

International Gamma Knife Research Foundation

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The International [Gamma Knife](#) Research Foundation consists of academic and clinical centers of excellence where brain [Stereotactic Radiosurgery](#) is performed using the Leksell [Gamma Knife](#). All participating centers have a track record of outcomes research and participation in clinical trials.

The primary goal of the IGKRF is to facilitate retrospective and prospective clinical trials and outcomes analysis that evaluate the role of Gamma Knife radiosurgery in a wide spectrum of clinical indications.

Because individual centers may evaluate only a small number of patients with rare conditions, pooling of information is critical to evaluate and to improve outcomes. Each center has a professional team consisting of one or more neurological surgeons, radiation oncologists, and medical physicists. Participation is by invitation of the Board of Directors. The IGKRF is a non-profit scientific, educational, and research entity incorporated in the state of Pennsylvania.

Case series

2017

Multicenter, retrospective cohort study to evaluate the outcomes after single-session stereotactic radiosurgery (SRS) for SM Grade IV-V AVMs and determine predictive factors.

Patibandla et al. 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 cm³, 17.3 Gy, and 84.5 months, respectively. Statistical analyses were performed to identify factors associated with post-SRS outcomes.

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.

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 ¹⁾.

Ding et al. evaluated and pooled AVM radiosurgery data from 8 institutions participating in the [International Gamma Knife Research Foundation](#). Patients with unruptured AVMs and ≥ 12 mo of follow-up were included in the study cohort. Favorable outcome was defined as AVM obliteration, no postradiosurgical hemorrhage, and no permanently symptomatic radiation-induced changes.

The unruptured AVM cohort comprised 938 patients with a median age of 35 yr. The median nidus volume was 2.4 cm³, 71% of AVMs were located in eloquent brain areas, and the Spetzler-Martin grade was III or higher in 57%. The median radiosurgical margin dose was 21 Gy and follow-up was 71 mo. AVM obliteration was achieved in 65%. The annual postradiosurgery hemorrhage rate was 1.4%. Symptomatic and permanent radiation-induced changes occurred in 9% and 3%, respectively. Favorable outcome was achieved in 61%. In the multivariate logistic regression analysis, smaller AVM maximum diameter ($P = .001$), the absence of AVM-associated arterial aneurysms ($P = .001$), and higher margin dose ($P = .002$) were found to be independent predictors of a favorable outcome. A margin dose ≥ 20 Gy yielded a significantly higher rate of favorable outcome (70% vs 36%; $P < .001$).

Radiosurgery affords an acceptable risk to benefit profile for patients harboring unruptured AVMs. These findings justify further prospective studies comparing radiosurgical intervention to conservative management for unruptured AVMs ²⁾.

2016

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.

The mean maximum AVM diameter was 2.3 cm, with a mean volume of 4.3 cm³. A mean margin dose of 20.5 Gy was delivered. Mean follow-up was 7 years (range 1-20 years). Overall obliteration was 64.7%. Post-GRKS hemorrhage occurred in 165 patients (annual risk 1.1%). Radiation-induced imaging changes occurred in 29.2%; 9.7% were symptomatic, and 2.7% had permanent deficits. Favorable outcome was achieved in 60.3% of patients. Patients with prior 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.

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 ³⁾.

1)

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. Stereotactic radiosurgery for Spetzler-Martin Grade IV and V arteriovenous malformations: an international multicenter study. *J Neurosurg*. 2017 Sep 8;1-10. doi:

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2)

Ding D, Starke RM, Kano H, Lee JYK, Mathieu D, Pierce J, Huang P, Missios S, Feliciano C, Rodriguez-Mercado R, Almodovar L, Grills IS, Silva D, Abbassy M, Kondziolka D, Barnett GH, Lunsford LD, Sheehan JP. Radiosurgery for Unruptured Brain Arteriovenous Malformations: An International Multicenter Retrospective Cohort Study. *Neurosurgery*. 2017 Jun 1;80(6):888-898. doi: 10.1093/neuros/nyx181. PubMed PMID: 28431024.

3)

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. Stereotactic radiosurgery for cerebral arteriovenous malformations: evaluation of long-term outcomes in a multicenter cohort. *J Neurosurg*. 2016 Mar 4:1-9. [Epub ahead of print] PubMed PMID: 26943847.

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