

Clinical Article

Radiosurgical Considerations in the Treatment of Large Cerebral Arteriovenous Malformations

Sung Ho Lee, M.D., Young Jin Lim, M.D., Seok Keun Choi, M.D., Tae Sung Kim, M.D., Bong Arm Rhee, M.D.

Department of Neurosurgery, School of Medicine, Kyung Hee University, Seoul, Korea

Objective : In order to establish the role of Gamma Knife radiosurgery (GKS) in large intracranial arteriovenous malformations (AVMs), we analyzed clinical characteristics, radiological features, and radiosurgical outcomes.

Methods : Between March 1992 and March 2005, 28 of 33 patients with large AVMs (> 10 cm³ in nidus-volume) who were treated with GKS underwent single session radiosurgery (RS), and the other 5 patients underwent staged volumetric RS. Retrospectively collected data were available in 23 cases. We analyzed treatment outcomes in each subdivided groups and according to the AVM sizes. We compared the estimated volume, defined as primarily estimated nidus volume using MR images, with real target volume after excluding draining veins and feeding arteries embedded into the nidus.

Results : Regarding those patients who underwent single session RS, 44.4% (8/18) had complete obliteration; regarding staged volumetric RS, the obliteration rate was 40% (2/5). The complete obliteration rate was 60% (6/10) in the smaller nidus group (10-15 cm³ size), and 25% (2/8) in the larger nidus group (over 15 cm³ size). One case of cerebral edema and two cases (8.7%) of hemorrhage were seen during the latent period. The mean real target volume for 18 single sessions of RS was 17.1 cm³ (10.1-38.4 cm³), in contrast with the mean estimated volume of 20.9 cm³ (12.0-45.0 cm³).

Conclusion : The radiosurgical treatment outcomes of large AVMs are generally poor. However, we presume that the recent development in planning software and imaging devices aid more accurate measurement of the nidus volume, therefore improving the treatment outcome.

KEY WORDS : Gamma Knife radiosurgery · Arteriovenous Malformation · Intracerebral Hemorrhage · Obliteration · Complication · Outcome.

INTRODUCTION

For the treatment of intracranial arteriovenous malformations (AVMs), one of three established methods or combinations of them-microsurgery, embolization, and stereotactic radiosurgery- have been applied^{1,3,12,19,21,26}. For the large AVMs, however, none of them gave rise to clinically acceptable outcomes to date^{11,18,23,25}. The important prognostic factors that affect the outcomes in treating AVMs are the volume of the nidus and its location along with hemodynamic characteristics of the AVM itself in relation to the surrounding vasculature^{1,17}. In

radiosurgical field of AVM treatment, the volume is the single most important factor among the aforementioned prognostic factors, because in cases of large volume AVMs, sufficient radiation dose cannot be delivered for a number of reasons⁶. Therefore, planning for the minimization of target volume without surplus is the one of the most important procedures for the effective treatment. Aiming the goal of radiosurgery at delivering a sufficient dose to the AVM nidus itself while minimally affecting the normal brain tissue in vicinity¹⁹, we would like to introduce the dosimetry, obliteration rate and complications from our experiences of treating large AVMs.

METHODS AND MATERIALS

Patients and AVM characteristics

Patients were enrolled in this study according to the following criteria : 1) a large AVM defined as 10 cm³ or more in volume; 2) a clinical and radiological follow-up

• Received : June 15, 2009 • Revised : October 6, 2009
• Accepted : October 6, 2009
• Address for reprints : Young Jin Lim, M.D.
Department of Neurosurgery, School of Medicine, Kyung Hee University,
1 Hoegi-dong, Dongdaemun-gu, Seoul 130-702, Korea
Postal code: 130-702
Tel : +82-2-958-8408, Fax : +82-2-958-8380
E-mail : youngjins@yahoo.co.kr

period of at least 36 months; 3) those patients who showed early complete obliteration or those who died from hemorrhage. Between March 1992 and March 2005, 355 patients with intracranial AVMs were treated with GKS at our institution. Thirty-three patients (9.3%) had large AVMs, and 23 of these patients (16 male; 7 female) were included in this study. The mean age at the time of GKS was 34.3 years (range, 10-58 years). Their clinical and radiological data were retrospectively analyzed.

Eighteen patients (78.3%) had a history of hemorrhage, and four patients had undergone microsurgeries, such as partial nidus resection or hematoma evacuation, beforehand. Four patients had undergone intravascular embolization before radiosurgery. The radiological characteristics of the AVMs, including the Spetzler-Martin Scale and location, are summarized in Table 1.

Radiosurgical technique

Single session radiosurgery (RS) was performed in 18 patients and two-stage volumetric RS was performed in the other 5 patients. Cerebral angiography and magnetic resonance (MR) imaging were performed with fixation of a Leksell stereotactic instrument to the skull. As a radiosurgical planning tool, the KULA system was used until 2001, and the Leksell Gamma Plan system (Elekta AB, Stockholm, Sweden) has been used since then. During the planning, feeding arteries and draining veins were maximally excluded to minimize the target volume. As seen in Fig. 1, estimated target volume was defined as primarily estimated nidus volume using Gamma Plan based on gadolinium enhanced Tetravol of Fallot (TOF) MR images and real target volume as substantial volume after excluding draining veins embedded into the nidus and feeding arteries, which enables compaction of the target to be irradiated. In cases prior to 2001, KULA system was used with gadolinium enhanced T1 axial and coronal images as source. The gap between estimated target volume and real target volume was analyzed.

Follow-up evaluations

All patients were evaluated during follow-up visits at 1 week, 1 month, and 6 months, and then annually after GKS. Radiologic follow-up was done using MR angiography annually after GKS. Conventional angiography was performed for confirmation of complete obliteration when there was no visualization of the nidus on follow-up MRI, or for planning of retreatment of the remnant nidus, even 2-3 years after primary GKS. Additional visits or telephone counseling were recommended when new symptoms developed. Radiologic imaging,

including computed tomography (CT), was performed whenever needed.

Estimation of radiosurgical outcomes

Complete obliteration was defined as no remaining nidus

Table 1. Clinical and angiographic characteristics

Patient characteristic	No. of patients (%)
Presenting symptom	
Headache	18 (78.3)
Hemorrhage	18 (78.3)
Seizures	8 (34.8)
Sensory-motor deficit	11 (47.8)
Visual defect	2 (8.7)
Decreased mental status	2 (8.7)
Prior therapy	
Embolization	3 (13.0)
Surgical resection	4 (17.4)
Spetzler-martin grade	
II	7 (30.4)
III	10 (43.5)
IV	5 (21.7)
V	1 (4.3)
Deep venous drainage	10 (43.5)
Location	
Lobar	14 (60.9)
Thalamus/Basal ganglia	6 (26.1)
Cerebellum	1 (4.3)
Corpus callosum	2 (8.7)
Eloquent	11 (47.8)

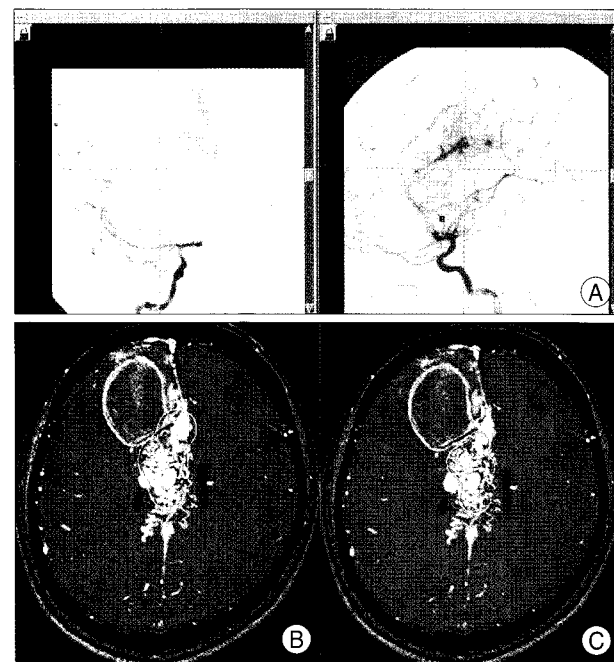


Fig. 1. An example of serial methods to minimize target volume is shown using Gamma Plan. A : Projective volume of nidus on conventional angiography. B : Primary target volume on TOF MR images. C : Minimized real target volume excluding draining vein and supplying arteries.

on angiography, and partial obliteration was defined as some obliteration on either MRA or angiography more than 3 years after GKS. Repeat GKS was considered in cases of partial obliteration.

To estimate outcomes in large AVM patients based on nidus volume, the authors classified the patients who received single session radiosurgery into two groups : a 10-15 cm³ group and a larger than 15 cm³ group. We also compared the treatment results between single session radiosurgery and staged volumetric radiosurgery patients. Complications following the treatments are also revised.

RESULTS

Follow-up and characteristics

The mean clinical follow-up period was 41.2 months (5.9-84.2 months) in all cases and 43.5 months (24.3-84.2 months) in non-bleeding cases. The mean nidus volume in the 23 AVM cases was 16.8 cm³ (range, 10.1-38.4 cm³). The prescription isodose lines ranged from 40% to 65% (mean 53%, median 50%). In single session RS cases, the mean marginal dose was 16.9 Gy (range, 7.2-25 Gy), and the mean nidus volume was 17.1 cm³ (range, 10.1-38.4 cm³). In two-stage volumetric RS cases, the mean nidus volume of 5 AVMs was 15.7 cm³ (range, 11.6-20.2 cm³), but the radiosurgical targets in 10 instances of GKS for these 5 AVMs ranged from 3.0 to 11.3 cm³ in size. The mean marginal dose was 20.8 Gy (range, 17.0-24.0 Gy) for 10 separate radiosurgical targets. The interval between two staged GKS treatments varied from 1 to 7 months.

The mean real target volume for 18 single sessions of RS was 17.1 cm³ (10.1-38.4 cm³), in contrast with the mean estimated target volume of 20.9 cm³ (12.0-45.0 cm³). The real and estimated target volume was compared in Fig. 2.

Nidus obliteration

The mean clinical follow-up period was 41.2 months (5.9-84.2 months) in all cases and 43.5 months (24.3-84.2

months) in non-bleeding cases. Complete obliteration was achieved in 8 of 23 (34.8%) single session RS cases and in 2 of 5 (40%) staged volumetric RS cases (Table 2). The largest volume of total obliteration was 25.3 cm³ (mean 13.4 cm³). The minimal marginal dose that resulted in total obliteration was 18 Gy. In two fatal bleeding cases,

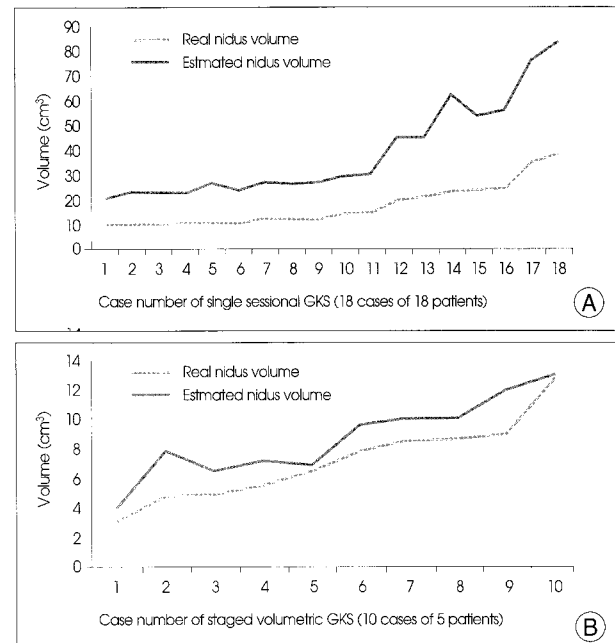


Fig. 2. Gadolinium enhanced Tetralogy of Fallot (TOF) MR images are incorporated into the Gamma Plan to assess estimated target volume (Black line) as a primarily estimated nidus volume. The gray line depicts substantial volume, which is the real target volume, where the embedded draining veins and feeding arteries have been removed. A : 18 cases of single sessional gamma knife radiosurgery (GKS). B : 10 cases of staged volumetric GKS.

Table 2. Radiosurgical outcomes

Outcome	Single session RS (%), n = 18	Staged volumetric RS (%), n = 5
Complete obliteration	8 (44)	2 (40)
Partial obliteration	6 (33)	3 (60)
Unchanged	2 (11.1)	0 (0)
Bleeding during follow-up	2 (11.1)	0 (0)

RS : radiosurgery

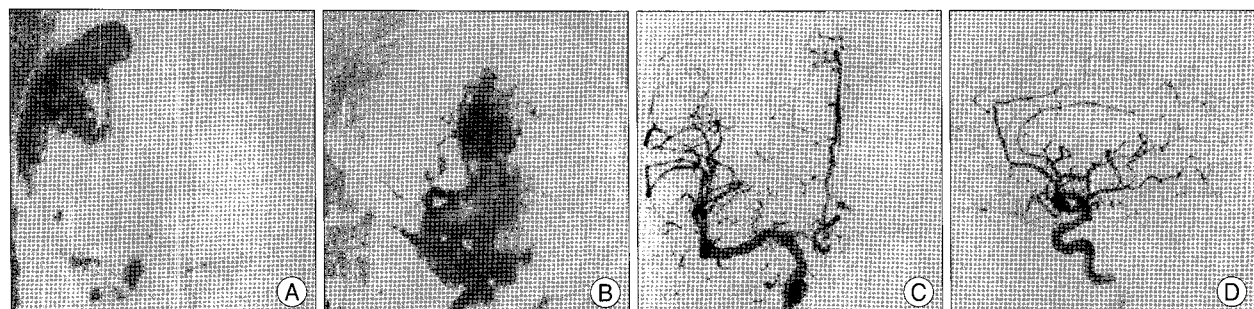


Fig. 3. A and B : Large arteriovenous malformation in the right frontoparietal lobe, fed by the ipsilateral anterior cerebral artery and the middle cerebral artery draining into the superior sagittal sinus in a 52-year-old man who presented with seizures. C and D : Complete obliteration is seen on follow-up conventional angiography 4 years after gamma knife radiosurgery. Target volume = 20.1 cm³, maximal volume = 50 Gy, marginal dose = 25 Gy.

AVM evaluation could not be obtained. A case of complete obliteration is shown in Fig. 3. In the single session RS group, the complete obliteration rate was 60% (6 of 10 cases) when the nidus volume was less than 15 cm³ and 25% (2 of 8 cases) when it was 15 cm³ or more. The obliteration rates for each volumetric group are shown in Table 3. Partial obliteration was seen in the other three patients who underwent staged RS, and all of them were re-treated with GKS thereafter.

Complications

ARE were found in 1 of 23 cases. A patient who received a marginal dose of 25.0 Gy and a maximal dose of 50.0 Gy suffered edema around the irradiated area. The patient had no distinguishable difference in either volume or dose compared to those patients who had no complications.

Bleeding occurred after GKS in 2 of 23 patients (8.7%); both died from hemorrhage. One of these patients had a history of hemorrhage prior to radiosurgery. Hemorrhage occurred at 5.9 months after radiosurgery in the first patient and at 36.5 months after radiosurgery in the other patient.

DISCUSSION

Although GKS is generally thought to be an effective treatment modality with great safety, the treatment results remain unsatisfactory for large AVMs^{14,19}. Several factors affect the results of radiosurgical treatment for large AVMs. Flickinger et al.⁴⁻⁷ reported that location, size, and hemodynamic characteristics should be considered in radiosurgical planning. Additionally, volume is one of most important factors influencing prognosis^{1,4,5,9}. Friedman et al⁹. reported a complete obliteration rate of 69% after radiosurgery for AVM nidi over 10 cm². Pan et al²⁰. reported a 77% complete obliteration rate in nidi 10 to 15 cm³ in size and a 25% complete obliteration rate in nidi over 15 cm³ during a follow-up period of 40 months. Moreover, with volumes over 15 cm³, the complete obliteration rate increased to 58% after a 50-month follow-up period. The investigators suggested that the latency period for large AVMs may be longer than that for small AVMs. In this study, the overall complete obliteration rate for single session RS was 44% (8 of 18 cases) : 60% when the nidus volume was less than 15 cm³ and 25% when it was 15 cm³ or more (Table 3).

The relatively low radiation dose could be one of the most potent factors contributing to the poor obliteration rate of large AVMs compared to small lesions²⁸. There is a tendency for the radiation dose to decrease as the volume of

Table 3. Radiosurgical planning and treatment outcomes based on nidus volume

Parameter	Nidus Volume	
	10-15 mm ³	≥ 15 mm ³
Marginal dose		
Mean (range)	20.3 Gy (18-25)	15.0 Gy (7.2-25)
Less than 20 Gy	4 (40%)	6 (75%)
20 Gy or more	6 (60%)	2 (25%)
Treatment outcome		
Total obliteration	6 (60%)	2 (25%)
Partial obliteration	2 (20%)	4 (50%)
No change	1 (10%)	1 (12.5%)
Bleeding during follow-up	1 (10%)	1 (12.5%)

the AVM increases, because normal intracranial structures surrounding the lesion might be irradiated in the case of larger AVM target volumes. Miyawaki et al.¹⁸ suggested that the dose-volume range for the optimal balance between successful obliteration and the risk of complications narrows as AVM size increases. In the present study of single session RS, the minimal marginal dose that resulted in total obliteration was 18 Gy. However, when the marginal dose was less than 20 Gy, the complete obliteration rate was only 25% (3 of 12 cases). The likelihood of cure has been shown to be dependent on the marginal dose^{8,15,16} whereas the risk of complications has been shown to be related primarily to the dose and volume irradiated⁵.

On the other hand, only two of five staged volumetric radiosurgery cases achieved complete obliteration. Through a decrease in the nidus volume to be irradiated, a higher marginal dose can be applied to the nidus²⁴. However, there are always limitations in the application of abundant radiation doses for fear of complications, resulting in partial obliteration during the latency period. If an effective dose can be given to the nidus, the outcome can be expected to improve.

Ten GKS treatments were delivered to 5 AVMs in this series of staged volumetric RS. Only three of 10 cases had marginal doses less than 20 Gy. Despite a sufficient marginal dose, complete obliteration was seen in only two of five AVMs, with partial obliteration seen in the rest. We concluded that several factors, including insufficient experience with multi-session RS, influenced the poor results (Fig. 4). Technical problems, especially planning errors, can also contribute to the higher rate of incomplete obliteration of large AVMs.

AVM nidus can be identified from conventional cerebral angiography and from gadolinium enhanced TOF MR images. From the angiographic images, projective volume of the nidus enables inclusion of the draining vein as illustrated in Fig. 5. On the other hand, from the TOF

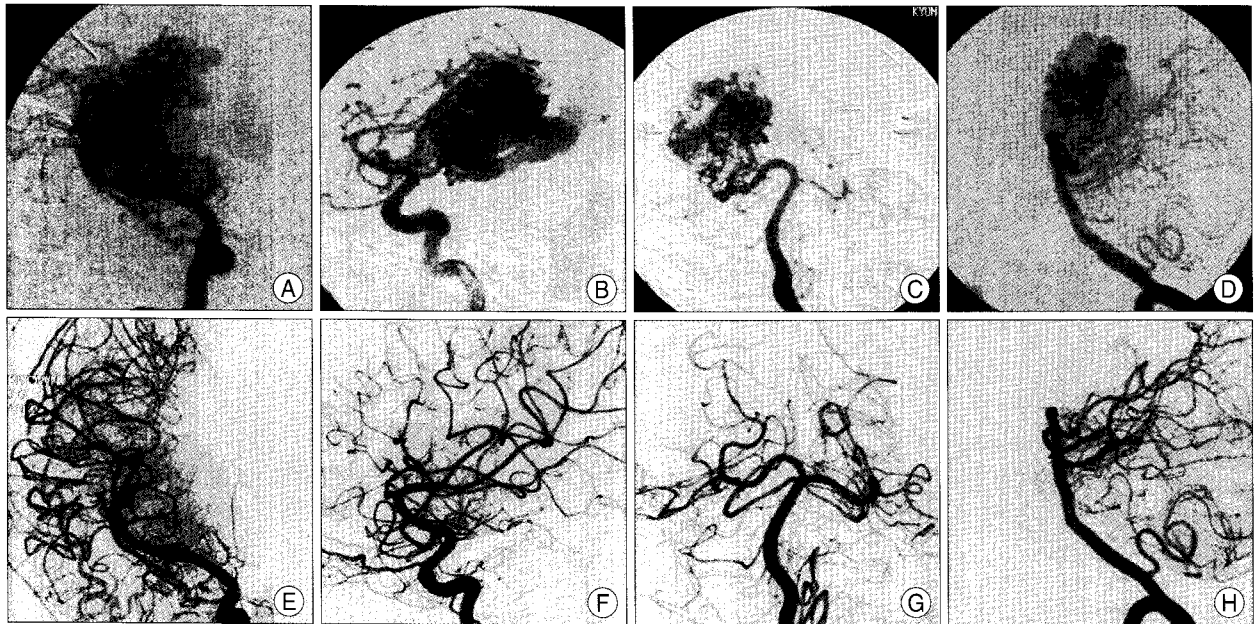


Fig. 4. A 27-year-old male patient who was treated with staged volumetric radiosurgery. A large arteriovenous malformation is supplied by both the anterior and posterior circulations. At first, the anterior compartment was irradiated with a marginal dose of 20 Gy on 11,300 mm³ (A and B). After 5 months, the posterior compartment was treated with a marginal dose of 24 Gy on 3,500 mm³ (C and D). On 5-year follow-up, angiography shows complete obliteration (E and F).

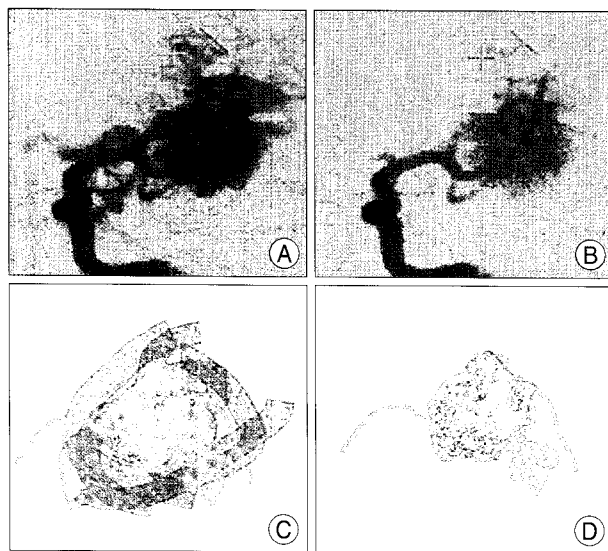


Fig. 5. The majority of the volume of the nidus is occupied by the enlarged vessels. Therefore, the definite target volume might have been smaller. Angiograms are shown in A and B, and corresponding schematic illustrations are shown in C and D.

MR images, tomographic volume of the malformed vessels excluding the draining veins comprises the supplying arteries. Therefore, as seen in Fig. 1, in combination of the two imaging techniques, the supplying arteries and draining veins could be discarded and true AVM nidus can be condensed. Recent developments in neurodiagnostic techniques allow accurate radiosurgical targeting which facilitates minimization of nidus volume to be irradiated. The present study also demonstrated that true large AVMs

may be fewer in number in these reasons.

Irradiation to surrounding normal tissues contributes to several AREs, such as cerebral edema, necrosis, vascular stenosis, cyst formation, and hemorrhage, and many previous studies have suggested that lower radiation dose decreases the incidence of ARE^{5,7,28}). Flickinger et al.⁵⁾ offered several hypotheses about complications related to AVM radiosurgery. They suggested that radiation-induced complications were due not only to irradiation of perilesional normal brain tissue, but also to irradiation of the AVM nidus inside the treatment volume. It is generally agreed that lower radiation dose decreases the incidence of ARE. Inoue et al.¹³⁾ reported a low incidence of ARE during a 10- to 15-year follow-up in 76 patients treated with doses lower than 20 Gy. In this study, cerebral edema occurred in one case in which the marginal dose was 25.0 Gy. The factor, which contributed to the development of edema after GKS, remains obscure, but relatively high dose irradiated or planning error could be one of most reliable reasons. Evolution of imaging tools like MR and angiogram serves more accurate images, which helps more effective planning.

Potent risk factors for AVM hemorrhage are most likely to correlate with AVM volume¹⁰). The hemorrhage risk correlated statistically with increasing AVM size, decreasing dose, and treatment isodose lines less than or equal to 70. The investigators also reported that neither patient age nor incidence of prior hemorrhage correlated with the risk of post-treatment bleeding. In a retrospective study, Friedman

et al.⁸⁾ found that 10 of 12 AVM cases with hemorrhage had angiographic risk factors, including arterial aneurysm, venous aneurysm, venous outflow stenosis, and periventricular location. They also found that GKS did not influence the hemorrhage rate of AVMs during the latency interval before obliteration. No protective benefit was conferred on patients who had incomplete nidus obliteration on early (< 60 mo) follow-up after radiosurgery²⁰⁾. Miyawaki et al.¹⁸⁾ reported that the rate of post-radiosurgical hemorrhage was 2.7% per person-year for AVMs with treatment volumes < 14 cm³ and 7.5% per person-year for AVMs > 14 cm³. There were two cases of fatal hemorrhage. One case of hemorrhage occurred at 5.9 months, which is latent period after GKS. The target volume was 12.1 cm³ and the marginal dose was 19.6 Gy. In the other case of hemorrhage, occurred at 36.5 months after radiosurgery, partial obliteration was shown at follow up angiogram.

CONCLUSION

Large AVMs are more fastidious, in terms of favorable treatment outcomes, compared to that of the smaller ones. The reason is that the larger AVMs cannot be irradiated with desired radiation dose with minimal effects on surrounding structures. Recent development of imaging devices and planning software, however, enable exclusion of feeding arteries and draining veins, thereby minimizing the target volume and delivery of sufficient treatment dose. We look forward to more investigations on various radiosurgical strategies in order for better outcomes with large AVMs.

References

1. Chang JH, Park YG, Choi JY, Chang JW, Chung SS : Factors Related to the Success of Gamma Knife Radiosurgery for Arteriovenous Malformations. *J Korean Neurosurg Soc* 30 : 1406-1416, 2001
2. Chang SD, Marcellus ML, Marks MP, Levy RP, Do HM, Steinberg GK : Multimodality treatment of giant intracranial arteriovenous malformations. *Neurosurgery* 61 : 432-442; discussion 442-444, 2007
3. Ellis TL, Friedman WA, Bova FJ, Kubilis PS, Buatti JM : Analysis of treatment failure after radiosurgery for arteriovenous malformations. *J Neurosurg* 89 : 104-110, 1998
4. Flickinger JC : An integrated logistic formula for prediction of complications from radiosurgery. *Int J Radiat Oncol Biol Phys* 17 : 879-885, 1989
5. Flickinger JC, Kondziolka D, Pollock BE, Maitz AH, Lunsford LD : Complications from arteriovenous malformation radiosurgery : multivariate analysis and risk modeling. *Int J Radiat Oncol Biol Phys* 38 : 485-490, 1997
6. Flickinger JC, Lunsford LD, Kondziolka D, Maitz AH, Epstein AH, Simons SR, et al. : Radiosurgery and brain tolerance : an analysis of neurodiagnostic imaging changes after gamma knife radiosurgery for arteriovenous malformations. *Int J Radiat Oncol Biol Phys* 23 : 19-26, 1992
7. Flickinger JC, Pollock BE, Kondziolka D, Lunsford LD : A dose-response analysis of arteriovenous malformation obliteration after radiosurgery. *Int J Radiat Oncol Biol Phys* 36 : 873-879, 1996
8. Friedman WA, Blatt DL, Bova FJ, Buatti JM, Mendenhall WM, Kubilis PS : The risk of hemorrhage after radiosurgery for arteriovenous malformations. *J Neurosurg* 84 : 912-919, 1996
9. Friedman WA, Bova FJ, Mendenhall WM : Linear accelerator radiosurgery for arteriovenous malformations : the relationship of size to outcome. *J Neurosurg* 82 : 180-189, 1995
10. Gobin YP, Laurent A, Merienne L, Schlienger M, Aymard A, Houdart E, et al. : Treatment of brain arteriovenous malformations by embolization and radiosurgery. *J Neurosurg* 85 : 19-28, 1996
11. Gobin YP, Vinuela F, Gurian JH, Guglielmi G, Duckwiler GR, Massoud TF, et al. : Treatment of large and giant fusiform intracranial aneurysms with Guglielmi detachable coils. *J Neurosurg* 84 : 55-62, 1996
12. Han JH, Kim DG, Chung HT, Park CK, Paek SH, Kim JE, et al. : Clinical and neuroimaging outcome of cerebral arteriovenous malformations after Gamma Knife surgery : analysis of the radiation injury rate depending on the arteriovenous malformation volume. *J Neurosurg* 109 : 191-198, 2008
13. Inoue HK : Long-term results of Gamma Knife surgery for arteriovenous malformations : 10- to 15-year follow up in patients treated with lower doses. *J Neurosurg* 105 Suppl : 64-68, 2006
14. Karlsson B, Jokura H, Yamamoto M, Soderman M, Lax I : Is repeated radiosurgery an alternative to staged radiosurgery for very large brain arteriovenous malformations? *J Neurosurg* 107 : 740-744, 2007
15. Karlsson B, Lindquist C, Steiner L : Effect of Gamma Knife surgery on the risk of rupture prior to AVM obliteration. *Minim Invasive Neurosurg* 39 : 21-27, 1996
16. Lunsford LD, Kondziolka D, Flickinger JC, Bissonette DJ, Jungreis CA, Maitz AH, et al. : Stereotactic radiosurgery for arteriovenous malformations of the brain. *J Neurosurg* 75 : 512-524, 1991
17. Maruyama K, Kondziolka D, Niranjana A, Flickinger JC, Lunsford LD : Stereotactic radiosurgery for brainstem arteriovenous malformations : factors affecting outcome. *J Neurosurg* 100 : 407-413, 2004
18. Miyawaki L, Dowd C, Wara W, Goldsmith B, Albright N, Gutin P, et al. : Five year results of LINAC radiosurgery for arteriovenous malformations : outcome for large AVMS. *Int J Radiat Oncol Biol Phys* 44 : 1089-1106, 1999
19. Pan DH, Guo WY, Chung WY, Shiau CY, Chang YC, Wang LW : Gamma knife radiosurgery as a single treatment modality for large cerebral arteriovenous malformations. *J Neurosurg* 93 : 113-119, 2000
20. Pollock BE, Flickinger JC, Lunsford LD, Bissonette DJ, Kondziolka D : Hemorrhage risk after stereotactic radiosurgery of cerebral arteriovenous malformations. *Neurosurgery* 38 : 652-659; discussion 659-661, 1996
21. Pollock BE, Flickinger JC, Lunsford LD, Maitz A, Kondziolka D : Factors associated with successful arteriovenous malformation radiosurgery. *Neurosurgery* 42 : 1239-1244; discussion 1244-1247, 1998
22. Pollock BE, Lunsford LD, Kondziolka D, Bissonette DJ, Flickinger JC : Stereotactic radiosurgery for postgeniculate visual pathway arteriovenous malformations. *J Neurosurg* 84 : 437-441, 1996
23. Sirin S, Kondziolka D, Niranjana A, Flickinger JC, Maitz AH, Lunsford LD : Prospective staged volume radiosurgery for large arteriovenous malformations : indications and outcomes in otherwise untreatable patients. *Neurosurgery* 58 : 17-27; discussion 17-27, 2006
24. Sirin S, Kondziolka D, Niranjana A, Flickinger JC, Maitz AH, Lunsford LD : Prospective staged volume radiosurgery for large arteriovenous malformations : indications and outcomes in otherwise untreatable patients. *Neurosurgery* 62 : 744-754, 2008
25. Steinberg GK, Chang SD, Levy RP, Marks MP, Frankel K, Marcellus

- M : Surgical resection of large incompletely treated intracranial arteriovenous malformations following stereotactic radiosurgery. *J Neurosurg* 84 : 920-928, 1996
26. Steiner L, Lindquist C, Adler JR, Torner JC, Alves W, Steiner M : Clinical outcome of radiosurgery for cerebral arteriovenous malformations. *J Neurosurg* 77 : 1-8, 1992
27. Yamamoto M, Barford BE : Gamma Knife Radiosurgery for Arteriovenous Malformations : Past Hope and Present Reality. *J Korean Neurosurg Soc* 39 : 1-10, 2006
28. Yamamoto Y, Coffey RJ, Nichols DA, Shaw EG : Interim report on the radiosurgical treatment of cerebral arteriovenous malformations. The influence of size, dose, time, and technical factors on obliteration rate. *J Neurosurg* 83 : 832-837, 1995