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Review

# Stereotactic radiosurgery for deep intracranial arteriovenous malformations, part 1: Brainstem arteriovenous malformations

Or Cohen-Inbar *, Dale Ding, Ching-Jen Chen, Jason P. Sheehan

*Department of Neurological Surgery, University of Virginia, PO Box 800212, Charlottesville, VA 22908, USA*

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ABSTRACT

The management of brainstem arteriovenous malformations (AVM) are one of the greatest challenges encountered by neurosurgeons. Brainstem AVM have a higher risk of hemorrhage compared to AVM in other locations, and rupture of these lesions commonly results in devastating neurological morbidity and mortality. The potential morbidity associated with currently available treatment modalities further compounds the complexity of decision making for affected patients. Stereotactic radiosurgery (SRS) has an important role in the management of brainstem AVM. SRS offers acceptable obliteration rates with lower risks of hemorrhage occurring during the latency period. Complex nidal architecture requires a multi-disciplinary treatment approach. Nidi partly involving subpial/epipial regions of the dorsal midbrain or cerebellopontine angle should be considered for a combination of endovascular embolization, micro-surgical resection and SRS. Considering the fact that incompletely obliterated lesions (even when reduced in size) could still cause lethal hemorrhages, additional treatment, including repeat SRS and surgical resection should be considered when complete obliteration is not achieved by first SRS. Patients with brainstem AVM require continued clinical and radiological observation and follow-up after SRS, well after angiographic obliteration has been confirmed.



## 1. Introduction

Arteriovenous malformations (AVM) are congenital vascular malformations with an incidence of 1:100,000, which present equally in men and women, and are typically diagnosed by the fourth decade of life [1,2]. An AVM is characterized by a nidus formed by direct arterial to venous connections without an intervening capillary network [3]. This abrupt transition from the high-pressure, thick-walled muscular arterial system to a low-pressure, dilated and thin-walled venous system leads to secondary intracerebral venous dilatation and engorgement, vessel wall arterialization, and vasogenic edema and inflammation of surrounding brain tissue. This pathological process and the associated hemodynamic derangements predispose the AVM nidus to rupture and intranidal or perinidal aneurysm formation [1–6].

Brainstem AVM constitute approximately 2–6% of all intracranial AVM [7–9]. The natural history of untreated AVM located in the brainstem suggests a higher risk of hemorrhage compared to AVM in other locations. Additionally, due to the density of critical structures in the brainstem, AVM hemorrhage in this location is associated with excessive rates of major morbidity or mortality [1,2,10–12]. Kiran et al. [13] reported an 81% incidence of hemorrhagic presentation in patients with deep-seated AVM in the basal ganglia, thalamus, and brainstem. This rate of hemorrhagic presentation was significantly higher than that reported in patients with AVM in other locations (67%). No single management strategy fits all, and the best course of treatment for a certain brainstem AVM is often tailored specifically.

With the advances made in neuroimaging and improved population education and vigilance, the number of unruptured AVM has increased to over half of all identified AVM [14]. These patients may suffer a multitude of other clinical manifestations, such as seizures, headache or focal neurological deficits. Several observational studies have suggested that the natural history of unruptured AVM may be different than that of ruptured AVM, carrying a lower risk of rupture [5]. This finding has incited a significant controversy regarding the best management of these unruptured AVM, with some physicians stating that intervention for unruptured AVM may yield worse outcomes than conservative management [15]. The short-term outcomes from A Randomized Trial of Unruptured Brain AVM (ARUBA) and the Scottish Audit of Intracranial Vascular Malformations (SAIVM) prospective AVM cohort study supported such a view [16].

* Corresponding author. Tel.: +1 434 924 8129; fax: +1 434 243 6726.
*E-mail address:* oc2f@virginia.edu (O. Cohen-Inbar).

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**Table 1**
AVM scales

| Parameter | Spetzler Martin scale [24,25] | | | | | Virginia Radiosurgery AVM Scale [29] | | | | | RBAS [28] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Variable | | Points | Outcome | | Coefficient |
| | | | | | | | | | Cumulative points | Favorable outcome (%)+ | |
| AVM size | <3 cm^Ω | 1 | | Surgical outcome | | <2 ml³ | | 0 | 0 | 83 | 0.1 |
| | 3–6 cm^Ω | 2 | Modified grade | Grade | Major, minor deficits (%) | 2–4 ml³ | | 1 | 1 | 79 | |
| | >6 cm^Ω | 3 | | | | >4 ml³ | | 2 | 2 | 70 | |
| AVM in eloquent location++ | No | 0 | A | 1 | 0, 0 | Frontal/temporal | 0 | 1 | 3 | 48 | 0.3 |
| | | | | 2 | 0, 5 | P/O/IV/CC/Cer | 1 | | | | |
| | Yes | 1 | B | 3 | 4, 12 | BG/TH/BS | 2 | | | | |
| Venous drainage | Super-ficial | 0 | C | 4 | 7, 20 | – | | – | | | – |
| | Deep | 1 | | 5 | 12, 19 | – | | | | | – |
| History of hemorrhage | – | – | – | – | – | – | | 1 | 4 | 39 | – |
| Patient age, years | – | – | – | – | – | – | – | – | – | – | 0.02 |
| | | | | | | | | | | | AVM RBAS score: (0.1) (AVM volume) + (0.02) (patient age) + (0.3) (AVM location) |

AVM = arteriovenous malformation, BS = brainstem, BG = basal ganglia, CC = corpus callosum, Cer = cerebellar, IV = intraventricular, O = occipital, P = parietal, RBAS = Radiosurgery Based Arteriovenous malformation Score [28], TH = thalamus.
Ω Diameter of the nidus.
+ Favorable outcome defined as both AVM obliteration and no post-treatment hemorrhage or permanent Gamma Knife (Elekta AB, Stockholm, Sweden) stereotactic radiosurgery associated symptoms.
++ In RBAS, when an AVM involves multiple sites, fractional values are used according to the number of sites (0.5 for two sites, 0.33 for three sites).

The goal of treating AVM with stereotactic radiosurgery (SRS) is to obliterate the nidus, and thereby completely eliminate any future hemorrhage risk. The occurrence of complete AVM nidus obliteration with SRS depends on several factors. The key factors are the volume of the AVM nidus (and its compactness) and the maximum safe radiosurgical margin dose allowed [1]. A general rule of thumb is a higher margin dose, within the therapeutic range of 10–30 Gy delivered in a single session, positively correlates with obliteration rate. Karlsson et al. [17] reported a series of 945 patients with an 80% overall obliteration rate. The obliteration rate was calculated in this report to be approximately 90%, 80%, and 70% for AVM given margin doses of 20 Gy, 18 Gy, and 16 Gy, respectively [17].

AVM in different locations pose distinct clinical challenges and can behave very differently, even after SRS. AVM of the brainstem have been shown to be associated with significant complications and a higher incidences of hemorrhage during the latency period [6,13,18,19] as well as lower obliteration rates compared with other locations [13,20].

## 2. Predicting outcome after SRS

The post-SRS effects in AVM patients, unlike that of microsurgery, may not fully manifest for many years. Both obliteration and complications occur in longer time scales after SRS compared to embolization or resection. In addition, the risk of hemorrhage from an SRS-treated AVM nidus persists, to some degree, during the latency period until obliteration. Given the fundamental difference between radiosurgical and microsurgical approaches, conventional grading scales characterizing AVM may seem insufficient for prognostic purposes. The time-honored Spetzler–Martin (SM) grading system [21,22], is mainly limited to distinguishing the size of brainstem AVM, because these are uniformly eloquent in location and drain deeply [18]. As such, these lesions are automatically classified at least as grade III in the old SM scale and as grade B in the new modified SM-system (Table 1). Nevertheless, the SM grading system has been shown to correlate with SRS outcomes [23–28].

Many designated grading scales have been created in an attempt to predict outcome following SRS [17,23,29–31]. These early scales were limited, in that they predicted obliteration based largely on treatment parameters (for example, radiation dose) [17,29], failing to account for the fact that as SRS dose increases, so does the likelihood of both obliteration and radiation-induced complications. Thus, as the radiosurgical field evolved, early models required modification to better predict overall clinical and radiographic outcome [30]. The potential benefit of increasing the radiation dose (higher obliteration rates) must always be weighed against the increased risk of accompanying neurological morbidity [32]. Flickinger et al. [33] suggested that a major determinant for increasing the rate of permanent radiosurgery-induced deficits was the volume of tissue receiving at least 12 Gy [33].

Newer scoring systems, such as the radiosurgery-based AVM score (RBAS) described by Pollock et al. [30] or the Virginia radiosurgery AVM scale (VRAS) [31] devised by our group, were constructed in an attempt to provide a stratified estimate of a composite radiologic and clinical outcome comprising nidus obliteration, hemorrhage, and radiation-related complications. These different scales are summarized in Table 1. The RBAS [30] was based on outcome analysis of 356 patients, 56% (n = 199) of whom harbored a deep-seated AVM. One caveat to the RBAS lies in the fact that it was designed to predict a patient outcome after a single radiosurgery procedure and not the overall results of radiosurgical management. The VRAS [31] was derived based on analysis of 1012 patients treated with Gamma Knife stereotactic radiosurgery