Gamma knife surgery for dural arteriovenous shunts: 25 years of experience

MICHAEL SÖDERMAN, M.D., PH.D., GÖRAN EDNER, M.D., KAJ ERICSON, M.D., PH.D., BENGT KARLSSON, M.D., PH.D., TIT RÄHN, M.D., PH.D., ELEFAR ULEARSSON, M.D., AND TOMMY ANDERSSON, M.D., PH.D.

Departments of Neuroradiology and Neurosurgery, Karolinska University Hospital, Stockholm, Sweden; and Department of Neurosurgery, West Virginia University, Morgantown, West Virginia

Object. The aim of this study was to assess the clinical efficacy of gamma knife surgery (GKS) in the treatment of dural arteriovenous shunts (DAVSs).

Methods. From a database of more than 1600 patients with intracranial arteriovenous shunts that had been treated with GKS, the authors retrospectively and prospectively identified 53 patients with 58 DAVSs from the period between 1978 and 2003. Four patients were lost to follow-up evaluation and were excluded from the series. Thus, this study is based on the remaining 49 patients with 52 DAVSs. Thirty-six of the shunts drained into the cortical venous system, either directly or indirectly, and 22 of these were associated with intracranial hemorrhage on patient presentation. The mean prescription radiation dose was 22 Gy (range 10–28 Gy).

All patients underwent a clinical follow-up examination. In 41 cases of DAVS a follow-up angiography study was performed. At the 2-year follow-up visit, 28 cases (68%) had angiographically proven obliteration of the shunt and in another 10 cases (24%) there was significant flow regression. Three shunts remained unchanged.

There was one immediate minor complication related to the administration of radiation. Furthermore, one patient had a radiation-induced complication 10 years after treatment, although she recovered completely. There was one posterior fossa bleed 2 months after radiosurgery; a hematoma, as well as a lesion, was evacuated, and the patient recovered uneventfully. A second patient had an asymptomatic occipital hemorrhage approximately 6 months postradiosurgery.

The clinical outcome after GKS was significantly better than that in patients with naturally progressing shunts (p < 0.01, chi-square test); figures on the latter have been reported previously.

Conclusions. Gamma knife surgery is an effective treatment for DAVSs, with a low risk of complications. Major disadvantages of this therapy include the time elapsed before obliteration and the possibility that not all shunts will be obliterated. Cortical venous drainage from a DAVS, a risk factor for intracranial hemorrhage, is therefore a relative contraindication. Consequently, GKS can be used in the treatment of both benign DAVSs with subjectively intolerable bruit and aggressive DAVSs not responsive to endovascular treatment or surgery.

KEY WORDS • dural arteriovenous shunt • arteriovenous fistula • gamma knife surgery • radiosurgery • treatment outcome

In adults, DAVSs, also called fistulas or malformations, are approximately 10 times less common than brain AVMs. Revealing neurological symptoms can include seizures, progressive dementia, or neurological deficits, often caused by a hemorrhage in the brain or subarachnoid space. Externally audible pulse-synchronous bruit and orbital venous hypertension are also common findings. The symptoms on presentation and the prognosis depend on the location and size of the shunt and, in particular, the venous drainage pattern.

A DAVS with direct or indirect CVD or reflux may cause intracranial hemorrhage. In a single-center retrospective study the annual incidence of intracranial hemorrhage after disclosure was 8%. Furthermore, it is clear from results of other studies that a DAVS with CVD entails a significant risk of intracranial hemorrhage as well as nonhemorrhagic neurological deficit. Therefore, most patients with a DAVS accompanied by CVD are quickly offered treatment, unless it is believed that the risk imposed by the remedy itself cannot be justified. Many patients with intolerable bruit but no CVD also receive treatment, as are patients with exophthalmos or chemosis from a DAVS draining through the superior ophthalmic vein.

Microsurgery and embolization are established treatment options for DAVSs, and the indications and methods have recently been well described. However, there are only a few case reports and single-center series concerning radiosurgery for DAVSs. In the present study we report on 25 years of experience in the treatment of DAVS using GKS at a single center.

Abbreviations used in this paper: AVM = arteriovenous malformation; CT = computerized tomography; CVD = cortical venous drainage; DAVS = dural arteriovenous shunt; GKS = gamma knife surgery; MR = magnetic resonance.
Clinical Material and Methods

From a database of more than 1600 patients with intracranial arteriovenous shunts that had been treated using GKS, we identified 53 patients with 58 DAVSs from the period between 1978 and 2003. From 1990 onward, patients with DAVSs were registered as a separate category. Four patients with six shunts were lost to follow-up evaluation and thus were excluded from the series; three of these patients had been referred from the same clinic outside of Sweden. Therefore, the present study was based on the remaining 49 patients with 52 DAVSs, each shunt being regarded as a separate case. The clinical study was limited to events before and during the 2 years after GKS. Follow-up angiography studies were performed within this 2-year period or later. Clinical data were extracted from hospital files. If data were missing or ambiguous, we contacted the referring physician or patient directly.

Neuroimaging Examinations and Target Definition

Results of all neuroimaging evaluations, including treatment and follow-up angiography data, were retrospectively reviewed by one author (M.S.). In cases treated in 1998 and later, stereotactic MR imaging with intravenously injected contrast medium was supplemented by stereotactic angiography with the aim of better discerning the dural wall. All stereotactic angiograms were analyzed based on whether the target volume had been correctly defined, and thus included the arteriovenous shunt (Fig. 1).

Treatment Parameters

Radiation dose data were available for all 52 treatments. Dose plans in 41 cases were reviewed by one author (M.S.); the remaining 11 cases were treated before the advent of modern dose-planning systems.

Venous Drainage Patterns

The venous drainage patterns of the DAVSs were assessed based on the stereotactic angiography data (M.S.). Classification systems by Cognard, et al.,31 (Cognard) and Borden, et al.,32 (Borden) were applied. Furthermore, the DAVSs were categorized as benign or aggressive according to the absence or presence of retrograde cortical venous blood flow.

Statistical Analysis

The chi-square test (degree of freedom 1) was applied to compare treatment results and the natural history of the DAVS. The Mann–Whitney U-test was used to analyze the dose-obliteration relationship.

Study Limitations

This is a retrospective single tertiary care center study of data from a time span of 25 years. Inclusion criteria, imaging methods, and dose planning have changed over time.

Results

Prior Treatment

Nine DAVSs were treated with embolization or surgery before radiosurgery (Table 1).

### Table 1

<table>
<thead>
<tr>
<th>No. of DAVSs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>GKS</td>
</tr>
<tr>
<td>2</td>
<td>none</td>
</tr>
<tr>
<td>3</td>
<td>none</td>
</tr>
</tbody>
</table>

Obliteration of DAVSs

Among the 41 cases with 2-year follow-up angiography data, 28 DAVSs were obliterated, 10 revealed flow regression, and three remained unchanged. Thus, the 2-year obliteration rate, proven with angiography studies, was 68% and the rate of significant regression was 24%. In two cases in which the shunts were only partially treated due to erroneous delineation, both malformations were obliterated within the treated portion. These two cases were included among the 10 with flow regression.
Twelve of 16 benign DA VSs were obliterated, whereas two had regressed significantly, leaving only minor arte-riovenous shunts. The patients in the remaining two cases refused to undergo follow-up angiography examination. All patients in these 16 cases were clinically cured of their symptoms, that is, pulse-synchronous bruit or chemosis.

Sixteen shunts among 36 cases of aggressive DA VSs were obliterated, eight regressed significantly, and three remained unchanged.

The patient who had experienced a hemorrhage 10 weeks after radiosurgery and emergency surgery was not included among the 41 patients with follow-up angiography data. One patient with severe renal insufficiency underwent MR imaging instead of conventional angiography, and the results were suggestive of obliteration. Two patients had undergone MR imaging or CT follow-up evaluations whose results showed a remaining DAVS; they were not examined using angiography. One patient with an MR image suggestive of obliteration refused to undergo a follow-up angiography study. Four patients, each harboring only one DAVS, refused follow-up angiography or any other neuroimaging examination. No patient died within the 2-year follow-up period.

**Time Until Clinical Effect of Treatment**

Eleven patients with bruit at the time of the treatment recalled that this symptom had disappeared 42, 34, 30, 25, 25, 17, 12, 12, 8, 3, and 2 weeks after GKS. Another patient re-

### TABLE 2

Summary of DAVS locations among 36 cases with CVD

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>Localization</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>falcotentorial region</td>
</tr>
<tr>
<td>9</td>
<td>transverse sinus &amp; sigmoid sinus</td>
</tr>
<tr>
<td>6</td>
<td>superior petrosal sinus &amp; petrous ridge</td>
</tr>
<tr>
<td>5</td>
<td>straight sinus &amp; vein of Galen</td>
</tr>
<tr>
<td>2</td>
<td>superior sagittal sinus</td>
</tr>
<tr>
<td>1</td>
<td>middle fossa</td>
</tr>
<tr>
<td>1</td>
<td>cribriform plate</td>
</tr>
</tbody>
</table>
ported that the bruit had disappeared only 1 day after GKS. Ten of these 12 patients had angiographically proven oblitera-
tions, whereas two refused follow-up angiography.

In addition, several of the patients with cavernous sinus DAVS had noted that their orbital symptoms disappeared quite soon after the treatment, but could not in retrospect recall the exact point in time. In the more recent years of GKS treatment, patients with bruit have been asked to contact us when the symptom disappeared. The first treated patient to be given that instruction noticed resolution after 8 weeks. A follow-up angiography study performed 2 weeks later showed that the shunt had indeed been obliterated (Fig. 2).

**Flow Regression**

Significant flow regression in the DAVS could be seen in 10 patients who had undergone an angiography study. Coverage was complete in eight of these cases and partial in two.

**Treatment Failure**

All of the five treatment failures, that is, cases in which the radiation had no discernible effect, occurred among the 36 cases with CVD. One patient had a high-flow petrous ridge DAVS draining into the lateral mesencephalic vein, which was treated with a minimal radiation dose of 19 Gy and a maximal dose of 27 Gy. Neuroimaging follow-up examination consisted of CT. Clinically, his condition was unchanged during the follow-up period. The second patient had a high-flow vein of Galen DAVS that was treated with a minimal radiation dose of 20 Gy and a maximal dose of 40 Gy. Neuroimaging follow up was performed using MR imaging (Fig. 3). A third patient harbored a high-flow DAVS located in the transverse sinus, which was treated with a minimal dose of 25 Gy and a maximal dose of 50 Gy. This patient’s condition deteriorated clinically because of progressive downstream sinus thrombosis (which was well outside the irradiated volume) and secondary increase in cortical venous reflux. The fourth patient received radiation at a minimal doses of 25 Gy and a maximal dose of 50 Gy for a vein of Galen DAVS that had previously been treated with coil placement and embolization (N-butyl cyanoacrylate). Clinically, the patient was in good condition. The GKS was unsuccessful in a fifth patient due to incorrect target delineation.

All three high-flow shunts in the series occurred among the five cases in which treatment had no apparent effect.

**Dose–Obliteration Relationship**

The relationship between the minimal radiation dose and the obliteration rate was analyzed. The 41 patients with 2-year angiography follow-up data and the two patients with residual DAVS on MR imaging or CT were included. The radiation dose was assumed to be 0 Gy in the patient in whom the target was missed altogether. The two patients with incompletely treated and partially obliterated shunts were included among those considered cured. Eight patients with flow regression were included among those considered not cured. In the present analysis, there was no statistically
significant relationship between the minimal radiation dose to the DAVS and the obliteration rate ($p < 0.1$).

**Intracerebral Hemorrhage**

Two posttreatment intracerebral hemorrhages occurred among the patients with aggressive shunts. One patient had a posterior fossa bleed 10 weeks after receiving a prescription dose of 25 Gy. Both the hematoma and the DAVS were evacuated, and the patient recovered uneventfully. The second patient had an asymptomatic occipital hemorrhage fortuitously discovered on a control MR image approximately 6 months posttreatment (prescription dose 20 Gy).

There was no case of intracranial hemorrhage among the patients without CVD.

**Treatment Complications**

One patient harboring a cavernous sinus DAVS who had been treated with a prescription dose of 25 Gy and a maximal dose of 50 Gy had a pretreatment sixth cranial nerve palsy that worsened after GKS. The palsy finally resolved,
although the time span involved is unclear. There was one case of a late radiation reaction, with hemorrhage occurring approximately 10 years after GKS with a prescription dose of 25 Gy and a maximal dose of 50 Gy. The patient recovered uneventfully. Another patient reported transient focal alopecia. There were also two minor transient complications related to the stereotactic and follow-up angiography studies. In no case was there any evidence of damage to the cortical veins or dural sinuses.

The downstream partial thrombosis of the sigmoid sinus in one patient was far away from the fistulous portion that received the radiation and was regarded as part of the natural history of the lesion.

**Comparison With the Natural History of DAVS**

The clinical outcome following treatment was compared with the data on the natural history of DAVS.14 The event and hemorrhage rates during the 2-year follow-up period did not differ significantly from those associated with the natural history of the malformation. The mortality rate was significantly lower in treated compared with untreated patients (p < 0.01).

**Discussion**

Dural arteriovenous shunts are acquired abnormal arteriovenous connections within the dura mater. Patients with these malformations can clinically present with a variety of symptoms, such as a neurological deficit from an intracranial hemorrhage, pulse-synchronous bruit, seizures, dementia, or orbital symptoms.55

**Pathophysiological Features**

The pathophysiology of spontaneous DAVS is related to venous thrombosis and venous hypertension, both before and after the emergence of the shunt.19,38 There is also evidence of an increased expression of angiogenic growth factors in established DAVSs, whose levels may perhaps be related to the nature of the shunt.7,8,11,13,17,23,28

**Presentation and Prognosis**

The presentation and significance of a DAVS depend on its location and venous drainage pattern.1,7,9,14,15,23,28 WIdely used classification systems combine anatomical location and venous drainage patterns, but these are useful for descriptive purposes only.45,11 Note that the venous drainage pattern alone determines prognosis. Thus, a patient harboring a DAVS without CVD, also called a "benign fistula," may often present with externally audible pulse-synchronous bruit or orbital symptoms but no bleeding. This phenomenon was also true in our series.

A patient harboring a DAVS with CVD, that is, an aggressive fistula, may present in a similar fashion or with a neurological deficit, frequently because of intracranial hemorrhage. Nineteen (53%) of the 36 cases with CVD in the present series were associated with hemorrhagic presentation.

After presentation the risk of intracranial hemorrhage in a patient with an aggressive DAVS may be considerable. For example, in a small series with 14 untreated and six previously treated patients, the annual hemorrhage rate was 8% and the annual mortality rate was 10%.7,23,40

**Management of DAVSs**

There are four treatment options for DAVSs: monitoring, microsurgery, embolization, and radiosurgery. Most patients harboring a DAVS with CVD receive treatment unless the risk imposed by the remedy itself cannot be justified. Many patients without CVD but with intolerable bruit or orbital symptoms also receive treatment. In a patient with limited symptoms and no CVD, observation is the proper course. Note, however, that such patients must be monitored closely both clinically and radiologically given that a benign DAVS may develop into an aggressive one. A change in symptoms—even an improvement in the level of bruit, for example—could indicate a conversion and warrants an angiography study. Among the possible remedies, each method has its specific advantages and disadvantages, which overlap to some extent. Sometimes the different treatment modalities can be used in combination. Embolization and microsurgery have been utilized for many years, and the indications and methods have been well described elsewhere.31 There are only a limited number of case reports and small studies on radiosurgery for DAVSs.2,3,7,10,17,19,26,28,31,33,35,37 The minimal published data and the consequent lack of clear indications for radiosurgery for DAVS may be the reason for the sometimes strong opposition to this treatment method.35

**Obliteration Rate**

In the present study the 2-year obliteration rate, proven by angiography data, was 68%, and the rate of significant flow regression was 24%. The former is very close to the 70% obliteration rate predicted by the Karlsson and colleagues’ obliteration model for the treatment of brain AVMs using the same radiation doses.20 Some may argue that the obliteration rate should have been calculated from complete patient material; in that case, 28 obliterations among 58 treatments were proven on angiography, that is, a 48% obliteration rate. In contrast, if we include cases with MR imaging—demonstrated control (two with proven nonobliteration and two with probable obliteration), clinically proven control only (cure), and in-field obliteration, the obliteration rate can be said to be 75%, that is, 38 obliterations following 51 treatments.

We consider the values derived from angiography results alone to be the most reliable, particularly given that there was no selection bias in terms of angiograms being obtained only in cases in which a cure was expected based on a previous CT or MR image.

The time span between GKS and symptom cure—and, in some cases, proven obliteration—was in many cases remarkably short. In one case obliteration was proven by an angiography study obtained 10 weeks after radiosurgery (Fig. 2). Thus, the obliteration process can occur very quickly, with a subsequent reduction in the time a patient remains at risk for hemorrhage. It may be reasonable to assume that there is a dose-effect relationship similar to the one established in radiosurgery for a brain AVM.20 If so, one would expect that the higher the radiation dose, the higher the obliteration rate. However, we could show no relationship between the minimal radiation dose and the obliteration rate. Likely, the absence of a relationship is due to the limited number of patients in the present study. Furthermore, data may be skewed given that the group of four cav-
Radiosurgery of dural arteriovenous shunts

ernous sinus DAVSs, which had been treated using a 10-Gy prescription dose, were all obliterated. It is unclear whether this rather low dose of radiation was sufficient or whether spontaneous cures occurred among the patients with slow-flow lesions. Data from one center demonstrated that symptoms improved or resolved without treatment in 81% of 32 patients with benign lesions, and 10% of 20 patients with aggressive DAVSs experienced spontaneous occlusion.\textsuperscript{23,43} It is possible that the DAVSs in some of the patients in the present study resolved spontaneously. Alternatively, the location within the dura mater and the usually rather narrow blood vessels these shunt zones represent may indeed render a reaction to radiosurgery that is different from that of brain AVMs, hence offering the possibility of faster obliteration.

Complication Rate

All observed complications related to angiography studies or the application of radiation were of little clinical significance and resolved without sequelae. One late cystic hemorrhagic complication was similar to those occasionally seen after radiosurgery for AVMs;\textsuperscript{21} it healed without clinical consequences.

Hemorrhage Rate

In the present series there was one case of rebleeding 2 days after the revealing hemorrhage and before treatment. In some of the cases, however, many years elapsed between the initial symptoms, which could consist of a hemorrhage or any other symptom, and GKS. This phenomenon does not agree with the very high risk of hemorrhage, both as an initial event and a rebleed, which has been reported by some authors regarding aggressive DAVSs; it does, however, coincide with the more conservative figures reported by others.\textsuperscript{6,16,41} A source of error in the present study was the fact that it was largely retrospective. We do not know how many patients died or were severely disabled while awaiting treatment and consequently never underwent GKS.

Two patients with CVD due to the DAVS bled during the 2-year follow-up period, that is, the annual incidence of hemorrhage after GKS was approximately 2.6% (two of 78 case-years).

Mechanism of DAVSs

In brain AVMs, the gradual occlusion of the nidus after GKS has been attributed to endothelial damage in pathological arteries inducing the proliferation of smooth-muscle cells and the elaboration of extracellular collagen by these cells, which in turn leads to progressive stenosis and obliteration of the AVM.\textsuperscript{36} The process may be similar in the DAVS, even though the nidus basically consists of normal vessels but still comprises thrombus, neovascularization, and medial hyperplasia.

The mechanism of the sometimes very rapid effect of GKS on the DAVS could involve direct damage to the endothelium together with subsequent thrombosis. To our knowledge there is no pathoanatomical study of the effect of GKS on a DAVS.

In the present series we noted that all three cases of high-flow shunts represented treatment failures. We speculate that this result may have occurred for simple geometrical reasons; that is, the vessel diameters were too large for thrombus formation and wall thickening to have the desired effect. This hypothesis concurs with the observation of other authors that plexiform brain AVMs may respond better to radiosurgery than fistulous AVMs in the brain.\textsuperscript{29}

Comparison With the Natural History of DAVSs

The natural history of DAVSs with CVD is not very well known, except that they entail a risk of intracranial hemorrhage. This alarming finding in a few single-center series has prompted a very active approach toward these lesions.\textsuperscript{1,5,11-13} The very low incidence of DAVSs (one tenth the incidence of brain AVMs) and the urge to treat these malformations rapidly to prevent hemorrhage may be the reasons for the small number of reports on their natural history. The best-documented material consists of data in 14 untreated and six previously treated patients who underwent follow-up evaluation, for a total of 90 patient-years.\textsuperscript{23,43} The annual incidence of hemorrhage based on that material was 8%. Among the patients treated using GKS in the present series, the annual incidence of hemorrhage was 2.6%, showing no significant difference between the two groups. This finding may be attributable to the small number of patients in both series. There was also no significant difference concerning the neurological event rate, perhaps for the same reason.

The annual mortality rate in the studies by Lasjaunias\textsuperscript{23} and van Dijk and colleagues\textsuperscript{41} was 10%. The mortality rate in the present study was 0%. The difference between these groups was significant (p < 0.01). The venous outlet thrombosis noted in one patient was explained as part of the natural history of the lesion and not as an adverse effect of the radiation treatment itself.\textsuperscript{11,21}

Previous Reports on Radiosurgery for DAVS

The high occlusion rate and low risk of complications in radiosurgery for cavernous sinus DAVSs were noted as early as 1982 and have been confirmed in other series.\textsuperscript{2,3,18,31} Likewise, the efficacy of GKS—either alone or in combination with embolization—for DAVSs in other locations has been documented.\textsuperscript{10,17,26,28,32,33,37} The results in the present study are very similar to those in previous reports.

Current Treatment Protocol

At our institution DAVSs are treated with radiation doses similar to those used in radiosurgery for AVMs in the brain. Thus, lesions remote from cranial nerves or other radiation-sensitive tissues are usually treated with 25 Gy to the 40 to 60% isodose line. Dose plans are adjusted according to the radiation sensitivity of adjacent structures. The volume of the lesion is usually less than 2 cm\textsuperscript{3} and is therefore not a limiting factor.

Conclusions

Gamma knife surgery is an effective treatment for DAVS, with a low risk of complications. Major disadvantages include the time required for the shunt to become obliterated and the fact that not all shunts respond to treatment. Cortical venous drainage from the DAVS, which is a risk factor for intracranial hemorrhage, is therefore a relative contraindication for GKS. Consequently, GKS can be used in the
treatment of benign DAVSs with subjectively intolerable brut and aggressive DAVSs not amenable to endovascular treatment or surgery.

Acknowledgments
We acknowledge Professors Ladislau Steiner and Christer Lindqvist for their pioneering work in GKS for intracranial arteriovenous shunts.

References

M. Söderman, et al.
Radiosurgery of dural arteriovenous shunts


Manuscript received September 5, 2005.
Accepted in final form January 20, 2006.
Address reprint requests to: Michael Söderman, M.D., Ph.D., Department of Neuroradiology, Karolinska University Hospital, SE-171 76 Stockholm, Sweden. email: michael.soderman@karolinska.se.