REVIEW ARTICLE

# Current Status of Radiosurgery for Arteriovenous Malformations

Michael Schwartz, Peter O'Brien, Phillip Davey,
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**ABSTRACT**: Cerebral arteriovenous malformations (AVM), regardless of the mode of discovery, have an annual risk of hemorrhage of approximately 4 percent. A progressive obliterative vasculitis culminating in the occlusion of an AVM may be induced by the administration of radiation doses of approximately 20 Gy given in a single fraction. The process takes about two years and occlusion occurs in approximately 80% of patients so treated. Such a dose may be accurately administered to AVMs up to 3 cm in diameter with very little radiation imparted to the adjacent brain by means of multiple highly collimated radially arranged cobalt sources (the Gamma Knife) or by means of a modified linear accelerator turned through an arc or arcs with the target AVM as the centre of rotation. The Gamma Knife and the modified linear accelerator have nearly equal accuracy. Recent experience with modified linear accelerators indicates efficacy equal to the Gamma Knife. Both devices are effective treatment for small AVMs but the cost of modifying a pre-existing linear accelerator is only a few percent of the acquisition and installation costs of the Gamma Knife.

**RÉSUMÉ: Radio-chirurgie dans le traitement des malformations artério-veineuses: état de la question** Les malformations artério-veineuses cérébrales (MAV), quel que soit la façon dont elles sont décelées, comportent un risque annuel d'hémorragie d'à peu près 4 pourcent. Une vasculite oblitérante progressive aboutissant à l'occlusion d'une MAV peut être induite par l'administration d'une dose de radiations d'à peu près 20 Gy, donnée en une seule fraction. Le processus prend environ deux ans et l'occlusion se fait chez à peu près 80% des patients ainsi traités. Une telle dose peut être administrée avec précision à des MAVs qui ont jusqu'à 3 cm de diamètre, avec peu d'irradiation aux tissus cérébraux adjacents, au moyen de sources de cobalt multiples, hautement collimatées et disposées radialement (le Couteau Gamma) ou au moyen d'un accélérateur linéaire modifié décrivant un ou des arcs ciblés sur la MAV comme centre de rotation. Le Couteau Gamma et l'accélérateur linéaire modifié ont presque le même degré de précision. Des expériences récentes avec des accélérateurs linéaires modifiés indiquent qu'ils ont une efficacité égale à celle du Couteau Gamma. Les deux techniques sont une forme efficace de traitement pour les petites MAVs, mais le coût de modification d'un accélérateur linéaire pré-existant n'est qu'un faible pourcentage des fais d'acquisition et d'installation d'un Couteau Gamma.

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It has been estimated that a patient who is found to have an unruptured, high flow cerebral arteriovenous malformation (AVM) has a 2 to 3 percent chance of suffering a hemorrhage in the first year and an approximately 30% chance of hemorrhage over the first 10 years. The likelihood of sustaining a significant cerebral neurological deficit from the hemorrhage is approximately 50% and the likelihood of dying approaches 10 percent.[1] More recent evidence[2] suggests that the mode of presentation, that is, seizure, hemorrhage, or incidental discovery may not influence the propensity to bleed and that the annual incidence of hemorrhage may be as high as 4 percent. With these risks in view, an appropriate treatment regimen must be designed from the therapies currently available. Relatively small and superficial arteriovenous malformations are best treated by craniotomy and complete surgical excision. Surgical excision of large lesions, especially those with particularly high flow can be made safer by preoperative partial endovascular obliteration (embolization).[3,4] Very large or very high flow arteriovenous malformations, especially those which are deep or delicately placed, are best treated by staged endovascular procedures without surgery.[5] Small arteriovenous malformations (or large ones made small enough by partial endovascular obliteration) that are deep and inaccessible to the surgeon are best treated by focused radiation. In considering how to treat a particular individual, there may be a spectrum of opinion regarding the best method. At Sunnybrook Medical Centre and the Toronto Bayview

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Regional Cancer Centre we have assembled a multidisciplinary committee to assess and review patients with AVM's referred for radiosurgery.

The immediate risk of bleeding for patients with unruptured AVM's is relatively small. It is reasonable, therefore, to choose a treatment modality that may confer delayed protection if it is safer than surgical excision which is effective as soon as the operation is completed. For recently ruptured arteriovenous malformations where the risk of rebleeding is higher and the need for immediate protection is greater, one might lean more toward surgical excision than if the lesion had not recently bled.

Since safe, effective embolization and focused radiation have only recently become available in most medical communities, these treatment modalities are still finding their place in the therapeutic armamentarium. It is expected that over the next several years, the criteria for choosing among the available therapeutic modalities will be more generally agreed upon.

When a high dose of radiation is given to an arteriovenous malformation, a progressive obliterative vasculitis is induced. Over a period of months to years, some lesions gradually disappear. Steiner[6] reports that 85% of irradiated arteriovenous malformations with follow up angiography are completely obliterated at two years. In an earlier report, Backlund[7] showed that the best results for AVM's were obtained when the whole nidus could be irradiated, not just the feeding vessels. The worst results were obtained when only some of the feeding vessels were included in the radiation field. The best radiation dose has not been definitively established. Doses up to fifty Gy in one or a very few fractions may be considered.[8] The volume of tissue that may safely be irradiated to this dose is probably a sphere of about 3 cm in diameter. For larger volumes the dose may need to be considerably smaller.

Taking these facts into consideration, it is generally accepted that small AVM's (less than 3 cm in diameter) or those reduced to this size by embolization, which are inaccessible to craniotomy and surgical excision are the lesions most suitable for focused radiation or radiosurgery.

There is a debate in the medical literature about what procedure is properly called radiosurgery.[9,10] The term radiosurgery was coined in 1951 by Lars Leksell but he did not specify the means of accurately delivering the radiation.[11] In our view, the terms focused radiation and radiosurgery may be used interchangeably.

What is the best means of delivering a high dose of radiation to the AVM while sparing the surrounding brain? Implanted radiation sources are clearly impractical because of the risk of bleeding. Available methods for external radiation include beams of charged particles (protons or helium ions) and photon radiation generated by an array of collimated radioactive sources or by a linear accelerator. The charged particles must be generated by a cyclotron which is a complex and expensive facility. The physics and technical considerations regarding charged particle irradiation are different from photon irradiation but both have in common that the obliteration of the AVM occurs slowly and continuously over a period of months to years.[12,13] Because of the expense and complexity of the cyclotron, it is unlikely that there will be many units available for the treatment of patients with arteriovenous malformations.

At the present time, there are two competing technologies for the delivery of focused photon irradiation. The first, popularly called the "Gamma Knife", consists of multiple (approximately 200) collimated sources of cobalt 60 radially directed at a central target at the focal point of the collimators. Using a stereotactic frame, the patient is positioned so that the arteriovenous malformation or tumor is centred at the focal point. Different collimators may be selected to irradiate a larger or smaller target. The dose is varied by varying the length of time the patient is positioned in the unit. For nearly 30 years, the Gamma Knife in Stockholm was the only unit in the world. Diffusion of this technology to other centres has been very slow. An article by Lunsford et al highlights the bureaucratic impediments that had to be overcome in the acquisition of a Gamma Knife by the Pittsburgh Presbyterian University Hospital.[8] Walton's[14] description of the Sheffield Stereotactic Radiosurgery Unit, in service since 1985, describes the physical characteristics of the Gamma Knife and the daunting technical problems of site preparation and radiation protection. In fact, despite modifications, the dose rates at points close to the shutter shielding the cobalt sources within the unit are still slightly higher than the British radiation code of practice recommends.

With more than a 30-year experience and approximately 2500 patients treated, the Gamma Knife is established as a safe and accurate device. It is estimated that the central axis of each of the radiation beams intersects at the focal point with a mechanical precision of ± 0.3 mm.[14] Alignment between the collimating helmet and the surrounding unit containing the cobalt sources is controlled by microswitches with a tolerance of ± 0.1 mm. Disregarding the error of stereotactic localization, which would be common to all devices using a stereotactic frame, the cumulative error in the radiation parts of the system is 0.4 mm or less. So far no patients have been harmed by misdirection of the radiation[8] and 85% of arteriovenous malformations radiated are obliterated at a 2-year angiographic follow up.[6]

A standard device in Canada for administering external radiotherapy is the linear accelerator which can generate a sharply collimated pencil of high energy photons. With simple modifications to the device, a patient's head may be positioned so that an intracerebral target is positioned at the centre of rotation of the gantry that carries the radiation source. The radiation couch on which the patient lies during the procedure may also be rotated in the horizontal plane about the same point. A high radiation dose at the target point with a steep reduction in radiation dose outside the target area is achieved by a tomographic effect. The target is always in the path of the collimated photon beam with the source swinging through an arc. The overlying tissue is exposed to the beam for only a short period of time as the radiation source passes over it. In the Harvard system which is essentially that originally proposed by Betti et al[15] and Colombo et al,[16] the radiation may be delivered as a system of noncoplanar arcs[17] by repositioning the radiation couch at a different angle for each pass of the gantry. In the "dynamic stereotactic radiosurgery" system described by Podgorsak et al[18] gantry and couch move together. The entering radiation beam remains centred on the target but sweeps through a complex pattern and never passes through the same point twice. Winston and Lutz[17] have examined the cumulative error for the former system. They found the treatment error vector for angiographically selected targets to have a value of 0.3 mm. CT scanning is less accurate than angiography. As a result, the treatment error

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vector for targets localized by CT scanning was found to be 0.64 mm. This loss of accuracy in localization by CT scanning would apply to any method for delivering focused radiotherapy including the Gamma Knife.

The radiation contour generated by the linear accelerators approximates that of the Gamma Knife. Podgorsak et al[18] report a steeper drop in radiation dose to brain adjacent to the target than do Winston and Lutz,[17] but do not address the question of target accuracy in any detail. In our own unit at the Toronto Bayview Regional Cancer Centre, modified after the Montreal system, we have used an anthropomorphic phantom to confirm the accuracy of dose delivery at the isocentre with measurements both ionometrically for large fields and with thermoluminescent detectors (TLD) for small fields. The disk-shaped TLD's were arrayed in stacks in drill holes in the phantom symmetrically placed with respect to a central aluminium target. The target was localized by means of CT scanning and then irradiated. In 3 independent experiments, the measurements agreed with predicted dose values to within 1 percent. Spatial accuracy was measured with the TLD arrays for the x, y and z stereotactic coordinates. The average combined error in localization was 0.93 mm.

There is a debate between proponents of the Gamma Knife and supporters of the modified linear accelerator. It is argued that the Gamma Knife is proven by 30 years of experience. Since the radiation sources and the patient are both static during the treatment, the precision of localization of the centre of the irradiated tissue volume is greater. The disadvantages of the Gamma Knife are high cost of installation and operation, and problems of radiation protection. The device, which may only be used for radiation of cerebral targets costs at least 5 million dollars at the present time to purchase and install. New cobalt sources, current price $500,000.00, must be purchased every seven years. In contrast, there are linear accelerators in every major cancer treatment centre. The cost of modifying a linear accelerator to do focused stereotactic radiotherapy, that is, to deliver up to 50 Gy in a single dose to a target chosen stereotactically, is between $50,000 and $100,000; that is, between 1 - 2% of the cost of a Gamma Knife! Furthermore, operating costs are embedded in the cost of running a radiotherapy unit, whereas for the Gamma Knife, at least some of the personnel would likely have to be dedicated to that unit alone.

If one is irradiating a nonspherical lesion, like an arteriovenous malformation, the likely error in choosing the target centre is at least 1 or 2 mm. The volume of a 25.4 mm diameter sphere is 8580 cubic mm. An error which shifts this volume one mm in one direction or another does not seem significant. One can reduce the treatment volume so that the 90% isodose curve is at least 1 mm within the volume of the lesion to be irradiated and compensate for any error.

Betti et al[15] have reported total obliteration of arteriovenous malformations in 27 of 41 patients followed at least two years after undergoing linear accelerator radiosurgery and Colombo and his colleagues[16] using a similar system report complete obliteration of radiated AVM's at two years in 15 of 20 patients. It is likely that over the next year reports from Boston and Montreal will also confirm the efficacy and safety of the method.

At the time of writing we have treated 11 patients with recurrent and surgically inaccessible cerebral metastases and 18 patients with AVM's. In a man with a 2.5 cm mesencephalic metastasis there was transient worsening of his neurological deficit. The growth, as indicated by CT scanning, of all metastases so treated has been arrested. One patient with a 2 cm AVM in the left angular gyrus became aphasic 6 hours after treatment but her deficit resolved virtually completely over the next 48 hours. No other patient has suffered neurological deficit. The longest follow-up of our AVM patients is now 21 months. We will be reporting our results as they accrue. With the OBT (Montreal) stereotactic frame, it is possible to obtain magnetic resonance images.[19] Since radiation changes are eventually visible on MR scanning,[20] the accuracy of radiation delivery can be verified.

What does the future hold? It is certain that there will be very few Gamma units because of their high cost and limited application. There will be an increasing number of linear accelerators modified to deliver focused radiotherapy. An increasing number of patients with arteriovenous malformations and suitable tumors will be treated by the linear accelerator with the result that there will not likely be sufficient cases to sustain even a few Gamma units in North America. In our opinion, it is probable that the results from the best centres utilizing linear accelerators will equal those produced by the Gamma Knife. Any hospital or health system that is contemplating the acquisition of a Gamma Knife can expect to have a facility that is overpriced and underutilized. The modified linear accelerator, carefully used, promises the safety and efficacy of the Gamma Knife at a fraction of the cost. Early results from the best linear accelerator units are very encouraging. Patients with arteriovenous malformations can now expect safe, effective treatment selected from the full range of therapeutic modalities.

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