Stereotactic radiosurgery for arteriovenous malformations of the postgeniculate visual pathway

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OBJECT A visual field deficit resulting from the management of an arteriovenous malformation (AVM) significantly impacts a patient’s quality of life. The present study was designed to investigate the clinical and radiological outcomes of stereotactic radiosurgery (SRS) performed for AVMs involving the postgeniculate visual pathway.

METHODS In this retrospective single-institution analysis, the authors reviewed their experience with Gamma Knife surgery for postgeniculate visual pathway AVMs performed during the period between 1987 and 2009.

RESULTS During the study interval, 171 patients underwent SRS for AVMs in this region. Forty-one patients (24%) had a visual deficit prior to SRS. The median target volume was 6.0 cm$^3$ (range 0.4–22 cm$^3$), and 19 Gy (range 14–25 Gy) was the median margin dose. Obliteration of the AVM was confirmed in 80 patients after a single SRS procedure at a median follow-up of 74 months (range 5–297 months). The actuarial rate of total obliteration was 67% at 4 years. Arteriovenous malformations with a volume < 5 cm$^3$ had obliteration rates of 60% at 3 years and 79% at 4 years. The delivered margin dose proved significant given that 82% of patients receiving ≥ 22 Gy had complete obliteration. The AVM was completely obliterated in an additional 18 patients after they underwent repeat SRS. At a median of 25 months (range 11–107 months) after SRS, 9 patients developed new or worsened visual field deficits. One patient developed a complete homonymous hemianopia, and 8 patients developed quadrantanopias. The actuarial risk of sustaining a new visual deficit was 3% at 3 years, 5% at 5 years, and 8% at 10 years. Fifteen patients had hemorrhage during the latency period, resulting in death in 9 of the patients. The annual hemorrhage rate during the latency interval was 2%, and no hemorrhages occurred after confirmed obliteration.

CONCLUSIONS Despite an overall treatment mortality of 5%, related to latency interval hemorrhage, SRS was associated with only a 5.6% risk of new visual deficit and a final obliteration rate close to 80% in patients with AVMs of the postgeniculate visual pathway.


KEY WORDS arteriovenous malformation; AVM; optic radiation; stereotactic radiosurgery; Gamma Knife; vision; vascular disorders

MANAGEMENT options for arteriovenous malformations (AVMs) have expanded and evolved over time. However, the underlying goal of intervention remains complete obliteration of the AVM and maintenance of neurological function.16,40,41 The rates of AVM occlusion after a single Gamma Knife surgery generally range from 70% to 80% over a 5-year observation period.6,11,19,25 In addition, stereotactic radiosurgery (SRS) has a relatively low risk profile for adverse radiation effects (AREs).23

The lateral geniculate nucleus gives rise to the sublenticular and retrolenticular segments of the optic radiation that travel through the temporal and parietal lobes, respectively, on a path that terminates in the striate cortex. Because the distance and fragility of these pathways create the opportunity for disruption by an AVM, associ-
ated hemorrhage, or procedural intervention, visual field deficits are a common risk. Visual field deficits are most apparent in the occipital lobe where homonymous field deficits have been reported, occurring in up to 81% of patients with AVM hemorrhages and in 36% of patients without a hemorrhage.13

New visual field deficits have been reported in all treatment paradigms and can occur in as many as 33% of microsurgical patients.1,3 Unfortunately, such deficits can be a significant disability that negatively impacts quality of life and can worsen long-term rehabilitation outcomes, especially when a homonymous hemianopia has occurred.5,8,32 A sparse collection of reports highlighting multimodality AVM treatment paradigms and visual field deficits has been published. However, an updated study focused on SRS treatment has been absent. In this study, we sought to evaluate the outcomes of Gamma Knife radiosurgery on postgeniculate visual pathway AVMs with a focus on visual field deficits.

Methods
Study Design
We conducted a single-institution retrospective analysis approved by the University of Pittsburgh Institutional Review Board. We evaluated outcomes for AVMs residing within the postgeniculate visual pathway and treated with Gamma Knife radiosurgery between 1987 and 2009. The AVMs occurred along the anatomically normal course of the optic radiation, which extends from the lateral geniculate body to the calcareous fissure. This course was further demarcated by Parraga et al., who indicated an anterior limit of the optic radiation at 5 mm posterior to the tip of the temporal horn and a lateral edge of approximately 20 mm from the cortical surface.28 The AVMs suitable for analysis were identified from our SRS database and were verified on imaging studies during the medical record review process independently conducted by two authors. Outcome data were collected through an independent medical record review and were analyzed by neurosurgeons who had not participated in the initial patient management.

Radiosurgery Technique
Expanded technical elements of the radiosurgery technique have been detailed in our previous publications.19,20 In brief, patients present on the day of treatment and intravenous conscious sedation is induced. The Leksell stereotactic frame is applied after a local anesthetic is administered to the pin sites. Axial high-resolution MRI is performed, followed by biplanar stereotactic angiography. The AVM nidus is outlined using a highly conformal radiosurgery dose plan that is created with Leksell GammaPlan software version 10 (Fig. 1). The selected margin dose was based on the volume and location of the AVM. In this study, we used Leksell Gamma Knife Models U, B, C, 4C, and Perfexion units (Elekta AB).

Patient Follow-Up
Clinical and imaging follow-up (MRI when possible) is requested at 6, 12, 24, and 36 months after SRS. All patients have serial clinical assessments of their visual fields using confrontation examinations. If a patient complains of a new visual field reduction or demonstrates such on confrontational examination, then a formal visual field test is requested. Furthermore, if any changes in neurological symptomatology, including visual disturbances, occur after SRS, the patient is promptly examined with imaging studies to assess for potential AREs. After 3 years, if MRI demonstrates total obliteration (no flow voids identified on T2-weighted MRI), then an angiography study is requested. Complete AVM obliteration on angiography is defined as the elimination of the AVM nidus and the absence of early draining veins.13 However, if a residual nidus is evident on imaging, then repeat SRS is recommended to achieve complete obliteration. Patients who undergo a second SRS procedure are again followed up with a similar protocol.

Statistical Analysis
Kaplan-Meier survival analysis was used to evaluate potential factors that affect results. Obliteration was calculated based on the time that MRI or angiography demonstrated complete occlusion of the AVM. The accuracy of MRI confirmation of obliteration is 96%, as demonstrated by Pollock et al.30 We have shown that both MRI and angiography provide satisfactory evidence of AVM obliteration.11,37 Cox regression was used in a univariate analysis to calculate significant interactions between obliteration rates and related factors. A p value < 0.05 was defined as statistically significant.

Hemorrhage results were calculated based on the time of a postradiosurgical bleeding event or loss to follow-up. The hemorrhage statistics were obtained through Kaplan-Meier survival analysis. The annual hemorrhage rate during the latency period was calculated based on the years of at-risk follow-up and the number of hemorrhages that occurred. Comparisons between various groups were performed as appropriate, using the Fisher exact and Mann-Whitney tests.

Results
Patient Population and AVM Characteristics
One hundred seventy-one patients underwent an initial single-stage SRS. At the time of SRS, the median patient age was 37 years (range 4–73 years). Eighty-nine patients were female and 82 were male. Arteriovenous malformations were functionally located within the postgeniculate optic radiation and anatomically located predominantly within the occipital lobe in 73 patients (43%), the temporal lobe in 67 patients (39%), and the parietal lobe in 31 patients (18%) (Table 1) The initial presentation of these patients included intracranial hemorrhage in 61 patients (36%), headaches in 54 (32%), seizures in 45 (26%), an incidental finding in 7 (4%), and a visual field deficit in 4 (2%). Neurological deficits were present before SRS in 50 patients (29%). The primary causes of these neurological deficits were hemorrhage in 24 patients, adverse outcomes from embolization in 9 patients, and unknown in 17 patients. A visual deficit was the primary neurological deficit in 41 patients, followed by hemiparesis (11 patients) and
speech difficulties (2 patients). Five patients had multiple deficits.

Formal visual field testing (Goldmann field examination) was conducted if a field deficit was clinically observed during a confrontation visual field exam, was reported by a patient, or was highly suspected given the AVM’s anatomical location. Thus, formal examinations were conducted in 97 patients. A homonymous hemianopia was seen in 11 patients, an upper quadrantanopia in 16, and a lower quadrantanopia in 14. The visual defect was caused by prior hemorrhage in 24 patients, related to prior embolization in 4 patients, detected after prior surgical intervention in 1 patient, and related to the anatomical AVM location in the remaining patients.

Additional AVM characteristics included a coexisting aneurysm in 15 patients (9%) and a venous outflow varix in 24 patients (14%). Endovascular embolization had been performed in 37 patients (22%) prior to the referral for SRS. Fifteen patients (9%) had undergone craniotomy before SRS; 6 patients had undergone hematoma evacuation, 5 a partial AVM resection, 3 an aneurysm clipping, and 1 a ventriculostomy. Two experienced neurosurgeons had determined the Spetzler-Martin grade before SRS. A Grade I AVM was diagnosed in 8 patients (5%), Grade II AVM in 36 (21%), Grade III in 86 (50%), and Grade IV in 41 (24%).

The median target volume was 6 cm³ (0.4–22 cm³). The median margin dose was 19 Gy (14–25 Gy), and the maximum median dose was 36 Gy (25–50 Gy). The median number of isocenters used was 4 (range 1–17). At the conclusion of treatment, all patients received 20–40 mg of intravenous methylprednisolone. Patient discharge from the hospital occurred within 2–24 hours postprocedure.

**Arteriovenous Malformation Response**

The median imaging follow-up after SRS was 74 months (5–297 months). Obliteration of the AVM was confirmed after initial SRS by using MRI or angiography in 80 patients. Actuarial rates of confirmed obliteration were 38% at 3 years and 67% at 4 years (Fig. 2). The median time until obliteration was 31 months (6–70 months). Fifty-eight patients had obliteration confirmed by angiography. As documented in previous studies, angiography results alone are falsely lowered because of patients who decline repeat angiography after obliteration is determined on MRI.11,15,17

Several variables were significantly associated with AVM obliteration, according to univariate analysis. The
median AVM target volumes were large in this series, which predictably affected obliteration rates. Arteriovenous malformations with a volume < 5 cm³ had an obliteration rate of 60% at 3 years and 79% at 4 years (Fig. 3). These smaller AVMs had a statistically higher obliteration rate with MRI confirmation (p < 0.001). As the maximum AVM diameter increased, the rate of obliteration decreased (p < 0.001). Eighty-two percent of patients receiving a margin dose ≥ 22 Gy had total AVM obliteration (p < 0.001; Fig. 4). Patients who had a prior AVM hemorrhage had improved obliteration rates (p = 0.035). In contrast, patients who had a prior embolization had lower obliteration rates (p = 0.029).

**Visual Field Deficits**

Forty-one patients had a detected visual deficit prior to SRS. Thirty-six percent of patients with a hemorrhage at presentation had a visual deficit, compared with 19% of patients without a hemorrhage at presentation (Fig. 3). These smaller AVMs had a statistically higher obliteration rate with MRI confirmation (p < 0.001). As the maximum AVM diameter increased, the rate of obliteration decreased (p < 0.001). Eighty-two percent of patients

### Table 1. Summary of demographic and lesion characteristics in 171 patients with AVMs of the postgeniculate visual pathway

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Cases (%)</th>
</tr>
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<tbody>
<tr>
<td>Patients</td>
<td>171</td>
</tr>
<tr>
<td>Median patient age in yrs</td>
<td>37</td>
</tr>
<tr>
<td>Range of patient ages in yrs</td>
<td>4–73</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>82 (48)/89 (52)</td>
</tr>
<tr>
<td>AVM location</td>
<td></td>
</tr>
<tr>
<td>Occipital lobe</td>
<td>73 (43)</td>
</tr>
<tr>
<td>Temporal lobe</td>
<td>67 (39)</td>
</tr>
<tr>
<td>Parietal lobe</td>
<td>31 (18)</td>
</tr>
<tr>
<td>Prior visual field deficit</td>
<td>41 (24)</td>
</tr>
<tr>
<td>Type of visual field deficit</td>
<td></td>
</tr>
<tr>
<td>Homonymous hemianopia</td>
<td>11</td>
</tr>
<tr>
<td>Upper quadrantanopia</td>
<td>16</td>
</tr>
<tr>
<td>Lower quadrantanopia</td>
<td>14</td>
</tr>
<tr>
<td>Prior embolization</td>
<td>37 (22)</td>
</tr>
<tr>
<td>Prior surgery</td>
<td>15 (9)</td>
</tr>
<tr>
<td>Varix present</td>
<td>24 (14)</td>
</tr>
<tr>
<td>Coexisting aneurysm</td>
<td>15 (9)</td>
</tr>
<tr>
<td>Spetzler-Martin grade</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8 (5)</td>
</tr>
<tr>
<td>II</td>
<td>36 (21)</td>
</tr>
<tr>
<td>III</td>
<td>86 (50)</td>
</tr>
<tr>
<td>IV</td>
<td>41 (24)</td>
</tr>
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</table>
Latency Interval Hemorrhage and Complication Risks

Fifteen patients (9%) had a single hemorrhage during the latency period at a median of 12 months (2–53 months). Eight patients died as a result of hemorrhage after SRS. Two patients died of unrelated cancer, and 5 patients died of undetermined causes. The cumulative rate of AVM hemorrhage after SRS was 5% at 1 year, 9% at 3 years, and 10% at 5 years. The total number of hemorrhages was correlated with 387 patient-years of estimated hemorrhage risk, for an overall annual rate of 2.0% during the latency interval (the time from SRS treatment until obliteration or the last follow-up of a patient with a known residual AVM). No patient sustained a hemorrhage after MRI or angiography had confirmed AVM obliteration.

### TABLE 2. Visual field deficits before and after the SRS procedure

<table>
<thead>
<tr>
<th>Category</th>
<th>No. of Deficits</th>
<th>Cause of Visual Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Visual</td>
<td>Homonymous Hemianopia</td>
</tr>
<tr>
<td></td>
<td>Deficits</td>
<td></td>
</tr>
<tr>
<td>Prior to SRS</td>
<td>41</td>
<td>11</td>
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<tr>
<td>Single SRS</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Repeat SRS</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hemorrhage</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

NA = not applicable.

FIG. 5. A Kaplan-Meier survival curve depicting a new or worsened visual field deficit. The number of patients remaining in the analysis at 3, 5, and 10-years, with each of these years marked by a vertical line, is indicated on the graph.

Seven patients (4%) developed symptomatic AREs, defined as new T2 signal change surrounding the AVM target and associated with the development of new neurological signs in the absence of hemorrhage. Three patients had new or worsening seizure activity. Seizure activity returned to baseline in 2 of these patients after the administration of a short course of oral corticosteroids. As mentioned previously, 3 patients had a new or worsening visual field deficit. One patient exhibited new mild hemiparesis. Delayed cyst formation in the target region was detected in 4 individuals. The median time until cyst detection was 28 months (11–67 months). The cysts were asymptomatic in 3 patients, while 1 patient required surgical cyst fenestration.

Repeat SRS

Thirty patients with residual AVMs underwent a second SRS procedure at a median of 40 months (30–126 months) after the initial procedure. Twelve of these patients had confirmed obliteration on angiography, and 18 patients had confirmed obliteration on MRI or angiography at a median interval of 40 months (30–86 months) after the second SRS procedure (Fig. 6). One patient developed a new visual deficit (right homonymous hemianopia), which was identified 94 months after repeat SRS. A second patient developed a visual field deficit 165 months after a single SRS procedure. Eight of these patients demonstrated improvement in their visual field deficit. The resulting deficits included superior quadrantanopia in 5 patients, inferior quadrantanopia in 3 patients, and complete homonymous hemianopia in 1 patient (Table 2).
of patients receiving when a higher margin dose was applied. In this study 82% associated risk of AREs.6,33,40 Patients with a prior AVM empirical balance between the goal of obliteration and the with smaller AVMs, the optimal dose still represents an While higher doses are more often prescribed for patients zation material obscuring the AVM and late revasculariza- zation had a decreased rate of total obliteration. This find after SRS. Finally, patients previously treated with emboli- hemorrhage had a greater likelihood of AVM obliteration which corresponds to the volume effect noted in previous studies.10,12,25,43 A VMs has been estimated to be 1%.27 Thirty-six percent of annually devastating. An annual risk of death due to untreated hemorrhage risk has long been considered to be 2%–4%, the risk of a visual deficit alone remains notable in the untreated population. Fortunately, from a treatment standpoint, Gamma Knife radiosurgery is associated with a relatively low risk profile. Less than 6% of patients developed a treatment-related visual field deficit, and only 1 patient developed a homonymous hemianopia after a single procedure in our study.23 Pollock et al. described a series of 34 patients treated at the University of Pittsburgh, which this study builds upon.31 Those authors identified 2 patients (6%) who had developed a new visual field deficit. Compared with theirs, our data set has increased 5-fold to better evaluate risks and the correlation between AVM treatment and visual field preservation. Nonetheless, our results appear to correlate with the data published 17 years ago. We identified negative changes to visual fields in 9 (5.6%) of 160 patients (11 patients excluded because of homonymous hemianopia at presentation). The actuarial rates of a visual deficit were 3% at 3 years, 5% at 5 years, and 8% at 10 years. The median interval until deficit detection was 25 months. Several factors appeared to be associated with the occurrence of a deficit. Women had an increased risk of a visual deficit, as did patients who developed reactive edema on follow-up imaging. Incomplete obliteration requiring a second SRS procedure also increased the risk of a new visual deficit. Moreover, there was a trend toward larger-volume AVMs resulting in an increased risk of a visual field deficit, but this trend did not reach statistical significance. Several smaller SRS studies have demonstrated a wide distribution of new visual field deficits, with results ranging from 0% to 55%.7,14,34 Maruyama et al. investigated the effect of radiation on the optic radiation through tractography based on diffusion tensor MRI in 10 simulated Gamma Knife treatments.22 Their data indicated that a maximum dose of 12 Gy or less to the optic radiation did not lead to new visual field deficits. This finding is not unexpected based on accepted brain tolerances of radiation, but it is below the standard margin dose required to effectively treat an AVM.

Surgical intervention and its effects on visual fields have been well documented in the literature on temporal and occipital AVMs. The reported rate of visual field deficits after the microsurgical management of AVMs in the occipital lobe ranges from 17% to 33%.13,35 Sinclair et al. reported on multimodal treatments for occipital lobe AVMs, Arteriovenous malformations within the optic radiation provide a challenge for clinical decision making because of the high risk of a new visual deficit that can impair quality of life, social functioning, and rehabilitation outcomes, especially if a homonymous hemianopia has occurred.5,32 Previous studies have indicated that a homonymous visual field deficit occurs in 67%–81% of patients with a previous hemorrhage and in 25%–36% of unruptured AVM cases in the occipital lobe.13,21 However, the natural history rate for visual field deficits in optic radiation AVMs is largely unavailable. In this study 36% of patients with a prior hemorrhage and 12% of those without had a visual field deficit at presentation, rates consistent with the results of Dehdashti et al.5 Microsurgical publications have documented rates of visual deficit from a prior hemorrhage as 26%–77%.18,24 If these data are extrapolated based on an annual AVM hemorrhage rate between 2% and 4%, the risk of a visual deficit alone remains notable in the untreated population.
with a surgical risk of 17% and a visual field deficit occurring in 21.7% of patients after combined embolization and surgery.34 Dehdashti et al. concluded that they would not recommend surgery unless the patient was aware of the risks, as the surgical arm of their study had a much higher rate of visual field deficits.3 These results are comparable to those of Lopez-Ojeda et al. in the temporal lobe, where the microsurgical management of AVMs resulted in a transient visual field deficit in 24% of patients and in long-term deficits in 16% of patients.18 This finding is supported by Boström et al., who showed a new significant postoperative visual field deficit in 19% of patients and worsening of pre-existing visual field deficits in 43% of patients.4 Successful complete surgical removal provides the benefit of early hemorrhage protection but is associated with a higher risk of visual field deficits compared with SRS.

Research of stroke data has revealed a visual field loss rate of 40% with lesions in the occipital lobe, 30% with lesions in the parietal lobe, and 25% with lesions in the temporal lobe.27 However, the locations of all visual deficits in our study were relatively consistent across the lobes (30% occipital, 32% parietal, and 27% temporal), which demonstrates the sensitivity of the white matter tracts of the optic radiation.7 Kupersmith et al. reported that spontaneous recovery occurred in 24% of visual field deficits after hemorrhage.13 We noted improvement in a similar number of patients who had presented with a visual field deficit.

Repeat SRS was undertaken when incomplete AVM obliteration was noted on MRI at 3 or more years after initial SRS to reduce the hemorrhage risk.29,39 Total obliteration was then confirmed in 18 of 30 patients. Furthermore, only one additional non–hemorrhage-related visual field deficit was identified in this group. Previous studies have reported permanent neurological deficits ranging from 2.8% to 3.6% in retreatment groups.11,42

Study Limitations

Limitations of this study largely relate to the duration of follow-up and the retrospective review of outcomes. In this subseries the average AVM volume was large, which often leads to the need for a second SRS. The timing and consistency of visual field testing (clinically performed in every patient) are also limitations, as not every patient underwent a formal visual field examination. Visual acuity was not assessed in this study since the major impact of postgeniculate optic pathways would be visual field loss rather than the visual acuity loss more commonly associated with anterior visual pathway dysfunction. Future studies can provide these additional data.

Conclusions

Postgeniculate visual pathway AVMs that were smaller than 5 cm³ in volume, that received ≥ 22 Gy at the margin, or that had not been treated with prior embolization had the highest rates of total obliteration. New or worsened visual field deficits were identified in 5.6% of patients after a single SRS procedure. Female sex, the need for a second SRS procedure, and post-SRS edema were risk factors for a visual field deficit. In addition, we noted a trend toward a larger AVM volume as a risk factor. A homonymous hemianopia occurred in only one patient. This study indicates that Gamma Knife radiosurgery, compared with other modalities, was a relatively safe procedure and provided an effective means of treating a large percentage of the AVMs situated within the postgeniculate visual pathway.

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**Author Contributions**

Conception and design: Kano, Bowden, Lunsford. Acquisition of data: Kano, Bowden, Caporosa, Tonetti. Analysis and interpretation of data: Bowden. Drafting the article: Kano, Bowden, Lunsford. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Kano. Study supervision: Kano.

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