Control of epilepsy associated with cerebral arteriovenous malformations after radiosurgery

Hiroki Kurita, Shunsuke Kawamoto, Ichiro Suzuki, Tomio Sasaki, Masao Tago, Atsuro Terahara, Takaaki Kirino

Abstract

Objective—To investigate the effect of radiosurgery for symptomatic epilepsy associated with cerebral arteriovenous malformations (AVMs).

Methods—Thirty five patients with unruptured epileptogenic AVMs were studied with a mean follow up of 43.0 months. The duration of epilepsy before radiosurgery ranged from 2 months to 21 years (mean 2.8 years). Fifteen patients showed partial seizures; eight of these had associated secondary generalisation. The remaining 20 patients showed only generalised seizures without preceding focal seizures.

Results—At the final follow up examination, 28 patients remained seizure free, whereas seizures continued in seven. Variables significantly associated with continuity of seizures after radiosurgery were the number of seizures before therapy ($p<0.01$) and duration of epilepsy ($p<0.05$). According to Engel's classification, the 10 patients with intractable seizures before treatment included five with grade I, four with grade III, and one with grade IV. The frequency of seizures began to decrease several months after radiosurgery; much shorter than the time required for morphological change in the AVMs.

Conclusions—Radiosurgery seems to be beneficial for seizure control in patients with unruptured epileptogenic AVM.

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Keywords: arteriovenous malformation; symptomatic epilepsy; gamma knife; radiosurgery

Department of Neurosurgery

H Kurita
S Kawamoto
I Suzuki
T Sasaki
T Kirino

Department of Radiology, Faculty of Medicine, University of Tokyo, Tokyo, Japan
M Tago
A Terahara

Correspondence to:
Dr Hiroki Kurita,
Department of
Neurosurgery, Faculty of
Medicine, University of
Tokyo, 7-3-1, Hongo,
Bunkyo-ku, Tokyo 113-8655,
Japan. Telephone 0081 3
3815 5411; fax 0081 3 5800
8655.

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Table 1 Initial manifestations of 315 patients radiosurgically treated for AVM

Symptoms	Patients	
	No	%
Haemorrhage	228	72.4
Seizure	42	13.3
Headache	15	4.8
Neurological deficits	10	3.2
Others	3	1.0
Incidental	17	5.4
Total	315	100.0

Table 2 Location of arteriovenous malformations (AVMs) and type of seizures

Location of AVM	Patient No	Side		Type of seizures		
		L	R	SPS	CPS	SG
Frontal	10	7	3	2	1	10 (8*)
Parietal	7	5	2	3	1	3 (3*)
Temporal	13	9	4	1	3	11 (9*)
Occipital	5	1	4	5	0	4 (0*)
Total	35	22	13	11	5	28 (20*)

SPS=simple partial seizure; CPS= complex partial seizure; SG=secondarily generalised seizure.
*Generalised seizure without aura or focal symptoms.

Various therapeutic alternatives are currently available for eliminating the risk of bleeding from cerebral arteriovenous malformations (AVMs), and the reported treatment results have been favourable in terms of overall morbidity and mortality. However, the prognosis of epilepsy associated with cerebral AVMs has received little attention. Controversy exists on the surgical treatment of AVMs associated with epilepsy, and seizure outcome after AVM radiosurgery has not been documented in detail.

In this study, we analysed the characteristics and frequency of seizures in 35 patients with epileptogenic unruptured AVMs after gamma knife radiosurgery. A retrospective survey of 22 additional patients with unruptured non-epileptogenic AVMs was also done to assess the development of seizures after the procedure. Here we report the early effect of focused irradiation on seizures associated with AVMs and discuss the various factors that influence the prognosis.

Patients and methods

PATIENT POPULATION

Between June 1990 and December 1995, 315 patients with angiographically demonstrable cerebral arteriovenous malformations (AVMs) underwent radiosurgical treatment at our institution. The initial manifestation at diagnosis was haemorrhage in 228 (72.4%), seizure in 42 (13.3%), headache in 15 (4.8%), progressive or stable neurological deficits in 10 (3.2%), and other clinical symptoms in three (1.0%). In the remaining 17 patients (5.4%), AVM was an incidental finding (table 1).

From 42 patients who had epilepsy as a diagnostic symptom, we excluded five who underwent surgical resection or had a bleeding episode before radiosurgery, one whose AVM bled during the latent interval after radiosurgery, and one who had an infratentorial AVM. The present retrospective study was based on 35 patients with epileptogenic unruptured supratentorial AVMs with a clinical follow up of at least 18 months (mean 42.9 (SD 17.6) months).

There were 22 males and 13 females, aged between 12 and 50 years (mean 31.5 (SD 11.6)

Table 3 Clinical summary of patients with epileptogenic/non-epileptogenic AVMs

Variable	Patients with epileptogenic AVM (n=35)	Patients with non-epileptogenic AVMs (n=22)
Males/females	22/13	15/7
Age at radiosurgery	31.5 (11.6) (12–50)	34.2 (13.2) (13–56)
Mean nidus diameter (mm)	17.0 (7.5) (0.6–36.0)	19.5 (5.6) (11.2–33.7)
Nidus volume (cm ³)	3.9 (4.3) (0.1–25.0)	4.7 (4.4) (0.7–20.0)
R/L	13/22	17/5
Temporal/extratemporal lobe	13/22	7/15
Cortical/subcortical	21/14	9/13
Superficial/deep drainage	27/8	17/5
Duration of follow up	43.0 (20.0) (18–83)	30.2 (15.4) (12–62)

Figures in parentheses are (SD) (range).

years) at radiosurgery. The patients were aged 9 to 48 (mean 28.7 (SD 11.9 years) at seizure onset and had an average seizure history of 2.8 years (range 2 months to 21 years). Five patients had complex partial seizures, and 11 had simple partial seizures (focal motor in four cases, somatosensory in two, visual in five, and aphasic in two; two patients had two types of

simple partial seizures, including one who had both simple and complex partial seizures. Eight patients with partial seizure had associated secondary generalisation. In 20 patients, only generalised seizures, which were presumably preceded by partial seizures, were noticed. At radiosurgery, all patients except one, who refused medication, were given antiepileptic drugs for seizure prophylaxis with a mean duration of 2.0 (SD 4.3) years. Patients were divided into two groups according to the number of seizures: few ($\leq$ five and frequency $\leq$ 1/month, 25 patients including 18 with single seizure) or numerous ($>$ five and frequency $>$ 1/month, 10 patients).

Before irradiation, the AVMs were partially obliterated by transarterial embolisation in seven patients (total 16 procedures; mean 2.3 procedure/patient). Seizure frequency remained unchanged during the interval between embolisation and radiosurgery (mean 3.3 months, range 1 to 6 months). The patients were mentally and neurologically normal except for one with hemiparesis of the upper limbs due to polio and one with hemianopsia.

Table 4 Seizure free rate according to clinical characteristics

Characteristic	Seizure free rate	Statistic	95%CI	p Value
Patient's characteristics				
Age (y):				
≤34	0.789 (15/19)	0.177	(−0.241 to 0.289)	NS
>34	0.813 (13/16)			
Sex:				
Male	0.864 (19/22)	1.229	(−0.116 to 0.460)	NS
Female	0.692 (9/13)			
Characteristics of seizure				
Number of pretreatment seizures:				
≤5	0.920 (23/25)	2.806	(0.093 to 0.747)	<0.01
>5	0.500 (5/10)			
Duration of seizure history (months):				
≤6	0.944 (17/18)	2.200	(0.046 to 0.548)	<0.05
>6	0.647 (11/17)			
Age at seizure onset (y):				
≤32	0.789 (15/19)	0.177	(−0.241 to 0.289)	NS
>32	0.813 (13/16)			
Seizure type:				
Partial seizure without generalisation	0.571 (4/7)	1.692	(−0.102 to 0.674)	NS
Secondary generalised seizure	0.857 (24/28)			
Characteristics of AVM				
Side:				
Right	0.846 (11/13)	0.521	(−0.190 to 0.336)	NS
Left	0.773 (17/22)			
Location:				
Temporal	0.923 (12/13)	1.400	(−0.039 to 0.431)	NS
Extratemporal	0.727 (16/22)			
Cortical	0.857 (18/21)	1.362	(−0.137 to 0.423)	NS
Subcortical	0.714 (10/14)			
Drainage:				
Superficial	0.875 (7/8)	0.602	(−0.711 to 0.905)	NS
Deep	0.778 (21/27)			
Nidus diameter (mm):				
≤18.1	0.778 (14/18)	0.341	(−0.219 to 0.311)	NS
>18.1	0.824 (14/17)			
Nidus volume (cm ³):				
≤3.1	0.778 (14/18)	0.341	(−0.219 to 0.311)	NS
>3.1	0.824 (14/17)			
Treatment parameter				
Central dose delivered (Gy):				
≤40	0.880 (22/25)	0.839	(−0.195, 0.455)	NS
>40	0.750 (6/8)			
Marginal dose delivered (Gy):				
≤20	0.769 (20/26)	0.774	(−0.141, 0.381)	NS
>20	0.889 (8/9)			
Follow up findings				
Angiographical cure:				
yes	0.905 (19/21)	1.899	(−0.018, 0.542)	NS
no	0.643 (9/14)			
Radiation-induced edema:				
yes	0.750 (9/12)	0.535	(−0.214, 0.366)	NS
no	0.826 (19/23)			
AED treatment at last follow up:				
yes	0.750 (18/24)	1.089	(−0.084, 0.402)	NS
no	0.909 (10/11)			
Length of follow-up (months):				
≤36.0	0.778 (14/18)	0.341	(−0.219, 0.311)	NS
>36.0	0.824 (14/17)			

CHARACTERISTICS OF AVMs

In all cases, the AVM characteristics were defined by cerebral angiography. Most of the lesions in this series were small ($<$ 3 cm in diameter). The diameter ranged from 0.6 to 36 mm (mean 17.0 (SD 7.5 mm)), and the volume from 0.1 to 25 cm³ (mean 3.9 (SD 4.3) cm³). In 21 patients (60.0%), the AVMs were located in the cerebral cortex (cortical AVMs), and the other 14 in the white matter (subcortical AVMs). Seventeen AVMs (48.6%) were located in the eloquent area of the brain, and eight (22.8%) drained into deep veins. The most frequent location was the temporal lobe, followed by the frontal, parietal, and occipital lobes. The types of seizures and locations of the AVMs are summarised in table 2.

To investigate the development of new seizures after radiosurgery, we also undertook a retrospective survey of 22 patients with AVMs with no history of seizures, haemorrhages, neurological deficits, or surgical resection treated in the same period (non-epileptogenic AVMs). There were no significant differences in the demographic characteristics of the patients between the epileptogenic and non-epileptogenic AVM groups (table 3).

GAMMA KNIFE RADIOSURGERY

Radiosurgery was performed using a 201 source ⁶⁰Co gamma unit. The definition of the nidus and localisation of the irradiation target were done on biplane stereotactic cerebral angiography. After April 1992, thin slice high resolution dynamic stereotactic CT was used in combination to obtain precise information on the three dimensional shape of the nidus. A MicroVAX computer system (Digital Equipment Corporation, Westminister, MA, USA) was used for complex dose planning. The radiation dose delivered to the margin of the nidus, and the number and configuration of irradiation isocentres were determined jointly by neurosurgeons and radiation oncologists.

Table 5 Clinical summaries and responses to irradiation in 10 patients with numerous seizures before radiosurgery

Patient	Age/sex	Seizure duration	Seizure type	Seizure frequency	Antiepileptic drug	Volume of AVM (cm ³)	Location of AVM	Central/peripheral dose (Gy)	AVM response
1	15 F	5 y	1, SPS(m) 2, SPS(s)	1, monthly 2, monthly	PHT, PB	25.0	R parietal	30/15	NC (6 y)
2	32 F	11 y	CPS, SG	Weekly	PHT, PB	3.9	R temporal	40/20	CR (3 y)
3	26 M	1 y	CPS	Weekly	CBZ, PHT, VPA	5.5	R temporal	1st: 40/20 *2nd: 40/20	PR (3 y) CR (1.5 y)
4	14 F	1.5 y	1, CPS, 2, SPS(m), SG	1, weekly 2, monthly	CBZ, PB, VPA	2.6	L frontal	40/20	PR (5 y)
5	34 F	19 y	SPS (v), SG	Monthly	PHT, PB	3.3	R occipital	40/20	CR (3 y)
6	41 M	3 y	SPS (v)	†Daily	CBZ	5.6	R occipital	40/20	CR (3 y)
7	43 F	8 y	SG	Monthly	PB	1.1	L temporal	40/20	CR (2.5 y)
8	44 F	3.5 y	SG	Monthly	VPA	0.4	L temporal	40/20	PR (2 y)
9	17 F	0.5 y	CPS	Weekly	ZNS	0.6	R parietal	44.4/20	PR (1.5 y)
10	34 M	3.5 y	SPS (s)	Monthly	refused	6.9	R parietal	40/20	CR (1 y)

NC = no therapeutic response; PR = partial obliteration of the AVM; CR = total obliteration of the AVM; SPS = simple partial seizures: (m); motor, (s); somatosensory, (v); visual; CPS = complex partial seizure; SG = secondary generalized seizure; PHT = phenytoin; PB = phenobarbitone; CBZ = carbamazepine; VPA = valproate sodium; ZNS = zonisamide.

* Small remnant of AVM was reirradiated 3 years after radiosurgery.

† Seizure frequency before introduction of CBZ, which was introduced 6 months before radiosurgery and discontinued 1 year later.

All patients continued to have antiepileptic drugs at radiosurgery. In patients who had multiple seizures before radiosurgery, phenobarbitone was administered intramuscularly immediately after the procedure.

FOLLOW UP EVALUATION

Clinical examinations and radiological check ups (MRI, or contrast CT, or both, and cerebral angiography in selected patients) were performed at 6 month intervals. In patients whose AVMs had disappeared on MRI or CT, cerebral angiography was performed. Most patients were maintained on the same dose of antiepileptic drugs after radiosurgery; slow drug withdrawal was then offered if they were seizure free for 2 years. For patients living away from our institution, radiological imaging, clinical examinations, and antiepileptic medication were provided by the referring neurosurgeons or neurologists and reviewed at our institute.

TERMINOLOGY

Patients were classed as “seizure free” if they had not experienced a seizure for at least 1 year at the final follow up examination, with or without antiepileptic medication. Seizures that occurred immediately after radiosurgery (<24 hours) were excluded from the analysis. Seizure outcome in patients with numerous seizures before radiosurgery was graded according to a simplified version of Engel’s classification¹ (grade I: seizure free except for an occasional aura, grade II: rare seizures; 1–2/year, grade III: worthwhile reduction in frequency or severity of seizures, grade IV: no worthwhile improvement).

STATISTICAL ANALYSIS

All data were presented as mean (SD). A test for proportion was used to identify clinical features associated with seizure control after irradiation. Continuous variables were dichotomised at their median values. The Mann-Whitney rank test was used for non-parametric variables. The level of significance was $p < 0.05$.

Results

SEIZURES IMMEDIATELY AFTER RADIOSURGERY

Of 35 patients with a seizure history, four (11.4%) had a seizure within 24 hours after radiosurgery, whereas the corresponding incidence was one of 22 patients (4.5%) without a seizure history. In four of these five patients, the AVMs were located in the cerebral cortex. All of these patients remained seizure free subsequently, except for one who had an increased seizure frequency for several months after radiosurgery.

SEIZURE DEVELOPMENT AFTER RADIOSURGERY

Of the 22 patients with no history of seizures, 21 did not experience seizure after radiosurgery within a mean follow up period of 33.5 months (range 12–62 months). One patient had seizures immediately after irradiation, but no recurrence was seen during follow up without medication. No patient developed late seizures after radiosurgery.

SEIZURE CONTROL AFTER RADIOSURGERY

Of the 35 patients with a seizure history before radiosurgery, 28 (80%) were classed as “seizure free” at the last follow up examination. Of these patients, 10 were seizure free without receiving antiepileptic drugs, and four were in the process of tapering off. Another 14 patients continued the treatment regimen, including four in whom seizures had recurred 13–60 months after withdrawal of antiepileptic drugs. Among seven patients classed as “not seizure free” (at least one attack within the final year of follow up), seizure frequency was decreased in four and unchanged in two. Only one patient had increased seizure frequency several months after radiosurgery. After radiosurgery, 34 patients received antiepileptic drugs with a mean duration of 2.9 (SD 1.6) years. At final follow up, 24 of 35 patients (68.6%) continued receiving antiepileptic drugs; however, the medical status did not influence the seizure outcome.

On the other hand, the seizure free rate achieved 92% (23/25) in patients with few seizures before radiosurgery whereas the rate remained 50% (5/10) in patients with numerous seizures. The difference was significant ($p < 0.01$). Patients with a short history of

Table 5 Continued

Brain oedema	Change in seizure frequency	Follow up (months)	Seizure outcome (Engel grade)
No	1, free since 8 months 2, no change	83	Grade 3 AED continued
No	Decreased since 4 months free since 37 months	78	Grade 1 AED discontinued
No	Decreased since 3 months free since 41 months	67	Grade 1 AED reduced
No	1, no change 2, free since radiosurgery	70	Grade 3 AED continued
Local	Decreased since 4 months free since 35 months	55	Grade 1 AED continued
Local	Free since radiosurgery	48	Grade 1 AED discontinued
No	Free since radiosurgery	32	Grade 1 AED reduced
No	No change	24	Grade 4 AED continued
Local	Decreased since 3 months	20	Grade 3 AED continued
Local	Decreased since 5 months	18	Grade 3 AED refused

seizures (≤ 6 months) were also associated with significantly higher seizure free rate (94.4%; 17/18) than patients with a long seizure history (64.7%; 11/17) ($p<0.05$). No other initial characteristics, treatment variable, or follow up findings influenced the seizure free rates. Variables examined and their significance are summarised in table 4.

RESPONSE TO IRRADIATION IN PATIENTS WITH NUMEROUS SEIZURES BEFORE RADIOSURGERY
Ten patients had experienced numerous seizures (>10 times, with a frequency ≥ 1 /month) before radiosurgery. Table 5 shows the clinical characteristics of the patients and their responses to irradiation. All patients had frequent seizures despite antiepileptic medication except two; one who had refused medication (patient 10), and one in whom seizure prophylaxis was introduced only for a few months before and after radiosurgery (patient 6). Seizure history ranged from 6 months to 19 years (mean 5.6 years).

After radiosurgery, the seizures disappeared in two patients. They could discontinue antiepileptic drugs or reduce its dose. Seizure frequency was decreased in five patients from several months after radiosurgery, and the seizures disappeared subsequently in three of them. In two patients having two types of seizure (two types of simple partial seizures in one, and simple partial seizures and complex partial seizures in another), one type disap-

Figure 1 (A) Brain CT with contrast enhancement of patient 2 before radiosurgery, showing a right anteromedial temporal AVM with a maximum diameter of 2.5 cm. (B) and (C) Stereotactic right internal carotid angiography (ICAG); frontal and lateral projections showing the AVM. At radiosurgery, 20 Gy was delivered to the 50% isodose line (maximum dose 40 Gy). (D) Contrast CT; (E) and (F) right ICAG 1 year after radiosurgery, showing no morphological therapeutic response. (G) Contrast CT; and (H) and (I) right ICAG 3 years after radiosurgery, showing total obliteration of the AVM.

Figure 2 T2 weighted imaging of patient 3 before radiosurgery, demonstrating (A) a right posteromedial temporal AVM with a maximum diameter of 2.5 cm. (B) and (C) Right vertebral angiogram (VAG). Frontal and lateral projections before radiosurgery, showing the partially obliterated AVM after transarterial embolisation. A total of 20 Gy of irradiation was delivered to the periphery of the AVM at the first radiosurgical treatment. (D) T2 weighted MR image, and (E) and (F) right VAG 6 months after first radiosurgery, showing no morphological therapeutic response or adverse reactions to irradiation. Subsequently the patient underwent a second radiosurgery 2.5 years later to obliterate the small remnant of the AVM. (G) T2 weighted MR image, and (H) and (I) right VAG 1.5 years after second radiosurgery (4.5 years from first irradiation) confirming that the AVM was totally obliterated.

peared after radiosurgery, whereas the other type showed no change in frequency. Only one patient had seizures at the same frequency as that before radiosurgery.

Total obliteration of the AVM was confirmed in six patients (one of whom required further radiosurgery for residual AVM 3 years after initial irradiation), and five of them remained seizure free at the time of final evaluation. The AVMs were partially obliterated or showed no change in size in four patients, although seizure frequency was reduced with the exception of one. Asymptomatic radiation induced transient brain oedema was seen in four patients (40%).

As a result, Engel grade I seizure outcome was attained in five patients, grade III in four, and grade IV in one. A positive effect of irradiation for seizure control was found in nine of 10 patients (90%) with numerous symptomatic seizures associated with AVMs. The effect began to appear several months after

irradiation, much earlier than, or even without, the morphological therapeutic response of the AVMs or any adverse effect on the surrounding brain tissue.

ILLUSTRATIVE CASES

Patient 2

This 32 year old woman had had an initial attack of generalised seizure at the age of 11 years. Despite antiepileptic medication, complex partial seizures developed subsequently. As she grew older, the frequency of complex partial seizures increased, reaching two to three times a week, occasionally associated with secondary generalisation. Before radiosurgery, an interictal scalp EEG showed sharp waves in the right temporal region. Brain CT with contrast medium showed a right anteromedial temporal AVM (fig 1 A). Cerebral angiography disclosed a high flow AVM fed mainly by the right anterior temporal artery, which drained into both

the cortical and basal veins. Gamma knife radiosurgery was performed in December 1990. A total of 20 Gy of radiation were delivered in a single dose to the periphery of the nidus (fig 1 B,C). The seizures seemed unchanged for about 4 months after irradiation, and then decreased in frequency. At her 1 year follow up, CT and angiography showed no morphological therapeutic response (fig 1 D,E,F). However, seizure frequency decreased to one every several months, and EEG showed a decrease of epileptic discharges. Total obliteration of the AVM was confirmed 36 months (fig 1 G,H,I) after radiosurgery, and the last seizure occurred 37 months after radiosurgery. After that time, she had been totally seizure free for 3 years with tapering off of antiepileptic drugs, and remained neurologically intact.

Patient 3

This 26 year old man had had a history of complex partial seizures for 1 year before diagnosis of AVM. The attacks recurred weekly despite antiepileptic medication. After partial obliteration of the nidus by transarterial embolisation in another hospital, he was transferred to our institution for radiosurgical treatment. Brain MRI showed a right posteromedial temporal AVM (fig 2 A). Cerebral angiography demonstrated a partially obliterated AVM fed mainly by the temporal branches of the posterior cerebral artery and lateral posterior choroidal artery, and drained into the Galenic system (fig 2 A,B,C). He underwent gamma knife radiosurgery in March 1991. The AVM was totally covered with more than 20 Gy. Seizure frequency decreased from 3 months after radiosurgery. At his 6 month follow up, seizure frequency had improved to one a month without any morphological response or an adverse effect of irradiation (fig 2 D,E,F). He experienced his last attack 41 months after irradiation. Subsequently, he underwent further radiosurgery for his small AVM remnant 3 years after initial radiosurgery, and total obliteration was confirmed 1.5 years later (fig 2 G,H,I). Although he has continued to take a low dose of antiepileptic drugs, he has been totally seizure free for more than 2 years.

Discussion

EPILEPSY ASSOCIATED WITH AVM

Epilepsy is the second most common mode of presentation of cerebral AVMs. The reported incidence varies from 18% to 60%.²⁻¹¹ However, compared with the numerous reports concerning the risk of bleeding,^{3 8 12-15} the natural history of AVMs in relation to the risk of epilepsy and the factors influencing the epilepsy development remain less clear.

Several authors have suggested that seizures associated with AVMs are easy to control,^{5 7 12 16 17} and that surgery allows good control of epilepsy.^{5 9 17-21} Trumpy and Eldevik¹⁷ cured 50% of patients with preoperative seizures due to AVMs. Guidetti and Delitala¹⁸ reported that seizures were improved in 53% of patients after AVM surgery. Heros *et al*⁵ reported that over half of all preoperative seizures were cured or greatly improved after

resection of AVMs, and that only 12.7% worsened. In a recent report by Piepgras *et al*,⁶ the seizure free ratio after surgery was as high as 83% in patients with preoperative seizures and 94% in patients without. Several authors have recommended more radical resection including cortical excision of the epileptogenic foci around the AVMs.¹⁹⁻²¹

However, several studies disclosed that epileptogenic foci secondary to AVMs become progressively more intractable,^{22 23} or that surgery cannot contribute to seizure control.^{2 7 16 24 25} Forster *et al*²⁵ reported that only 4% of patients with epileptogenic AVMs were seizure free after surgery. Parkinson and Bachers¹⁶ stated that patients with preoperative seizures were likely to have them postoperatively. Drake²⁶ concluded that excision of an AVM alone would not relieve associated epilepsy. The reported risk of new epilepsy after AVM surgery also varies, ranging from <10% to >50%.^{5 7 12 16 17 24 25}

SEIZURE OUTCOME IN PATIENTS WITH RADIOSURGICALLY TREATED AVMs

Although the primary aim of radiosurgery for cerebral AVMs is to obliterate the nidus and eliminate the risk of bleeding, a positive effect of radiosurgery for seizure control has also been reported by several gamma knife users.²⁷⁻³¹ Steiner *et al*²⁹ reported that 69% of 59 patients with seizures became seizure free or were significantly improved after radiosurgery. In their series, 11 patients with medically intractable seizures became seizure free with or even without AVM obliteration. Lunsford *et al*²⁸ noted that 51% of 43 patients showed improved seizure control, and only one showed deterioration. At the Mayo Clinic,^{27 31} 20% of 59 patients with a seizure history showed a seizure decrease or elimination at the last follow up. Sutcliffe *et al*³⁰ reported that 38% of 49 patients with seizures had no further seizures after radiosurgery, 22% improved, and 6% showed deteriorated seizure control. Similar effects of radiosurgery have been reported for different types of penetrating radiation, including protons,^{4 32} heavy charged particles,^{33 34} and α irradiation.³⁵ On the contrary, Colombo *et al*³⁶ stated that there was no significant influence of x ray irradiation on seizure frequency or symptoms. Seifert *et al*³⁷ reported an increase in seizure frequency in seven of 39 patients after proton beam irradiation.

These reports suggest that focused single high dose irradiation does have some beneficial effects on seizures related to AVMs in a proportion of cases. However, the frequency and severity of seizures before irradiation or course of seizure improvement after radiosurgery have not been well documented. Furthermore, the effect of irradiation has not been quantified because of the complexity of the variables affecting seizure control, such as medication, presence or absence of previous haemorrhage or surgery, and psychological factors.

ANALYSIS OF THE PRESENT SERIES

In this series, four of 35 patients (11.4%) with epileptogenic AVM, and one of 22 patients (4.5%) with non-epileptogenic AVM had a seizure within 24 hours after irradiation. This so-called immediate epilepsy has been noted by several authors^{27 28 30 38} as an acute morbidity of radiosurgery. However, this acute exacerbation effect of irradiation on seizure activity seems to be transient in most cases, and, with a few exceptions, does not affect long term seizure control.³⁰ In fact, all of our patients with immediate epilepsy attained good seizure control afterwards, and none of 22 patients without seizures developed late seizures after radiosurgery within a mean follow up period of 33.5 months. Although this incidence compared favourably with reported surgical series, more long term follow up is necessary to determine whether radiosurgery has a protective effect against future development of epilepsy. On the other hand, 80% of 35 patients with epileptogenic AVMs remained seizure free, and epilepsy improved or disappeared in nine of 10 patients who had numerous seizures before radiosurgery. It must be plainly stated that there are no adequate controls in the present study, and the observation period for judging seizure control is not long enough to make definite conclusions. However, our experience suggests that radiosurgery allows seizure control in a proportion of treated patients with epileptogenic AVMs.

Analysis of factors affecting seizure control showed that a longer history and increased number of seizures were associated with a worse seizure outcome. Comparable findings have also been reported for AVM surgery.^{9 20 21} In such cases, epileptogenic foci occurring at a distance from the AVM should be considered.^{39 40}

On the other hand, the patients with angiographical obliteration tended to be associated with higher seizure free rate than non-obliterators (90.5% *v* 64.3%). Indeed, ischaemia of the surrounding brain is considered to be one of the pathophysiological factors of epilepsy, and amelioration of the arteriovenous shunt should be expected to alter regional blood flow resulting in relief of epilepsy.

The mechanism of seizure control in the present series remains unresolved; however, our findings may provide some basis for considering the efficacy of irradiation on epileptic activity in the surrounding gliotic brain.⁴¹ Because the frequency of seizures began to decrease several months after irradiation, much earlier than, or even in the absence of morphological change in the AVMs. Similar putative therapeutic efficacy of irradiation has been seen in patients with tumour related epilepsy.⁴²⁻⁴⁷ Although there is only a small amount of solid evidence, irradiation of the epileptogenic focus has been reported to have a curative effect in selected series.⁴⁸⁻⁵¹ The dose delivered to the foci has varied, the seizures began to improve after a period of between several months and one year, similar to our findings.

In conclusion, a single standard radiosurgical dose of irradiation can improve symptomatic epilepsy associated with AVMs in a proportion of treated patients. Our present findings should contribute to decision making when treating patients with epileptogenic unruptured AVMs.

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