STEREOTACTIC RADIOSURGERY OF ARTERIOVENOUS MALFORMATIONS
Clinical White Paper

Despite the low prevalence—between 0.04% and 0.52%—in the general population\(^1\), intracranial arteriovenous malformations (AVMs) are the leading cause of nontraumatic intracerebral hemorrhage in people younger than 35 years old\(^2\). Intracranial AVMs are congenital anomalies developing between the fourth and eighth week of intrauterine life. They consist of the persistence of connections between an artery and a vein without the interposition of a capillary bed, typically under a high-flow regimen\(^3\). This entanglement of blood vessels is often called a nidus.

Intracranial AVMs may present with intracerebral hemorrhage, seizures, neurologic deficit, headaches or occasionally as incidental findings on neuroimaging studies\(^4\). The risk of hemorrhage from AVMs without a previous event is about 3% per year\(^5\). An aggressive therapeutic approach is appropriate for preventing a fatal intracranial hemorrhaging caused by these lesions\(^6\).

The goal of AVM treatment should be complete removal or obliteration of the nidus, while preserving the functionality of the adjacent brain tissue. The successful treatment of AVMs remains a challenge with current options, including microsurgical resection, embolization and stereotactic radiosurgery (SRS)\(^7\). The adequate use of each of these tools as a single or combined treatment modality is necessary to successfully complete the treatment.

As the traditional treatment modality, microsurgical resection is an effective method to quickly eliminate the risk of hemorrhage\(^6\). However, large lesions in deep, eloquent regions of the brain are not amenable to microsurgery because of associated morbidity and mortality. Adjuvant embolization is also useful in the treatment of AVMs, but the associated risks can be high and the long-term efficacy of the treatment is not well understood\(^4\). There may be a risk of recanalization after embolization, even with recent novel materials.

Over the years, SRS has provided an elegant means of safely treating AVMs\(^10-17\). Because AVM tissue responds slowly to radiation, several months may follow SRS treatments before complete nidus obliteration\(^18\). The significant risk of hemorrhage during this latency period mandates diligent neuroimaging follow-up of the radiosurgical patients until complete obliteration of the nidus is angiographically confirmed\(^19\).

Several imaging modalities, such as digital subtraction angiography (DSA), computerized tomography angiography (CTA), magnetic resonance angiography (MRA) or combinations of these, may be used to create images of the nidus for SRS target definition. Despite the major disadvantage of being a two-dimensional imaging technique, DSA remains the gold standard for AVM imaging because it provides unique temporal information.

A summary of the most important SRS treatment parameters, together with the expected outcome of some dedicated SRS studies of the treatment of intracranial AVMs, is presented in the table below. A recent experience on repeat SRS for large AVMs is also included\(^17\). Hypofractionation trials for the stereotactic radiotherapy treatment of intracranial AVMs are currently underway; however, the results are still preliminary and are therefore not included.
In general, patients are immobilized with a frame and a single mean dose of 15 to 19 Gy is prescribed to the 80% isodose line. The dose is typically delivered by four to eight arcs—for spherical lesions, conical collimators can be preferred over high-resolution multi-leaf collimators.

Intracranial AVMs are often classified according to a grading score developed by Spetzler and Martin\textsuperscript{20} and the prescribed dose is related to the initial AVM grade, since complete nidus obliteration rates were found to depend mainly on the AVM volume and the SRS dose\textsuperscript{11,13,15}.

The overall incidence of radiation-induced complications ranges from 3 to 6% and the reported neurological deficits are often of transient nature\textsuperscript{16-17}.

It is therefore concluded that SRS is a safe and effective intracranial AVM treatment option, as long as careful neuroimaging follow-up is guaranteed to monitor the nidus response.

### Overview of the recent clinical literature on SRS for arteriovenous malformations

<table>
<thead>
<tr>
<th>Author</th>
<th>Institution</th>
<th>Year</th>
<th># Lesions</th>
<th>% Prior Treatment</th>
<th>Mean Vol (cm(^3))</th>
<th>Mean Dose (Gy)</th>
<th># Fractions</th>
<th>% IDL covering PTV</th>
<th>% Complete Obliteration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobin\textsuperscript{11}</td>
<td>University of California, Davis</td>
<td>1999</td>
<td>50</td>
<td>36</td>
<td>23</td>
<td>16</td>
<td>1</td>
<td>80</td>
<td>45 at 20 months</td>
</tr>
<tr>
<td>Pedroso\textsuperscript{15}</td>
<td>David Geffen School of Medicine, Los Angeles</td>
<td>2004</td>
<td>44</td>
<td>30</td>
<td>18</td>
<td>15</td>
<td>1</td>
<td>80</td>
<td>52 at 37 months</td>
</tr>
<tr>
<td>Buis\textsuperscript{12}</td>
<td>VU University Medical Center, Amsterdam</td>
<td>2005</td>
<td>31</td>
<td>32</td>
<td>3</td>
<td>19</td>
<td>1</td>
<td>80</td>
<td>77 at 33 months</td>
</tr>
<tr>
<td>Scarbrough\textsuperscript{14}</td>
<td>The Melbourne Cancer Center, Melbourne</td>
<td>2005</td>
<td>39</td>
<td>8</td>
<td>7</td>
<td>17</td>
<td>1</td>
<td>80</td>
<td>87 at 24 months</td>
</tr>
<tr>
<td>Zabel-du Bois\textsuperscript{13}</td>
<td>University of Heidelberg</td>
<td>2006</td>
<td>22</td>
<td>36</td>
<td>4</td>
<td>18</td>
<td>1</td>
<td>80</td>
<td>65 at 48 months</td>
</tr>
<tr>
<td>Huang\textsuperscript{16}</td>
<td>Ghang Gung Memorial Hospital, Taiwan</td>
<td>2006</td>
<td>34</td>
<td>14</td>
<td>2</td>
<td>16</td>
<td>1</td>
<td>80</td>
<td>NA</td>
</tr>
<tr>
<td>Moreno-Jiménez\textsuperscript{10}</td>
<td>Natl Institute of Neurol &amp; Neurosurg, Mexico</td>
<td>2007</td>
<td>40</td>
<td>40</td>
<td>8</td>
<td>15.4</td>
<td>1</td>
<td>80</td>
<td>63 at 29 months</td>
</tr>
<tr>
<td>Raza\textsuperscript{17}</td>
<td>The Johns Hopkins Hospital, Baltimore</td>
<td>2007</td>
<td>14</td>
<td>47</td>
<td>25</td>
<td>36</td>
<td>3</td>
<td>NA</td>
<td>36 at 31 months</td>
</tr>
</tbody>
</table>

Complete obliteration implies that the nidus is no longer visible angiographically and that the circulation time and the afferent and efferent vessels that had supplied the malformation have returned to normal. For angiographically occult lesions like low-flow cavernous malformations, studied by Huang et al., there is currently no gold standard for demonstrating the obliteration.

### References

1. Pollock B.E. et al., Stroke 27, 1, 1996
8. Lawton M.T., Neurosurg 52, 740, 2003
11. Mobin F. et al., Stereotact Funct Neurosurg 73, 50, 1999
17. Lawton M.T., Neurosurg 52, 740, 2003