 0.186$ ) despite a higher proportion of patients who described their workplace activity as improved compared with their pre-radiosurgical activity at the last follow-up evaluation. **CONCLUSIONS:** Radiosurgery may improve QOL and employment status in AVM patients, especially patients who experience seizure freedom or AVM obliteration.

**[139] Stereotactic radiosurgery for arteriovenous malformations located in deep critical regions.**

*Neurosurgery.* 2012;70(6):1458-69; discussion 1469-71

Nagy G, Major O, Rowe JG, Radatz MW, Hodgson TJ, Coley SC, Kemeny AA

PMID: 22186841 DOI: 10.1227/NEU.0b013e318246a4d0

**BACKGROUND:** Radiosurgery is widely used to treat deep eloquent arteriovenous malformations (AVMs). **OBJECTIVE:** To evaluate how anatomic 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 2 cm (range, 0.02-50) for supratentorial and 0.5 cm (range, 0.01-40) for brainstem AVMs; the marginal treatment doses were 17.5 to 25 Gy. After single treatment, obliteration was achieved in 65% of the brainstem, in 69% of the supratentorial, and 40% of the peritectoral AVMs. Obliteration of lesions <4 cm was better in the brainstem (70%) and in the supratentorium (80%), but not in the peritectoral region (40%). Complications were rare (6%-15%) and mild (<= modified Rankin scale [MRS] 2). Rebleed rate increased with size, but was not higher than before treatment. AVMs >4 cm in the brainstem were treated with unacceptable morbidity and low cure rate. Obliteration of large supratentorial AVMs was 65% to 47% with more complications >= MRS3. Repeat radiosurgical treatment led to obliteration in 66% of the cases with minor morbidity. **CONCLUSION:** Deep eloquent AVMs <4 cm can be treated safely and effectively with radiosurgery. Obliteration of peritectoral AVMs is significantly lower after a single treatment. However, morbidity is low, and repeat treatment leads to good obliteration. Radiosurgical treatment >4 cm in the brainstem is not recommended. Supratentorial deep AVMs >8 cm 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.

**[140] Cerebral arteriovenous malformations and seizures: differential impact on the time to seizure-free state according to the treatment modalities.**

*Acta neurochirurgica.* 2012;154(6):1003-10

Hyun SJ, Kong DS, Lee JI, Kim JS, Hong SC

PMID: 22492295 DOI: 10.1007/s00701-012-1339-8

**BACKGROUND:** To determine the prognostic factors for the incidence and the outcome of seizure in patients with cerebral arteriovenous malformation (AVM) and to identify the time to seizure-free state according to the treatment modalities. **MATERIAL AND METHODS:** Between 1995 and 2008, the multidisciplinary team at our institution treated 399 patients with cerebral AVMs. Treatment consisted of surgical resection, radiosurgery, and embolization, either alone or in combination. The median follow-up period was 6.0 years (range, 3.0-16.2 years). Eighty-six patients (21.5%) experienced seizures before treatment. We investigated the variables associated with seizure incidence and seizure outcome and analyzed the outcomes of seizure among each treatment modality. **RESULTS:** After treatment, 60 (70%) patients were seizure-free. Compared with 313 patients who did not experience seizures, we found that younger age (<= 35 years), size

>= 3 cm, and location of temporal lobe were associated with seizures ( $p < 0.05$ ). Short seizure history, accompanying intracerebral hemorrhage, generalized tonic-clonic type seizure, deep-seated or infratentorial AVM, complete obliteration of AVM, and a favorable neurological outcome at 12 months were closely associated with Engel Class I outcomes ( $p < 0.05$ ). Seizure-free outcomes after microsurgery, radiosurgery, or embolization were 78 %, 66 %, and 50 %, respectively. The overall annual bleeding rate was 1.0 % and 2.2 % in microsurgery-treated and radiosurgery-treated AVMs, respectively. In the surgery group, the median time to seizure-free status was 1.1 months (95 % CI, 0.7-1.2 months), whereas the radiosurgery group and embolization-alone group showed 20.5 months (95 % CI, 18.3-23.8 months), and 8.1 months (95 % CI, 6.0-13.5 months), respectively.

**CONCLUSIONS:** A multidisciplinary team approach for cerebral AVMs achieved satisfactory seizure control results. Microsurgery led to the highest percentage of seizure-free outcomes and had the lowest annual bleeding rate, whereas radiosurgery had a higher bleeding rate. Median time to seizure-free status in surgically treated patients was shorter than in patients who underwent radiosurgical or endovascular treatment.

**[141] Radiosurgery for unruptured cerebral arteriovenous malformations: long-term seizure outcome.**

*Neurology.* 2012;78(17):1292-8

Yang SY, Kim DG, Chung HT, Paek SH

PMID: 22459685 DOI: 10.1212/WNL.0b013e31825182c5

**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.

**[142] Gamma Knife surgery for basal ganglia and thalamic arteriovenous malformations.**

*Journal of neurosurgery.* 2012;116(4):899-908

Cheng CH, Crowley RW, Yen CP, Schlesinger D, Shaffrey ME, Sheehan JP

PMID: 22264181 DOI: 10.3171/2011.12.JNS11542

**OBJECTIVE:** Gamma Knife surgery (GKS) has emerged as the treatment of choice for small- to medium-sized cerebral arteriovenous malformations (AVMs) in deep locations. The present study aims to investigate the outcomes of GKS for AVMs in the basal ganglia and thalamus. **METHODS:** Between 1989 and 2007, 85 patients with AVMs in the basal ganglia and 97 in the thalamus underwent GKS and were followed up for more than 2 years. The nidus volumes ranged from 0.1 to 29.4 cm<sup>3</sup> (mean 3.4 cm<sup>3</sup>). The mean margin dose at the initial GKS was 21.3 Gy (range 10-28 Gy). Thirty-six patients underwent repeat GKS for residual AVMs at a median 4 years after initial GKS. The mean margin dose at repeat GKS was 21.1 Gy (range 7.5-27 Gy). **RESULTS:** Following a single GKS, total obliteration

of the nidus was confirmed on angiograms in 91 patients (50%). In 12 patients (6.6%) a subtotal obliteration was achieved. No flow voids were observed on MR imaging in 14 patients (7.7%). Following single or repeat GKS, total obliteration was angiographically confirmed in 106 patients (58.2%) and subtotal obliteration in 8 patients (4.4%). No flow voids on MR imaging were observed in 18 patients (9.9%). The overall obliteration rates following one or multiple GKSs based on MR imaging or angiography was 68%. A small nidus volume, high margin dose, low number of isocenters, and no history of embolization were significantly associated with an increased rate of obliteration. Twenty-one patients experienced 25 episodes of hemorrhage in 850 risk-years following GKS, yielding an annual hemorrhage rate of 2.9%. Four patients died in this series: 2 due to complications of hemorrhage and 2 due to unrelated diseases. Permanent neurological deficits caused by radiation were noted in 9 patients (4.9%). **CONCLUSIONS:** Gamma Knife surgery offers a reasonable chance of obliterating basal ganglia and thalamic AVMs and does so with a low risk of complications. It is an optimal treatment option in patients for whom the anticipated risk of microsurgery is too high.

**[143] A historical analysis of single-stage gamma knife radiosurgical treatment for large arteriovenous malformations: evolution and outcomes.**

*Acta neurochirurgica.* 2012;154(3):383-94

Nagy G, Rowe JG, Radatz MW, Hodgson TJ, Coley SC, Kemeny AA

PMID: 22173687 DOI: 10.1007/s00701-011-1245-5

**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<sup>3</sup> 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 isocenters and a marginal dose of 23 Gy covering 45-70% of the AVM (median volume 15.7 cm<sup>3</sup>). From 1994 to 2000 (225 patients) plans became more sophisticated, a median of 5 isocenters was used, covering 64-95% of the AVM (14.6 cm<sup>3</sup>), with a marginal dose of 21 Gy. Since 2000, MRI has been used with angiography to plan for 182 patients. Median isocenters increased to 7 with similar coverage (62-94%) of the AVM (14.3 cm<sup>3</sup>) 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.

**[144] Outcomes of diffusion tensor tractography-integrated stereotactic radiosurgery.**

*International journal of radiation oncology, biology, physics.* 2012;82(2):799-802

Koga T, Maruyama K, Kamada K, Ota T, Shin M, Itoh D, Kunii N, Ino K, Terahara A,

Aoki S, Masutani Y, Saito N

PMID: 21277103 DOI: 10.1016/j.ijrobp.2010.11.046

**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.

[145] Pretreatment predictors of adverse radiation effects after radiosurgery for arteriovenous malformation.

*International journal of radiation oncology, biology, physics.* 2012;82(2):803-8  
Hayhurst C, Monsalves E, van Prooijen M, Cusimano M, Tsao M, Menard C, Kulkarni AV, Schwartz M, Zadeh G  
PMID: 21345621 DOI: 10.1016/j.ijrobp.2010.12.014

**PURPOSE:** To identify vascular and dosimetric predictors of symptomatic T2 signal change and adverse radiation effects after radiosurgery for arteriovenous malformation, in order to define and validate preexisting risk models. **METHODS AND MATERIALS:** A total of 125 patients with arteriovenous malformations (AVM) were treated at our institution between 2005 and 2009. Eighty-five patients have at least 12 months of clinical and radiological follow-up. Any new-onset headaches, new or worsening seizures, or neurological deficit were considered adverse events. Follow-up magnetic resonance images were assessed for new onset T2 signal change and the volume calculated. Pretreatment characteristics and dosimetric variables were analyzed to identify predictors of adverse radiation effects. **RESULTS:** There were 19 children and 66 adults in the study cohort, with a mean age of 34 (range 6-74). Twenty-three (27%) patients suffered adverse radiation effects (ARE), 9 patients with permanent neurological deficit (10.6%). Of these, 5 developed fixed visual field deficits. Target volume and 12 Gy volume were the most significant predictors of adverse radiation effects on univariate analysis ( $p < 0.001$ ). Location and cortical eloquence were not significantly associated with the development of adverse events ( $p = 0.12$ ). No additional vascular parameters were identified as predictive of ARE. There was a significant target volume threshold of 4 cm<sup>3</sup>, above which the rate of ARE increased dramatically. Multivariate analysis target volume and the absence of prior hemorrhage are the only significant predictors of ARE. The volume of T2 signal change correlates to ARE, but only target volume is predictive of a higher volume of T2 signal change. **CONCLUSIONS:** Target volume and the absence of prior hemorrhage is the most accurate predictor of adverse radiation effects and complications after radiosurgery for AVMs. A high percentage of permanent visual field defects in this series suggest the optic radiation is a critical radiosensitive structure.

[146] Arteriovenous malformation-associated aneurysms in the pediatric population.

*Journal of neurosurgery. Pediatrics.* 2012;9(1):11-6  
Anderson RC, McDowell MM, Kellner CP, Appelboom G, Bruce SS, Kotchetkov IS, Haque R, Feldstein NA, Connolly ES, Solomon RA, Meyers PM, Lavine SD  
PMID: 22208314 DOI: 10.3171/2011.10.PEDS11181

**OBJECTIVE:** Conventional cerebral angiography and treatment for ruptured arteriovenous malformations (AVMs) in children are often performed in a delayed fashion. In adults, current literature suggests that AVM-associated aneurysms may

be more likely to hemorrhage than isolated AVMs, which often leads to earlier angiography and endovascular treatment of associated aneurysms. The nature of AVM-associated aneurysms in the pediatric population is virtually unknown. In this report, the authors investigate the relationship of associated aneurysms in a large group of children with AVMs. **METHODS:** Seventy-seven pediatric patients ( $\leq 21$  years old) with AVMs were treated at the Columbia University Medical Center between 1991 and 2010. Medical records and imaging studies were retrospectively reviewed, and associated aneurysms were classified as arterial, intranidal, or venous in location. Clinical presentation and outcome variables were compared between children with and without AVM-associated aneurysms. **RESULTS:** A total of 30 AVM-associated aneurysms were found in 22 children (29% incidence). Eleven were arterial, 9 intranidal, and 10 were venous in location. There was no significant difference in the rate of hemorrhage ( $p = 0.91$ ) between children with isolated AVMs (35 of 55 [64%]) and children with AVM-associated aneurysms (13 of 22 [59%]). However, of the 11 children with AVM-associated aneurysms in an arterial location, 10 presented with hemorrhage (91%). An association with hemorrhage was significant in univariate analysis ( $p = 0.045$ ) but not in multivariate analysis ( $p = 0.37$ ). **CONCLUSIONS:** Associated aneurysms are present in nearly a third of children with AVMs, and when arterially located, are more likely to present with hemorrhage. These data suggest that early angiography with endovascular treatment of arterial-based aneurysms in children with AVMs may be indicated.

[147] Stereotactic radiosurgery for arteriovenous malformations, Part 5: management of brainstem arteriovenous malformations.

*Journal of neurosurgery.* 2012;116(1):44-53  
Kano H, Kondziolka D, Flickinger JC, Yang HC, Flannery TJ, Niranjan A, Novotny J Jr, Lunsford LD  
PMID: 22077450 DOI: 10.3171/2011.9.JNS11176

**OBJECTIVE:** 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<sup>3</sup> (range 0.1-13.4 cm<sup>3</sup>). 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.

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

*Journal of neurosurgery.* 2012;116(1):11-20  
Kano H, Lunsford LD, Flickinger JC, Yang HC, Flannery TJ, Awan NR, Niranjan A,



Novotny J Jr, Kondziolka D  
PMID: 22077452 DOI: 10.3171/2011.9.JNS101740

**OBJECTIVE:** 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.

[149] Stereotactic radiosurgery for arteriovenous malformations, Part 4: management of basal ganglia and thalamus arteriovenous malformations.

*Journal of neurosurgery.* 2012;116(1):33-43  
Kano H, Kondziolka D, Flickinger JC, Yang HC, Flannery TJ, Niranjan A, Novotny J Jr, Lunsford LD  
PMID: 22077451 DOI: 10.3171/2011.9.JNS11175

**OBJECTIVE:** 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.

[150] Stereotactic radiosurgery for arteriovenous malformations, part 2: management of pediatric patients.

*Journal of neurosurgery. Pediatrics.* 2012;9(1):1-10  
Kano H, Kondziolka D, Flickinger JC, Yang HC, Flannery TJ, Awan NR, Niranjan A, Novotny J, Lunsford LD  
PMID: 22208313 DOI: 10.3171/2011.9.PEDS10458

**OBJECTIVE:** 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.

[151] Stereotactic radiosurgery for arteriovenous malformations, Part 6: multistaged volumetric management of large arteriovenous malformations.

*Journal of neurosurgery.* 2012;116(1):54-65  
Kano H, Kondziolka D, Flickinger JC, Park KJ, Parry PV, Yang HC, Sirin S, Niranjan A, Novotny J Jr, Lunsford LD  
PMID: 22077447 DOI: 10.3171/2011.9.JNS11177

**OBJECTIVE:** The object of this study was to define the long-term outcomes and risks of arteriovenous malformation (AVM) management using 2 or more stages of stereotactic radiosurgery (SRS) for symptomatic large-volume lesions unsuitable for surgery. **METHODS:** In 1992, the authors prospectively began to stage the treatment of anatomical components to deliver higher single doses to AVMs with a volume of more than 10 cm(3). Forty-seven patients with such AVMs underwent volume-staged SRS. In this series, 18 patients (38%) had a prior hemorrhage and 21 patients (45%) underwent prior embolization. The median interval between the first-stage SRS and the second-stage SRS was 4.9 months (range 2.8-13.8 months). The median target volume was 11.5 cm(3) (range 4.0-26 cm(3)) in the first-stage SRS and 9.5 cm(3) in the second-stage SRS. The median margin dose was 16 Gy (range 13-18 Gy) for both stages. **RESULTS:** In 17 patients, AVM obliteration was confirmed after 2-4 SRS procedures at a median follow-up of 87 months (range 0.4-209 months). Five patients had near-total obliteration (volume

reduction > 75% but residual AVM). The actuarial rates of total obliteration after 2-stage SRS were 7%, 20%, 28%, and 36% at 3, 4, 5, and 10 years, respectively. The 5-year total obliteration rate after the initial staged volumetric SRS with a margin dose of 17 Gy or more was 62% ( $p = 0.001$ ). Sixteen patients underwent additional SRS at a median interval of 61 months (range 33-113 months) after the initial 2-stage SRS. The overall rates of total obliteration after staged and repeat SRS were 18%, 45%, and 56% at 5, 7, and 10 years, respectively. Ten patients sustained hemorrhage after staged SRS, and 5 of these patients died. Three of 16 patients who underwent repeat SRS sustained hemorrhage after the procedure and died. Based on Kaplan-Meier analysis (excluding the second hemorrhage in the patient who had 2 hemorrhages), the cumulative rates of AVM hemorrhage after SRS were 4.3%, 8.6%, 13.5%, and 36.0% at 1, 2, 5, and 10 years, respectively. This corresponded to annual hemorrhage risks of 4.3%, 2.3%, and 5.6% for Years 0-1, 1-5, and 5-10 after SRS. Multiple hemorrhages before SRS correlated with a significantly higher risk of hemorrhage after SRS. Symptomatic adverse radiation effects were detected in 13% of patients, but no patient died as a result of an adverse radiation effect. Delayed cyst formation did not occur in any patient after SRS. **CONCLUSIONS:** Prospective volume-staged SRS for large AVMs unsuitable for surgery has potential benefit but often requires more than 2 procedures to complete the obliteration process. To have a reasonable chance of benefit, the minimum margin dose should be 17 Gy or greater, depending on the AVM location. In the future, prospective volume-staged SRS followed by embolization (to reduce flow, obliterate fistulas, and occlude associated aneurysms) may improve obliteration results and further reduce the risk of hemorrhage after SRS.

[152] Stereotactic radiosurgery for arteriovenous malformations, Part 3: outcome predictors and risks after repeat radiosurgery.

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**OBJECTIVE:** 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<sup>3</sup> (range 0.2-26.3 cm<sup>3</sup>) at initial SRS but was reduced to 2.3 cm<sup>3</sup> (range 0.1-18.2 cm<sup>3</sup>) 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.