Guest Editorial

Microsurgery and radiosurgery in brain arteriovenous malformations

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The parallel development of microsurgery, endovascular procedures, and radiosurgery, used alone or in combination, has widened the scope of surgery for arteriovenous malformations (AVM's). The paper presented by Sisti, et al., is a contribution to the evolving discussion concerning the present and future share of the three techniques in the management of brain AVM's. Sisti, et al., report the outcome of microsurgery in a series of 67 cases of AVM's less than 30 mm in largest diameter. They achieved complete resection of the AVM nidus in 94% of their cases, with a surgical morbidity rate of 1.5% and no mortality. In 24 superficially located AVM's, there was no morbidity or mortality. They compared these results, representative of those obtained by experienced vascular neurosurgeons, with the outcome in series with radiosurgical AVM treatment.

It was refreshing to note that, in contrast to the large majority of neurosurgeons, Sisti, et al., recognized the usefulness of a stereotactic guide. They used (as did Riechert and also Guit, et al., 30 years ago) a probe to lead them to a deep-seated target. We prefer a guide with a laser beam. It is elegant andatraumatic, and thus fulfills its purpose better than a probe. The theoretical risk of brain shift with displacement of deep lesions following the lifting of the bone flap does not occur or is insignificant in our experience if the craniotomy is kept small.

The primary aim of Sisti, et al., was to compare the outcome of treating patients with AVM's by microsurgery to that achieved with using radiosurgery. Since they acknowledge the inherent flaws of the methods they used, we will not emphasize them. Instead, we will provide some facts for calm consideration.

Radiosurgery

The Latency Period

In our previous publications,7-9 we estimated the latency period between radiosurgical treatment and the onset of total obliteration of the AVM to be 1 or 2 years or more. This was based on angiographic follow-up studies, which used to be performed according to a strict protocol at 1, 2, or several years after the treatment. Hence, the real time of obliteration between two follow-up angiograms could not be established. With the introduction of magnetic resonance (MR) imaging, follow-up MR angiograms were carried out at 6 months, and occasionally at 3 and 9 months following treatment. Absence of flow-void areas on these studies prompted early follow-up angiography which documented that, in a number of cases, the AVM is obliterated before 1 year.10 Hence, the problem of latency — and the risk of rebleeding during the latency period — should be reassessed.

AVM Volume and Dose

In our publications,7-9 we stressed that the best target for radiosurgery is a lesion of small volume. This did not mean that we managed only small AVM's. In our series, 450 AVM's were larger than 30 mm and 120 were larger than 40 mm in greatest diameter. Parenthetically, it should be mentioned that to give the size of only one of the diameters of an AVM is of doubtful value. In our series, some AVM's had one diameter larger than 40 mm and the other two diameters between 6 and 30 mm; some AVM's have two diameters over 40 mm, while the third diameter is between 5 and 25 mm; and some AVM's have all three diameters larger than 40 mm. Obviously, this wide variation in the size of the three diameters may influence the outcome both in microsurgery and in radiosurgery.

The incidence of total AVM obliteration is dose-dependent, and rises with an increase in minimum AVM margin dose.11 In large AVM's treated with similar doses, comparable obliteration rates can be achieved, but at the price of higher risk.

Patency of Irradiated AVM's and Rebleeding

The issue of possible protection against hemorrhage in irradiated but still patent AVM's is highly contro-
versal. Like the majority of neurosurgeons, we believe that patients, whether treated by microsurgery, radiosurgery, or endovascular techniques, remain at risk for a rebleed as long as the malformation is still patent. Nonetheless, in a recent study using the Kaplan-Meier life-table estimates, we found that the shape of the curve could be interpreted as an indication of a sustained decrease in the risk of hemorrhage late in the follow-up period. However, we emphasized that this should be confirmed by larger series followed beyond the period represented by the plateau at the right side of a life curve.

Another piece of information related to rebleeding was derived from the group of our patients having subtotal obliteration. We acknowledge subtotal obliteration in cases with nonvisualization of the nidus but continued early venous opacification, indicating that shunting is still present. In our series, 89 AVM's showed subtotal obliteration and no recurrence of hemorrhage was observed in this group. From the time of angiographic assessment of subtotal obliteration, the follow-up period was 496 patient-years, an average of 5.5 years per patient. If we assume a 2% or 4% yearly risk of rebleeding, the probable number of hemorrhages should have been nine (95% confidence interval 7.7 to 10.6, 99.9% confidence interval 6.7 to 11.7) or 17 (95% confidence interval 14.4 to 19.6, 99.9% confidence interval 12.5 to 21.4). The weakness in this reasoning is that we do not know whether any of these AVM's became obliterated after the last follow-up angiography. Therefore, let us assume that there were only 248 risk-years. Even in such a scenario, with a 2% assumed yearly risk the number of hemorrhages would be 4.8 (95% confidence interval 4 to 5.6, 99.9% confidence interval 3.5 to 6.1) and with a 4% assumed yearly risk the number of hemorrhages would be 9.3 (95% confidence interval 7.8 to 10.8, 99.9% confidence interval 6.8 to 11.7).

Thus, the zero incidence of hemorrhage in our material seems remarkable indeed compared to the incidence of hemorrhage in the natural history of the disease. These new observations require critical open-minded consideration; if they hold, it will be necessary to revise present views on possible protection against hemorrhage in irradiated but still patent AVM's.

**Location of AVM**

Sisti, et al. state that location alone is not commonly an indication for one form of treatment over the other. Nevertheless, they extirpated only three (50%) of six brain-stem AVM's. In our Fig. 1, we illustrate a mid-brain AVM before and after radiosurgery. In our series of 57 AVM's of the brain stem treated with the gamma knife, a 2-year follow-up evaluation was obtained in 28 cases; 20 (71.4%) were completely obliterated and five (17.9%) were subtobly obliterated. We excluded from this group the malformations on the surface of the brain stem and included only those lesions directly in the midbrain, pons, peduncle, and medulla. The results of gamma knife surgery in thalamic AVM's (Fig. 2) also compare favorably to the results with microsurgery.

**Aneurysms Associated With AVM's**

Sisti, et al. indicate as one of the advantages of microsurgery for AVM's, the clipping of associated arterial aneurysms during extirpation of the malformation. We certainly agree that microsurgery is the appropriate technique for managing arterial aneurysms; we (L.S. and C.L.) performed microsurgery on close to 1500 arterial aneurysms, 715 of them operated on between 1970 and 1980. Nevertheless, we have obliterated intranidal and perinidal aneurysms with the gamma knife (Fig. 3). Moreover, when for some reason microsurgery could not be performed, we have occasionally used the gamma knife to obliterate aneurysms at a distance from the AVM or aneurysms without an AVM.

**Clinical Outcome**

Sisti, et al. in their Table 3 summarize the clinical condition of their patients at the onset of symptoms, at the time of microsurgery, and at follow-up evaluation a mean of 50 months after treatment. Between time of surgery and follow-up review, improvement to their Grade I group (neurologically normal) was seen in only
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Fig. 2. Angiograms in a 9-year-old boy with intracranial hemorrhage in the thalamus and midbrain. Left Pair: Left vertebral angiograms, lateral (A) and frontal (B) views, at the time of gamma knife surgery. An arteriovenous malformation (AVM) is located in the posterior thalamus and rostral midbrain. A follow-up magnetic resonance image (not shown) revealed no flow-void area 11 months after treatment; however, the patient's parents refused permission to perform follow-up angiography until 13 months following treatment. Right Pair: Left vertebral follow-up angiograms, lateral (C) and frontal (D) views. The AVM has been obliterated and the patient suffered no neurological deficits.

Four patients (6%): three patients in their Grade II group (minor neurological deficits) and one in their Grade III group (major neurological deficits). Between the onset and time of surgery, a significant decrease of 42% in the number of patients with severe neurological deficits occurred, while between the time of surgery and the follow-up evaluation there was a mere 1% decrease in cases with major neurological deficits.

Could it be that surgery arrested the ongoing restoration process? Actually, risk-benefit assessment is difficult because injuries inflicted by surgery are to a great extent masked by symptoms at the time of surgery and it cannot be excluded that these symptoms might have continued to improve if surgery had been delayed.

In Table 1, reproduced from Steiner, et al.,10 the neurological outcome in 228 cases of AVM treated by gamma knife surgery with a mean follow-up time of 7 years is given. The motor deficit completely resolved

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Neurological outcome following radiosurgery in 228 cases of arteriovenous malformation*</th>
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</thead>
<tbody>
<tr>
<td>Pretreatment Signs &amp; Symptoms</td>
<td>Incidence</td>
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<tr>
<td></td>
<td>No.</td>
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<td></td>
<td>No.</td>
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<tr>
<td>chronic headache</td>
<td>98</td>
</tr>
<tr>
<td>motor deficit</td>
<td>74</td>
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<tr>
<td>seizures</td>
<td>59</td>
</tr>
<tr>
<td>sensory deficit</td>
<td>46</td>
</tr>
<tr>
<td>memory disturbance</td>
<td>44</td>
</tr>
<tr>
<td>language dysfunction</td>
<td>35</td>
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* Reproduced from Steiner, et al.,10 with permission.
in 54% of cases and significantly resolved in 17.6%; the speech dysfunction completely resolved in 60% and significantly resolved in 14.3%; and the sensory deficit completely resolved in 41.3%.

Retrospective nonrandomized, nonstratified, and unmatched series should not be compared. Nonetheless, they could help the reader to see the facts provided both by us and by Sisti, et al., in an appropriate perspective.

**Adverse Effects**

In their Fig. 7, Sisti, et al., illustrate a case with edema and histologically proven delayed radionecrosis. In our material, changes reflecting a wide gamut of pathological, physiological, and clinical entities have been detected on computerized tomography scans in 11% and on MR images in 37% of cases. The onset of these changes was 3 to 15 months after treatment in 92.3% of the cases and more than 15 months in 7.7% of the cases.1

It is disturbing that Sisti, et al., provide one initial MR image without subsequent MR studies. In Figs. 4 and 5, we illustrate cases in our series with radiation-induced changes on MR images at the onset and the subsequent improvements on the follow-up studies. Progressive resolution of the radiation-induced adverse effects with small residual destruction of neural tissue in some cases is the usual course in such patients, with resolution observed 1 to 33 months (mean ± standard deviation 9 ± 8 months) following detection of changes. Neurological deficits occurred in 51 (6%) of 816 pa-

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**Fig. 4.** Magnetic resonance (MR) images in an 11-year-old boy with intracerebral hemorrhage. A: T2-weighted MR image obtained 4 months after radiosurgery for arteriovenous malformation (AVM). Edema surrounds the residual AVM nidus (arrow). B: T2-weighted MR image obtained 6 months after radiosurgery. The edema has increased and the AVM nidus (arrow) is still present. C: T2-weighted MR image obtained 11 months after radiosurgery. The edema has decreased and the flow-void areas of the AVM have disappeared. A follow-up angiogram revealed that the AVM has been obliterated (not shown). D: Contrast-enhanced T1-weighted MR image obtained 11 months after radiosurgery showing a small area of abnormal enhancement (arrow) located at the center of the treatment field. Moderate weakness in the left arm and leg persist; however, the boy leads a normal life including intensive sports activity.

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**Fig. 5.** T2-weighted magnetic resonance images in a 31-year-old woman with intracerebral hemorrhage. A: Study obtained 6 months after radiosurgery for an arteriovenous malformation (AVM) showing extensive edema surrounding the residual AVM nidus (arrow). B: Image obtained 7 months after radiosurgery. The edema has increased while the flow-void areas of the AVM have disappeared. A follow-up angiogram showed subtotal obliteration of the AVM (not shown). C: Image obtained 28 months following radiosurgery. Only a small area of abnormal increased signal remains at the center of the treatment field (arrow). Follow-up angiography is pending. Postoperatively, this patient works as before as a dental nurse. Her only complaint is that when she inserts a coin in an automated laundry machine, her fingers feel clumsy.

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tients: however, only 25 (3%) still had neurological
deficits at the latest follow-up review. Concerning the
histological changes, we extirpated a cavernous an-
gioma and obtained specimens from the surrounding
brain tissue where radiation-induced changes had oc-
curred and subsequently regressed. The histological
study revealed no pathological changes (L Steiner, et al.,
unpublished data).

Thus, it appears that presenting one image of a
radiation-induced adverse effect without subsequent
follow-up studies is misleading. The presumption of
Sisti, et al., that with time the number of complications
following radiosurgery increases is not borne out by the
facts. Actually, the risk of hemorrhage seems to decrease
over time, and an overwhelming majority of the radia-
tion-induced adverse effects following treatment re-
solve within 1 to 17 months. Necrosis of small volumes of
neural tissue in some cases compares favorably with
occasional postoperative changes.

**Tumors Induced Following Radiotherapy vs. Radiosurgery**

Tumor induction by radiotherapy has been reported
with both low and high doses. In the 25 years since the
introduction of radiosurgery, no tumors induced by the
treatment have been observed. One may speculate that
ionizing beams delivered over a long period are more
effective to induce tumor than single high doses given
over a short period. Although our observation time
does not exclude the possibility of future tumor cases,
their number, if any, will presumably be insignificant.

**Radiosurgery and Growth Hormone Deficit**

Growth hormone deficit is observed in 30% of chil-
dren following fractionated radiation therapy. In our
series of 126 children between 3 and 12 years of age,
treated with gamma knife radiosurgery, however, no
deficit of growth hormone was observed. This result is
presumably because relatively small tissue volumes
have been targeted and the hypothalamus has been
spared.

**Discussion**

**Failures in Radiosurgery**

Sisti, et al., point to our failure to obliterate totally
all AVM's treated. If we consider the first treatment as
well as repeated treatments, the incidence of total obli-
eration reached 87%. In addition, subtotal obliteration
occurred in 5% of the cases. Among the subtotally
obliterated AVM's, no rebleed was observed over an
average of 66 months of follow-up review. Moreover,
the initial technique was crude compared to that we use
today. A review of the cases where radiosurgery failed
identified errors that could be avoided with the now
available planning system. The "learning curve effects"
heavily influence even our present statistics. The fast-
moving developments include the new computerized
three-dimensional planning system, improving imaging
techniques, new insights in the mechanisms of radia-
tion-induced vasogenic edema, evolving new treatment
strategies like targeting of embryologically determined
strategic spots in AVM's, second factors, sensitizers,
and nerve tissue protective agents, to name only a few.
Radiosurgery, like microsurgery or endovascular sur-
gery, has not yet reached the limits of its potentials.

**Are the Indications for Radiosurgery Too Broad?**

Sisti, et al., believe that too many cases are treated
by radiosurgery. In this respect, it should be remem-
bered that our 1800 AVM's were treated over a period
of 22 years. For a long period of time, we were the only
institute in the world where cases could be referred for
radiosurgery. Parallel with the use of the gamma knife,
microsurgery has been performed on 147 AVM's in
Stockholm and 72 in Charlottesville, a total of 219
patients. The cases for microsurgery were referred, as
we presume were the cases reported by Sisti, et al.,
from a limited patient population, compared to the radio-
surgical cases coming to us from 40 countries on five
continents. This means 81 radiosurgical cases per year
or (if we calculate only for the last 15 years) 120 cases
per year from a patient population spread throughout
the world. Considering the recent numbers in the
United States, we treated roughly 3% of the yearly
available new AVM cases. The rest of the gamma knife
centers together treated an additional 7% and centers
using the linear accelerator, 4%.

We share the suspicion that radiosurgery occasion-
ally is overused. It happens with all new methods with fast
proliferation. There are 12 gamma knife centers and
more than 100 centers using linear accelerators in the
United States. Enthusiasm and inexperience may un-
duly expand indications. Notwithstanding, it seems fu-
tile to argue whether the appropriate share of radiosur-
gery should be 14% or 3% as Sisti, et al., believe. The
percentage of treated patients will be different in differ-
ent services, since decision-making depends not only
upon the natural history and the parameters of the
AVM and of the patient, but also upon the pattern of
referral, and the parameters of the neurosurgeon. The
advent of MR imaging and the detection of increasing
numbers of asymptomatic or slightly symptomatic
AVM's further complicate decision-making. In spite of
the fact that we agree with Sisti, et al., that superficial
AVM's even in eloquent areas can be extirpated with
low risk, there will be neurosurgeons and patients who
will not easily accept open surgery in such cases. In fact,
only the future will tell whether such a decision is totally
wrong.

Any discussion concerning the share of the existing
techniques in the treatment of AVM's should be based
on matured data, which are not yet available. The
evolving facts should be evaluated *sine ira et studio*.
One should try to elevate the discussion to a higher
level, aiming not to prevail but to reach the truth, and
to adjust one's policy in the management of the AVM
to the new insights. Moreover, it would benefit our
patients indeed if in our decision-making we remember
the words of Born: "Ideas such as absolute certitude,
absolute exactness, final truths, are figments of the
imagination which should not be admissible into any
field of science. Because the belief in a single truth and
in being the possessor of it is the root cause of all evil in this world.

Conclusions

We consider the article of Sisti, et al., to be useful despite several lapses. It emphasizes that microsurgery is a straightforward method which should not be easily discarded in decision-making, that overuse of the radiosurgical tool should be avoided, and that AVM’s should be managed by neurosurgeons who do master both microsurgery and radiosurgery. On the other hand, Sisti, et al., occasionally with truncated presentation of facts, failed in their apparent aim of an unbiased assessment of results with microsurgery versus radiosurgery in AVM’s. Sisti, et al., have triggered a discussion that presumably will follow the Hegelian pattern — thesis, antithesis, synthesis — and will reach the conclusion that microsurgery, radiosurgery, and endovascular surgery are compatible and complementary.

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References


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