

Radiosurgery for Arteriovenous Malformations Using Micro–Multi-leaf Collimators: Analyses of Outcome

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Abstract

Aim To assess the outcome of patients with AVMs treated using micro-MLC–based radiosurgery at Regional Cancer Centre (RCC), Thiruvananthapuram.

Materials and Methods During January 1 to December 31, 2012, 24 patients were treated with stereotactic radiosurgery (SRS) at RCC. The median age was 28 years (range: 8–58 years). There were 11 males and 13 females. Fifteen patients had prior embolization. All patients were treated with a frameless radiosurgery system using micro-MLC–based linear accelerator (LINAC). Obliteration of the lesion was assessed with either magnetic resonance angiogram (MRA) or digital subtraction angiography (DSA).

Results Nineteen patients who underwent an assessment procedure were evaluable for this study. At median follow-up of 12 months, nearly two-thirds of patients had complete obliteration of the AVM and the rest had partial obliteration. Among patients with complete obliteration, seven patients had an AVM volume of ≤ 3 cc and three-fourths of the patients had AVM score of < 1.5 . Further, marginal dose of > 18 Gy resulted in higher obliteration. One patient had an episode of seizure after SRS. No complications or bleed was seen in any of the patients after treatment.

Conclusion Our experience correlates with the existing literature reports, without any significant complications. Longer follow-up is required to assess the complete obliteration and late complications.

Keywords

- venous malformation
- stereotactic radiosurgery
- LINAC
- micro–multi-leaf collimators

Introduction

Arterio venous malformations (AVM) of the brain are sporadic congenital vascular malformations, and their exact cause or

pathogenesis is not known. The anomalous connection between the arteries and veins without an intervening capillary system results in causing a high-pressure flow system, with a potential for fatal intracranial hemorrhages.

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The gold standard for treatment is surgery whenever feasible. However, alternate modalities such as embolization and stereotactic radiosurgery (SRS) are offered when the nidus is deep seated, in eloquent location, and/or when the risk of hemorrhage is high with surgical intervention.

Radiosurgery involves localizing the target with three-dimensional coordinates and delivering a single fraction of high-dose conformal radiation, aimed at obliterating the vascular nidus, thus reducing the risk of hemorrhage. Traditionally, radiosurgery was delivered using the Gamma knife or cone-based LINAC systems mostly suited for circular targets.

With the advent of modern linear accelerators (LINAC) and micro-multi-leaf collimators (mMLCs), it is possible to perform the same function with comparable results. The success of radiosurgery depends on the lesion size and the marginal dose delivered to the nidus volume.¹

In this retrospective analysis, our experience in treating AVM with SRS using modern LINAC with mMLC is presented.

Materials and Methods

Patients with digital subtraction angiography (DSA)-proven AVM who were treated with mMLC-based SRS during January 1 to December 31, 2012, were identified from the hospital records. The patient demographic, clinical, radiologic, and follow-up details were collected from the hospital records at the Regional Cancer Centre (RCC), Thiruvananthapuram, and the Sree Chitra Tirunal Institute of Medical Sciences (SCTIMST) where most patients underwent initial diagnosis with or without intervention such as embolization prior to SRS.

A total of 24 patients were identified and included in this analysis. The mean age was 30.4 years (range: 8–58 years); there were 11 males and 13 females. The presenting symptoms included headache in 10 (41.7%), intracranial bleed in 7 (29.2%), focal neurologic deficit in 4 (16.6%), and seizures in 3 (12.5%) patients. The onset of symptom was sudden in 8 (33.3%) patients. For the remaining 16, the mean duration of symptoms was 20.6 months (range: 1–120 months). Most patients (54.1%) had Spetzler-Martin (S-M) grade II AVM. The AVM score was < 2.5 in all patients. Fifteen patients underwent prior embolization with onyx. One patient had embolization twice and another patient thrice. The patient characteristics are summarized in ►Table 1.

The mean volume of AVM was 2.7 cc (range: 0.2–10.1 cc). The mean prescription dose was 17.7 Gy (range: 14–21 Gy), and marginal dose to AVM was 16.85 Gy (range: 12.3–20.2 Gy). Number beams used ranged from 8 to 15. The mean 12-Gy brain volume was 11.11 cc (range: 32.9–2.04 cc). The mean brainstem dose was 0.62 Gy (range: 0.06–3.76 Gy), optic chiasm dose was 0.4 Gy (range: 0.06–2.76 Gy), and mean dose to cochlea was 0.5 Gy (range: 0.04–6 Gy).

Results

The mean conformity index (Radiation Therapy Oncology Group) was 2 (range: 1.39–2.98). Among them four patients

Table 1 Patient characteristics

Age	
Mean age	30.4 y (8–58 y)
Sex	
Male	11
Female	13
Presentation	
Headache	10
Bleed	7
Neuro deficit	4
Seizure	3
Spetzler-Martin grade	
1	4
2	13
3	7
Previous embolization	
Nil	9
Once	13
More than once	2

each had conformity index ranging between 2 and 2.5 (defined as minor variation) and 2.51 and 3 (defined as major variation).

The median follow-up was 12 months (range: 9–32 months). Of the 24 patients, 19 patients had a follow-up imaging: DSA for 10 patients and magnetic resonance angiography (MRA) for 9.

Twelve out of 19 patients had complete obliteration of the nidus and the rest had a partial obliteration. Among them, nine patients had a complete obliteration at 1 year. The chance of obliteration was correlated with the AVM volume, S-M grade, AVM score, and marginal dose delivered to the nidus. Seven of the 12 patients had an AVM volume of ≤ 3 cc and a similar number of patients had a S-M grade of < 3. Three-fourths of the patients had AVM score of < 1.5. Further comparison with the marginal dose delivered to the nidus revealed that dose of > 18 Gy resulted in a higher obliteration rate (seven patients) ►Table 2 depicts AVM factors and correlation with obliteration.

One patient developed seizures immediately after SRS and was managed with antiepileptics. There were no patient reported symptoms or events during follow-up. One patient had nonspecific hyperintensity changes in the MRA at 1-year follow-up.

Discussion

In the present era, the linear accelerators have undergone several developments, especially with the introduction of mMLCs and circular cone collimators that can be used to generate miniature focused beam to treat small targets.

Table 2 AVM parameters and their correlation with obliteration

	n = 19	n = 12 (100% obliteration)
AVM volume		
< 3 cc	12	7
> 3 cc	7	5
AVM score		
< 1.5	16	9
> 1.5	3	3
Dose		
< 18 Gy	7	5
> 18 Gy	12	7
Spetzler-Martin grade		
Grade 1–2	12	7
Grade 3+	7	5
Prior embolization		
Yes	12	9
No	7	3

Abbreviation: AVM, arteriovenous malformation.

Along with a stereotactic localizing system, this has been widely used for radiosurgery. The main advantage of this is that the existing linear accelerator in a radiotherapy department can be modified to deliver stereotactic radiation treatment instead of investing in a dedicated radiosurgery unit like the Gamma knife. Both these radiation delivery systems differ in considerable aspects from treatment planning to delivery.

Gamma knife uses circular collimators, which focuses multiple pencil beams with variable diameter from 4 to 18 mm. On the other hand, the mMLCs in an LINAC can be used to conform the individual beams to the target. Further, the conformity depends on the width of the MLC, target shape, and target size (decreasing conformity for smaller targets). A smaller width of MLC helps better shape the beam and improve the conformity. In a study by Kubo et al, the conformity index was found to range between 1.5 and 2 for moderately irregular targets and 2.3 and 2.5 for highly irregular targets.² The overall mean conformity index in the same study was reported as 1.9. In comparison, the Gamma knife conformity index has been reported by various authors ranging from 1.24 to 2.2.^{3,4} At this center, a BrainLab m3 mMLC is used for all radiosurgeries. The calculated mean conformity index in our series is comparable with the existing reports. Although there were four patients with a conformity index > 2.5, the index does not account for the spatial distribution of the target.

In this series, patients were considered for radiosurgery when neither surgery nor embolization was a primary option for treatment, and also for obliterating the residual nidus after embolization. The first evaluation after

radiosurgery was done after at least 12 months for most patients. A complete obliteration demonstrated in angiography is the goal of treatment. However, the time to obliteration is not known precisely, but it generally varies between 2 and 3 years.^{5,6}

The obliteration depends on the volume of the nidus and the marginal dose delivered.^{7,8} In a retrospective analysis from a single institution, a nidus volume of < 1 cc had > 90% obliteration when compared with a 10-cc volume (obliteration rate of 36%) at mean follow-up of 31 months.⁹ Also, there was a significant increase in cure rates when at least 15 Gy was delivered to the periphery of the target. In this analysis, patients with AVM volume < 3 cc had a higher chance of obliteration compared with > 3 cc. A marginal dose delivered to the AVM of > 18 Gy was received by about two-thirds of the patient included in the outcome analysis. Among them, nearly 58% achieved complete obliteration.

Furthermore, various models have been proposed to predict the success of radiosurgery. Among them, the AVM score, which is calculated considering the volume of the nidus, the patient's age and location of AVM are widely accepted.¹⁰ Based on this score, the obliteration rate is 91.7% for a score of < 1, 74.1% for 1 to 1.49, 60% for 1.5 to 2, and 33.3% for > 2.¹¹ In our series, most patients had a score of < 1.5, hence favoring toward successful outcome. Only one patient had a score > 2; however, the follow-up angiography showed complete obliteration. Because the numbers of patients are less, a definitive correlation could not be achieved.

The serious complications of radiosurgery, in particular brain necrosis, depends on the volume of normal brain tissue receiving 12 Gy (V12) and the anatomic location of the AVM.¹² It was found that the volume receiving 12Gy was greater in the patient with nonspecific hyperintensity changes seen on follow-up. However, the patient is asymptomatic, and it cannot be definitely proven that it was due to increased volume of V12. Other rare events such as seizures and postradiation brain edema have been reported infrequently. The exact cause of seizures is not known, and it could probably due to low levels of blood antiepileptic drug.

Conclusion

Radiosurgery is a well-proven treatment modality for AVM. The modern-day LINACs have the capability to perform stereotactic treatments comparable with that of the traditional radiosurgery system such as Gamma knife. The prime factor in success of AVM obliteration depends on the volume of the nidus and the dose delivered. Our experience correlates well with the existing evidence.

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