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W Y Guo, D H Pan, H M Wu, W Y Chung, C Y Shiau, L W Wang, H J Chiou, M Y Yen and M M Teng

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Radiosurgery as a Treatment Alternative for Dural Arteriovenous Fistulas of the Cavernous Sinus

Wan-Yuo Guo, David H. C. Pan, Hsiu-Mei Wu, Wen-Yuh Chung, Cheng-Ying Shiau, Ling-Wei Wang, Hong-Jen Chiou, May-Yung Yen, and Michael M. H. Teng

PURPOSE: Radiosurgery is an effective treatment for cerebral arteriovenous malformations. We conducted the present study to investigate the feasibility and efficacy of gamma knife radiosurgery for dural arteriovenous fistulas (DAVFs) of the cavernous sinus.

METHODS: Eighteen patients (12 women and six men; 29–75 years old [mean age, 55 years]) with DAVFs of the cavernous sinus (Barrow's type B:1, C:7, and D:10) treated by gamma knife radiosurgery were enrolled in the study. DAVFs were bilateral in six patients and unilateral in 12. Stereotactic X-ray angiography and MR imaging were performed for targeting the radiosurgery. Areas of arteriovenous communication targeted for irradiation were first outlined on the X-ray angiograms. The target regions were then transferred to and displayed on the MR images. Dose planning was based on findings on the integrated images. Prescribed maximum target doses were 22 to 38 Gy (mean, 28 Gy). The targets were covered by 50% to 90% isodose levels. Radiation doses to the surrounding optic apparatus were kept to less than 8 Gy. The patients were followed up with color Doppler sonography and MR imaging. When noninvasive imaging suggested obliteration, X-ray angiography was performed to verify the results.

RESULTS: The DAVFs were totally obliterated in 12 (80%) of the 15 patients. In the other three, one was almost completely obliterated at 14 months and two were partially obliterated at 19 and 27 months, respectively, after radiosurgery. No complications or symptom worsening occurred during the follow-up period.

CONCLUSION: Gamma knife radiosurgery is a feasible, effective, and safe treatment for DAVFs of the cavernous sinus. Integration of stereotactic X-ray angiography and MR imaging not only aids treatment efficacy but also protects the relevant vital structures, especially the optic apparatus, from the hazards of radiation.

Gamma knife radiosurgery has been used in the treatment of many intracranial diseases with excellent results (1–10). One of the most successful examples is cerebral arteriovenous malformations (AVMs) (7, 9, 11). In gamma knife radiosurgery for cerebral AVMs, vascular injury is selectively induced in the AVM nidus embedded in basically normal brain tissue. The

hypothesis that medium and large vessels (feeding arteries and draining veins) are less radiosensitive than small vessels in the nidus constitutes the rationale for performing radiosurgery to correct AVMs. A therapeutic radiation dose, of 20 to 50 Gy results in a wide spectrum of vascular effects, including perivascular or subendothelial edema, fissuring of the walls, spot hemorrhages, thrombi, degeneration and necrosis of endothelial cells, increased interstitial colloids, and increased fibroblastic activity (7, 9, 11). Progressive reparative endothelial cell growth, medial thickening, fibrosis, and occlusion of small vessels are observed at a later stage; that is, 2 to 3 years after irradiation (7, 9, 11). With an optimal radiation dose and coverage, gamma knife radiosurgery has an approximately 85% cure rate for cerebral AVMs over a period of 2 to 3 years (7).

Dural arteriovenous fistulas (DAVFs) of the cavernous sinus constitute another category of intracranial AVMs, in which the abnormal arteriovenous

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From the Departments of Radiology (W.-Y.G., H.-M.W., H.-J.C., M.-M.H.T.), Neurosurgery (D.H.C.P., W.-Y.C.), Ophthalmology (M.-Y.Y.), and the Cancer Center (C.-Y.S., L.-W.W.), Veterans General Hospital-Taipei and the National Yang-Ming University, Taipei, Taiwan.

Address reprint requests to Wan-Yuo Guo, MD, PhD, Department of Radiology, Veterans General Hospital-Taipei, 1217 Taiwan.

TABLE: Patient data, types of DAVF(s), and treatment parameters

Patient	Age, y/Sex	Side of DAVF(s)	Type of DAVF(s)	Venous Drainage	Time from Diagnosis to Gamma Knife Radiosurgery, m	Maximum Target Dose/Isodose Level Coverage, Gy/%	Duration of Follow-up, m	Result of Treatment
1	60/F	L	D	SOV	3	25/80	7	CO
2	62/F	Bilateral	D	SOV, PS	30	28/50	10	CO
3	66/F	R	D	SOV, PS	2	23/70	12	CO
4	45/M	R	B	PS	6	38/50	9	*
5	56/F	Bilateral	D	SOV, PS	4	25/70	12	CO
6	53/M	Bilateral	D	SOV, PS	2	25/70	27	PO
7	68/F	Bilateral	C	SOV, PS, SPS	14	36/50	13	CO
8	75/M	R	C	SOV, PS	3	23/90	10	CO
9	65/M	R	D	SOV	6	27/70	12	CO
10	43/F	R	C	SOV, PS, CV	1	25/70	15	CO
11	29/F	R	D	SOV, PS	12	32/50	19	PO
12	55/M	Bilateral	D	SOV, PS, CV	4	28/70	14	ACO
13	41/F	L	D	SOV	8	28/90	11	CO
14	59/F	L	C	SOV, PS, CV	10	22/90	7	CO
15	45/F	L	D	SOV	4	30/60	10	CO
16	52/F	R	C	SOV, PS, CV	4	27/55	6	CO
17	47/M	L	C	SOV, PS, CV	2	25/70
18	62/F	Bilateral	C	SOV, PS, CV	2	25/70

Note.—CO, complete obliteration observed on X-ray angiogram; ACO, almost complete obliteration seen on X-ray angiogram; PO, partial obliteration; SOV, superior ophthalmic vein; PS, petrosal sinus; SPS, sphenoparietal sinus; CV, cortical vein.

* Died of other causes.

communication occurs in the walls or cavity of the cavernous sinus. Depending on the distribution of feeding arteries, shunting patterns, and probable causes of the disease, DAVFs of the cavernous sinus may be classified into four subtypes, proposed by Barrow et al (12): type A includes direct shunts between the internal carotid artery and the cavernous sinus; types B, C, and D are dural shunts. Type A DAVFs, also called direct carotid cavernous sinus fistulas (CCFs), are usually related to head trauma or aneurysmal rupture of the cavernous sinus segment of the internal carotid artery. Type B DAVFs are shunts between meningeal branches of the internal carotid artery and the cavernous sinus; type C are dural shunts between meningeal branches of the external carotid artery and the cavernous sinus; and type D are those between meningeal branches of both the internal and external carotid arteries and the cavernous sinus.

Endovascular treatment of DAVFs of the cavernous sinus via an arterial approach has been the method of choice for more than two decades (13). For complicated or residual CCFs, the transvenous approach is an effective alternative (14–16). Types B, C, and D DAVFs of the cavernous sinus, also called indirect CCFs, are relatively less virulent than type A DAVFs or cerebral AVMs. Although the cause of DAVFs (types B, C, and D) is not known with certainty, it is thought that vasculitis, minor trauma, or sinus thrombosis are possible mechanisms.

Clinical manifestations of DAVFs are stereotypical. Gradual onset of bruit, blurred vision, diplopia, proptosis, conjunctiva congestion, and glaucoma in middle-aged women are the most common signs and symptoms. In some rare cases, thrombosis develops

spontaneously or after only carotid-jugular compression. Nevertheless, Barcia-Saloria et al (17) made an important observation in a study of patients with DAVFs of the cavernous sinus, finding that the time between symptom onset and total obliteration was significantly shorter in patients treated by cobalt-60 radiosurgery than in those who received no treatment. Implications of their study are that while DAVFs of the cavernous sinus have to be treated, they may be treated by a less invasive strategy. Because of the high efficacy and noninvasiveness of gamma knife radiosurgery, we applied this technique to the treatment of DAVFs of the cavernous sinus.

Methods

Eighteen patients with DAVFs of the cavernous sinus constituted the study group. Twelve patients were women and six were men. Ages ranged from 29 to 75 years (mean age, 55 years). According to the distribution of feeders and to Barrow's system of classification, one DAVF was type B, seven were type C, and 10 were type D. They occurred bilaterally in six patients and unilaterally in 12. The DAVFs drained via the superior ophthalmic vein, the petrosal sinus, the sphenoparietal sinus, and the cortical veins in the temporal region. The angiographic data concerning the DAVFs are summarized in the Table. The interval between onset of signs and symptoms and gamma knife radiosurgery ranged from 1 to 30 months (mean, 7 months; see Table). In five patients, trauma history was traceable.

Targeting and Dose Selection

All gamma knife radiosurgeries were performed between 1993 and 1997. Stereotactic MR imaging and stereotactic X-ray angiography were used for targeting. Irradiation targets in which arteriovenous communication occurred were first outlined on the X-ray angiograms and were then transferred to and displayed on the stereotactic MR images. Subsequent dose

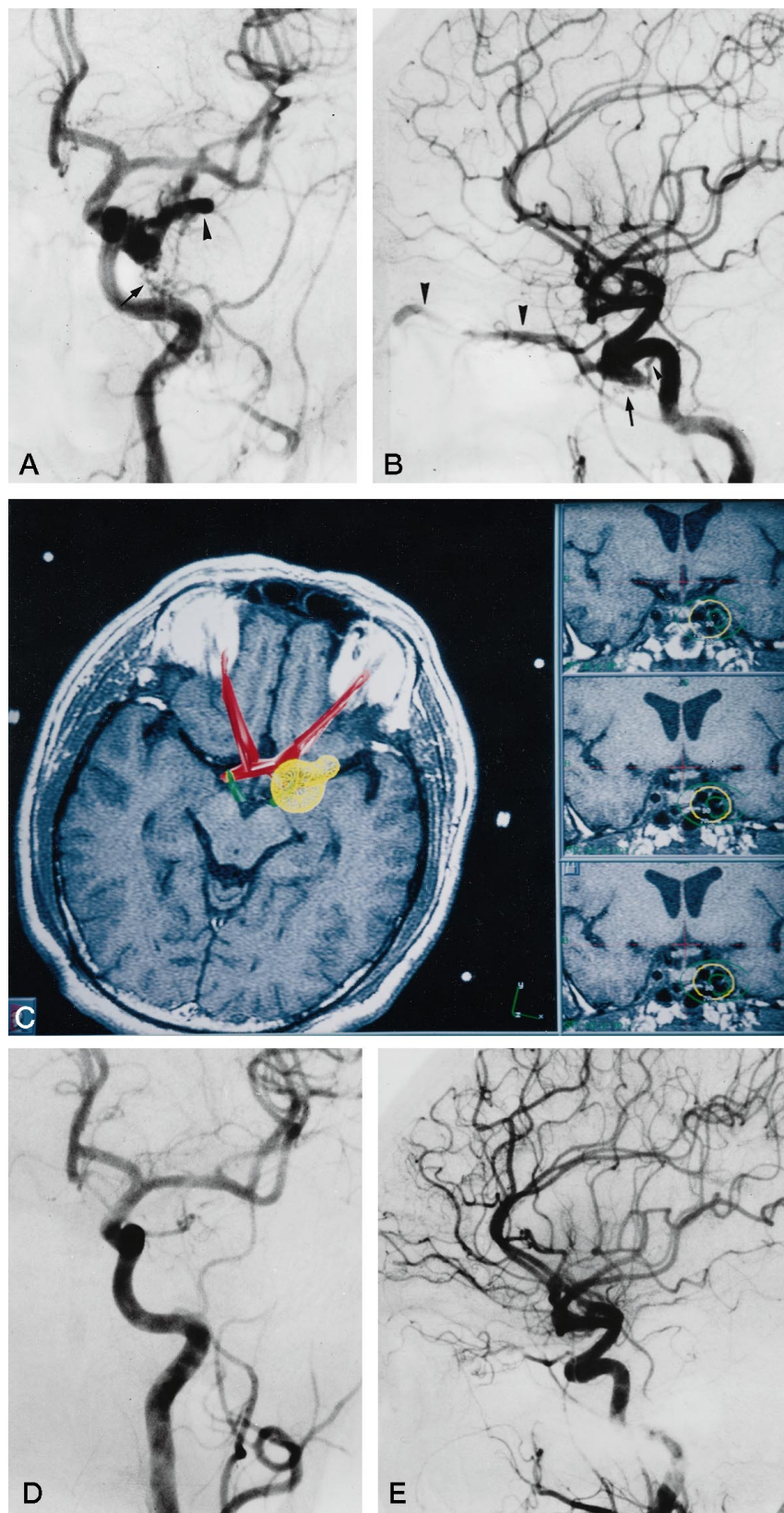


FIG 1. A and B, Anteroposterior (A) and lateral (B) views of carotid angiogram show a type D left-sided DAVF of the cavernous sinus. The DAVF is supplied by the inferior lateral trunk of the left internal carotid artery (*small arrowhead, B*) and by branches of the artery of the foramen rotundum (*arrow*). Drainage is via the superior ophthalmic vein (*large arrowheads*). The target for gamma knife radiosurgery is based first on the stereotactic X-ray angiogram; then, preliminary dose planning is performed. The isodose levels are retrieved and displayed on the stereotactic MR images (C).

C, On the right, three consecutive coronal views of T1-weighted MR images with superimposed isodose levels show the dose distribution in the target region. The yellow isodose lines indicate the effective radiation isodose levels. The optic apparatus is outside the irradiation field. On the left, the target volume (yellow), the optic nerve (red), and the oculomotor nerve (green) are superimposed on a stereotactic MR image, three dimensionally.

D and E, Eleven months after gamma knife radiosurgery, follow-up X-ray angiography shows complete obliteration of the DAVF on the anteroposterior (D) and lateral (E) views.

Obliteration rate

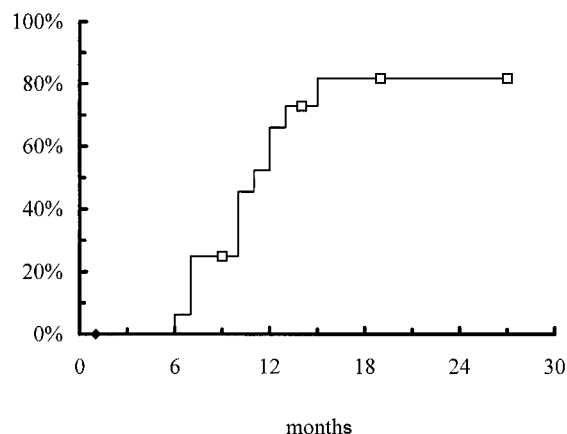


FIG 2. A Kaplan-Meier plot of the actuarial angiographic obliteration rate of the patients. The horizontal axis is the time after gamma knife radiosurgery in months. The vertical axis is the obliteration rate in percentages. The first open box indicates the patient who died of other causes 9 months after radiosurgery. The other three open boxes indicate that complete obliteration has not yet been obtained.

planning was based on findings on the integrated images (Fig 1). Targeting procedures using high-resolution MR imaging and gamma knife radiosurgery with steep dose gradients allowed us to give an effective high radiation dose to the area of arteriovenous shunting selectively and, at the same time, to protect the vital surrounding structures, especially the optic apparatus, from the hazards of radiation. The average prescribed maximum target dose was 28 Gy (range, 22 to 38 Gy). The targets were covered at 50% to 90% isodose levels. Doses to the optic apparatus were kept to less than 8 Gy. In most cases, single-shot radiation in 14- or 18-mm collimations was used.

Follow-up Strategy and Classification of Results

Regular clinical and imaging follow-up examinations were performed noninvasively after the gamma knife radiosurgery using color Doppler sonography and MR imaging/MR angiography. When findings on these noninvasive techniques suggested obliteration of the DAVFs, X-ray angiography was performed to verify the results. Fifteen of the 18 patients were followed up for at least 6 months (range, 6 to 27 months; median, 12 months) and constituted the result cohort. One patient who died of other causes at 9 months, and two patients who had less than 6 months' follow-up were excluded.

Results were classified as follows: 1) complete obliteration, meaning that X-ray angiography verified complete normalization of intracranial hemodynamics from the arterial to the venous phases; 2) almost complete obliteration, meaning that a small remnant of the DAVF was observed either on MR images or X-ray angiograms; and 3) partial obliteration, indicating that obviously decreased arteriovenous shunt was observed on MR images but that X-ray angiography is still pending.

Results

Twelve (80%) of the 15 DAVFs proved to be completely obliterated at X-ray angiography (Figs 1–3). One of the remaining three showed complete regression at MR imaging, but X-ray angiography at 14 months' follow-up showed a small remnant outside

the previous irradiation field. The treatment result was classified as almost complete obliteration (Fig 4). The other two DAVFs had relatively high-flow arteriovenous shunts before radiosurgery. The follow-up MR images and color Doppler sonograms showed small shunts remaining at 19 and 27 months, respectively. These results were classified as partial obliteration (see Table). The partially obliterated DAVFs had relatively high-flow arteriovenous shunts observed on X-ray angiograms as compared with the others. None of the patients had symptom worsening or complications during the follow-up period.

Discussion

Our study shows that gamma knife radiosurgery is an effective treatment strategy for DAVFs of the cavernous sinus (types B, C, and D). Interestingly, compared with cerebral AVMs, DAVFs of the cavernous sinus seem to react more promptly to the radiosurgery (ie, the time to complete obliteration was shorter in DAVFs, with the earliest complete obliteration observed at 6 months). This earlier treatment effect probably occurred because arteriovenous communication in the DAVFs was smaller than in the cerebral AVMs. Nevertheless, the delay between treatment and complete obliteration is a drawback of radiosurgery as compared with the endovascular approach. In the latter, when treatment is successful, immediate obliteration is obtained, and this may play an important role in protecting patients from deterioration in visual acuity, repeat hemorrhage, or other sequelae attributable to arteriovenous shunts in DAVFs. This is particularly true for high-flow DAVFs with reverse venous drainage. Radiosurgery followed by palliative embolization might be a good treatment alternative, providing that no additional risk from embolization is incurred (18).

We used the noninvasive techniques of MR imaging and color Doppler sonography to monitor the effects of treatment. Color Doppler sonography proved to be a good imaging tool for evaluating improvement in venous drainage via the superior ophthalmic vein if the DAVFs drained anteriorly. It also provided the means to obtain quantitative flow analysis. However, posterior venous drainage (eg, via the petrosal or sphenoparietal sinuses) is beyond the scope of Doppler sonography and it cannot be monitored by this technique. Both MR imaging and MR angiography were capable of showing increased flow in the cavernous sinus and draining veins. Although such observation on MR images only indirectly implies the existence of arteriovenous shunting, we found that these techniques were reliable follow-up imaging tools. In the current series, only one minute remnant of a DAVF was missed at follow-up MR imaging.

In terms of cost-effectiveness, gamma knife radiosurgery may be more expensive than other treatment techniques, such as endovascular and conventional radiotherapy (14–16, 19). Endovascular treatment also provides an immediate effect; however, even

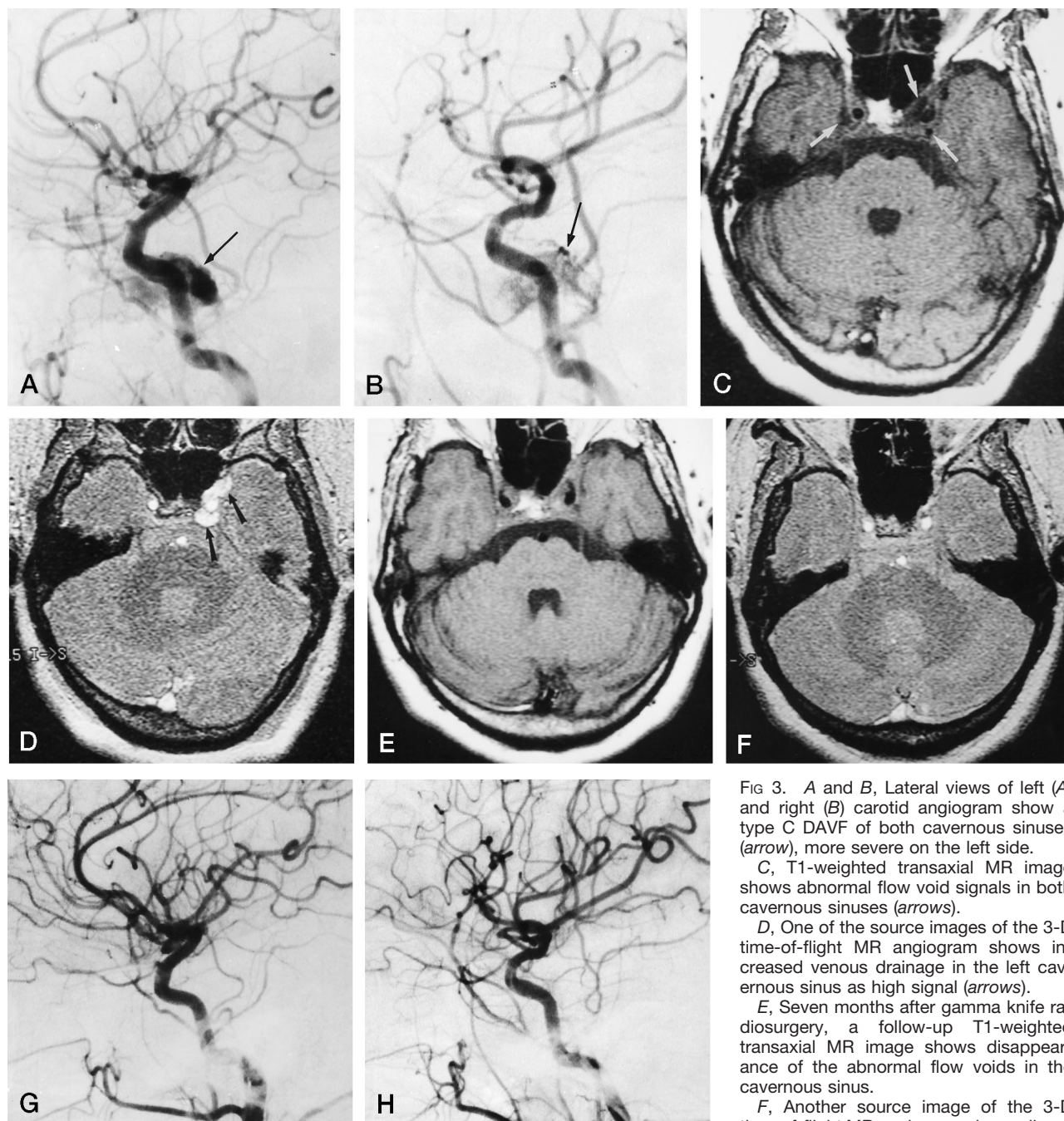


FIG 3. A and B, Lateral views of left (A) and right (B) carotid angiogram show a type C DAVF of both cavernous sinuses (arrow), more severe on the left side.

C, T1-weighted transaxial MR image shows abnormal flow void signals in both cavernous sinuses (arrows).

D, One of the source images of the 3-D time-of-flight MR angiogram shows increased venous drainage in the left cavernous sinus as high signal (arrows).

E, Seven months after gamma knife radiosurgery, a follow-up T1-weighted transaxial MR image shows disappearance of the abnormal flow voids in the cavernous sinus.

F, Another source image of the 3-D time-of-flight MR angiogram shows disappearance of the abnormal high signals in the left cavernous sinus.

G and H, Seven months after gamma knife radiosurgery, lateral views of the left (G) and right (H) carotid angiogram show complete obliteration of the DAVF.

when performed by an experienced interventional neuroradiologist, this approach carries the risk of permanent complications at a rate of up to 25% in difficult cases (20). A major difficulty is the complexity in vascular anastomoses of the head and neck region. While conventional radiotherapy may cost less, the number of treatments that may be performed is limited and the results are varied (19). The region of the cavernous sinus is critical, with many important structures located there—structures that can easily be included in the surgical field and that would suffer adverse effects of radiation. We integrated stereotac-

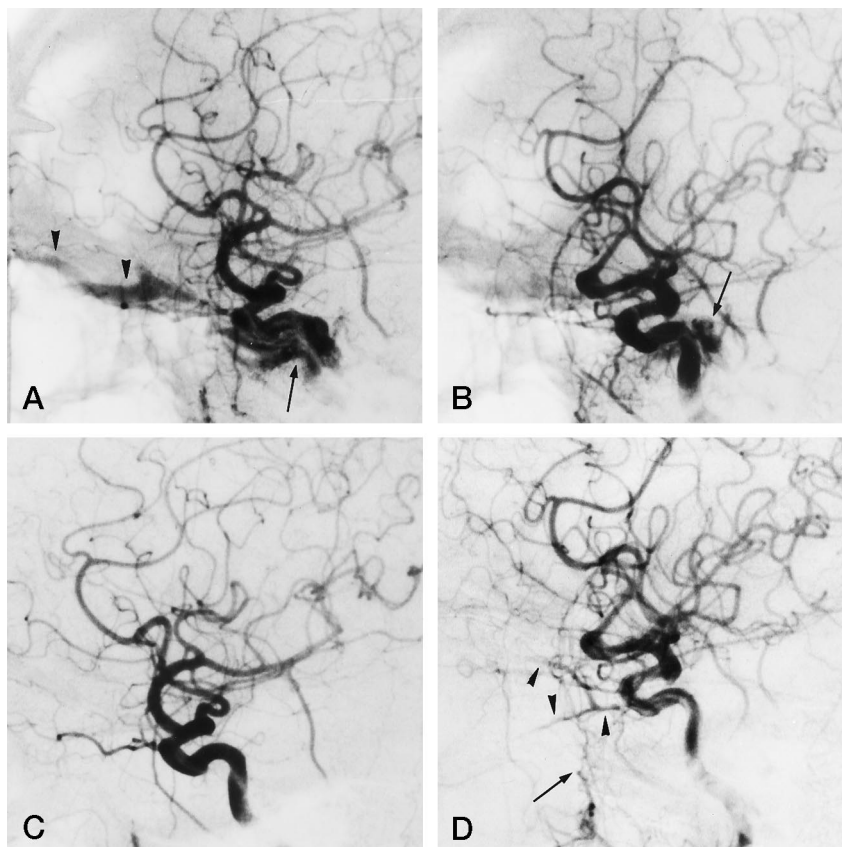
tic MR imaging and stereotactic X-ray angiography to target the DAVFs. This imaging technique is highly accurate and has been routinely used for cerebral AVMs in our institution (21).

The accuracy of the imaging technique and the steep dose gradient of gamma knife radiosurgery serve to protect the optic apparatus and brain stem from high-dose radiation (Fig 1). In the current series, no optic apparatus received more than 8 Gy of radiation, which is the safe dose to the optic nerve. Other cranial nerves in the cavernous sinus (ie, cranial nerves III, VI, V, and VI) are more radioresistant

FIG 4. A and B, Lateral views of left (A) and right (B) carotid angiogram show a type C DAVF, involving both cavernous sinuses, abnormal opacification of both cavernous sinuses (arrow), and venous drainage to the engorged right superior ophthalmic vein (arrowheads).

C, Lateral view of left carotid angiogram 14 months after gamma knife radiosurgery shows complete obliteration of the DAVF.

D, Lateral view of right carotid angiogram shows some prominent branches of the internal maxillary artery (arrow) and slightly engorged draining veins (arrowheads). The remaining feeders are outside the irradiation field of the previous gamma knife radiosurgery. Chemosis in the right eye remains, although it is improved. The result of treatment is classified as almost complete obliteration.



than the optic nerve. It has been reported that these nerves may tolerate up to 40 Gy single-fraction radiation dose (22). In the current series, the highest prescribed dose to the cavernous sinus was 38 Gy. In dose planning for these patients, we paid special attention to selecting isocenters for irradiation in order to avoid putting a hot spot of radiation on these nerves or on the internal carotid artery.

Conclusion

Gamma knife radiosurgery is a feasible, effective, and safe treatment alternative for DAVFs of the cavernous sinus. This is particularly true for those patients in whom endovascular treatment may result in a high risk of complication or when radiotherapy cannot provide a convincing cure rate.

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