https://doi.org/10.3329/bjns.v12i1.64017

Case Report

A Success Story of Cerebral Arteriovenous Malformation (AVM) Treated with Stereotactic Radiosurgery (SRS) in Bangladesh

Kumar N[1], Yasmin T[2], Appasamy M[3], Rana KMM[4], Kumar RA[5], Joardar A[6], Ahsan S[7], Alam S[8]

Conflict of interest: There is no Conflict of interest relevant to this paper to disclose.

Funding Agency: Was not funded by any institute or any group.

Contribution of Authors: Principal Investigator- Prof. Dr. Narendra Kumar

Manuscript preparation – Dr. Taohida Yasmin, Dr.Saiful Alam, Dr.Murugan Appasamy,

Data collection – Dr. KM Masud Rana, Dr. R. Arun Kumar

Editorial formatting – Dr. Aliuzzaman Joardar, Dr. Sania Ahsan

Received: 27 July, 2022
Accepted: 12 September, 2022

Abstract:

Purpose: *To share a case of cerebral Arteriovenous Malformation (AVM) patient, treated with Stereotactic Radiosurgery (SRS) at Evercare Hospital Dhaka, treatment process and successful outcome.*

Background: *Arteriovenous malformation is an anomaly, mostly congenital due to a misfit in vasculogenic, where arteries and veins come to a direct connection. Treatment options include observation, embolization, microsurgery, Stereotactic Radiosurgery (SRS) either alone or in combination. This report describes our experience in treating a patient of AVM by SRS. Stereotactic Radiosurgery is an established modality to achieve desired nidus obliteration, excellent compliance being noninvasive, and reduced treatment-related morbidity. This case report also reviewed the literature in detail. After a thorough literature search, to the best of our knowledge, this shall be the first published case report of AVM successfully treated with SRS in Bangladesh.*

Case Presentation: *In March 2019, 25-years old male presented in Radiation Oncology OPD as a diagnosed case of AVM, having complaints of headache for two years. Headache was occasional and often associated with vertigo and dizziness. He had no neurologic deficit. A radiological assessment revealed a large (4.6x4.4cm) AVM in the left parieto-occipital lobe showing serpiginous enhancement with IV contrast. After routine workup, he underwent stereotactic Radiosurgery in March'2019. A dose of 23Gy was delivered to the malformation, including all nidus. Acute radiation toxicity was noted as transient hair loss only over the irradiated area and no other side effect. Radiological Assessment was done at six months, 1year, and 2.5 years. After having a stable size at six months, complete nidus obliteration was achieved at one year. His last visit to our OPD was in July 2021, with radiologically complete nidus obliteration without any significant clinical symptoms.*

Conclusions: *Linear Accelerator-based SRS is an excellent treatment option for AVM, encouraging clinical outcomes for carefully selected patients.*

Keywords: *Arteriovenous Malformation, Linac-based SRS, Frameless Radiosurgery, Nidus obliteration.*

Bang. J Neurosurgery 2022; 12(1): 53-64

Introduction:

An arteriovenous malformation (AVM) is a vascular aberration characterized by arteriovenous shunt through tortuous vessels without an intervening capillary bed[1]. The annual incidence of AVM is approximately 1.3 per 100,000 population [2]. It is more common in males and personal with positive family history[3].

1. Dr. Narendra Kumar, Consultant and Head, Department of Radiation Oncology, Cancer Care Centre, Evercare Hospital Dhaka
2. Dr. Taohida Yasmin, Senior Specialist, Department of Radiation Oncology, Cancer Care Centre, Evercare Hospital Dhaka,
3. Dr. Murugan Appasamy, Chief medical physicist, Department of Radiation Oncology, Cancer Care Centre, Evercare Hospital Dhaka,
4. Dr. KM Masud Rana, Medical physicist, Department of Radiation Oncology, Cancer Care Centre, Evercare Hospital Dhaka,
5. Dr. R. Arun Kumar, Chief technologist, Department of Radiation Oncology, Cancer Care Centre, Evercare Hospital Dhaka,
6. Dr. Aliuzzaman Joardar, Consultant, Department of Neurosurgery, Evercare Hospital Dhaka,
7. Dr. Sania Ahsan, Senior Consultant, Department of Neuroradiology, Evercare Hospital Dhaka
8. Dr. Saiful Alam, Associate Professor, Department of Gamma Knife, National Institute of Neuroscience & Hospital, Dhaka, Bangladesh

Address of Correspondence: Prof. Dr. Narendra Kumar, Consultant & Head, Department of Radiation Oncology, Evercare Hospital Dhaka -1229, Bangladesh, Phone: +8801777763535, Email: drnarendra74@gmail.com, narendra.kumar@evercarebd.com

The pathogenesis of AVM has multiple schools of thought. It has been theorized that cerebral AVM is primarily congenital. The aberration of primordial capillary or venous formation during embryogenesis is believed to contribute AVM[4]. Another hypothesis supports AVM as a physiologic change or response to a stimulus ("Second hit") in genetically susceptible individuals. This stimulation can be mechanical, thermal, ischemic/hypoxemic, or inflammatory[5]. External insult such as stroke, brain contusion, encephalitis is believed to be linked with a higher Vascular endothelial growth factor (VEGF), which is hypothesized to be linked between such trigger & AVM formation[6,7]. In addition to that, there are also case reports of De novo AVM for existing anomalies, i.e., neuronal migration disorder, preexisting vascular pathology, venous hypertension, pathologically altered brain[8,9,10].

AVM commonly presents with hemorrhagic episodes in the second or third decade of life. However, other symptoms like seizure, stroke-like symptoms, or headache are also mentioned due to the involvement of eloquent areas of the brain and the pressure effect produced by the aberrant angioarchitectures itself[11,12]. In addition to that, AVM often remains clinically silent.

Cerebral arteriography, Computerized tomography (CT) scan, Magnetic resonance imaging (MRI) are the pivoting imaging techniques to diagnose & differentiate AVM. A contrast CT scan helps to apprehend the features about the feeding arteries & venous drainage and the presence of Hemorrhage. Cerebral angiography gives most details about location, maximum size, characteristics of the vessels and nidus, and deep venous drainage, which is helpful to determine the Spitzer-Martin or SM grading. In addition, MRI is sensitive to identify the subtle change in brain tissue related to AVM[13].

These malformations can be of different manifestations depending upon locations, Volume, and type of venous drainage. Therefore, to describe the severity and evaluate the risk of surgery, AVM is graded after the Spitzer-Martin (SM) classification. This SM-grading has three variables: the size of AVM, Eloquence of brain area, venous drainage. The grade ranges from I to V[14].

The treatment option of AVM includes observation, surgical resection alone, embolization alone, embolization and resection, Radiosurgery alone, Radiosurgery following embolization, Radiosurgery following surgical resection, etc.[15].

Conservative management and watchful observation are offered for asymptomatic individuals, older patients, patients with no hemorrhage event, or patients with high operative risk. However, individuals where the risk of Hemorrhage outweighs the risk of treatment or individuals expected to have good functional outcomes by treatment instead of enduring observation patients are discussed to undergo active management. Patients with epilepsy, even with larger AVM are advised for conservative management with antiepileptics[15].

Surgery alone is planned for smaller and accessible AVM with a higher risk of hemorrhage or patients with symptoms (ischemic, disturbance of consciousness). AVM diameter >4 cm in selected patients, <4cm with an increased chance of spontaneous Hemorrhage (young individual) is recommended for surgery. Diffuse AVM, eloquent location (Brainstem, thalamic, mesencephalic) is a contraindication of surgery. Several studies justify the size and location of AVM and the age of patients for selecting patients for AVM[15].

Embolization is typically incorporated as an adjunct in combined management. Detachable balloons, polymers, glue, metallic coils are used for embolization. The principal is to convert larger inoperable AVM into smaller one by occlusion of AVM nidus and thereby made fit for either surgery or Radiosurgery. Embolization alone can be approached for low—grade AVM with few feeder vessels where the complete occlusion of the nidus is predicted. However, due to the variable shrinkage rate resulting from partial occlusion, event of recanalization, or revascularization through a collateral blood vessel, embolization is best indicated as an adjunct in combination with other techniques[15].

Upfront Radiosurgery is indicated for AVM with small-sized, deep, midline, or inaccessible lesion or malformations involved with the eloquent cortex. When surgical excision is not realistic due to medical contraindication or the Patient's preference for a noninvasive approach, radiotherapy is a safe and efficient alternative option. In incompletely obliterated AVM's following embolization, Radiosurgery is also indicated to enhance the obliteration process and reduce the chance of Hemorrhage. Radiosurgery also has an adjuvant role in incomplete excision of AVM[15.]

AVM obliteration after SRS is a result of Endothelial proliferation followed by progressive thickening of the vessel wall. This is a pathophysiological response triggered by high Dose conformal radiation, eventually ending with luminal closure or nidus oblitetaration[16]. The concept of applying the benefit of radiation for AVM treatment was first introduced in Late1960's by Lars Lek shell and Ladislau Steiner. They utilized 1st generation Lekshell Gamma knife in Stockholm[17]. Afterward, newer techniques using an alternate form of radiation i.e., charged proton, helium ion, were investigated over time[18,19]. Using Linear Accelerator for treating AVM has been applied since the 1980s. Betti, Columbo et al. pioneered the SRS procedure using new generation Linear Accelerators (Linac)[20]. Linac-based SRS is a frameless SRS technique, which is a noninvasive & primarily outpatient procedure. With the advent of a modern treatment planning system, Linac can deliver precise radiation faster, safer, and effectively. In the modern era of radiation and high-quality neuroimaging, target volume for Radiosurgery is defined from the combined reference of contrast-enhanced computed tomography (CT), Magnetic Resonance Imaging (MRI)& cerebral angiography. Treatment planning systems ensure higher Dose to target with sharp Dose fall-off outside. Whereas beam shaping with a micro-multileaf collimator (MLC) increases the conformity of the target with better sparing of organ at risk (OAR). Published data by Peter et al. supports Linac-based SRS Treatment outcome, and it is comparable with that of gamma knife data with no statistical significance in terms of obliteration & long-term toxicity as well[21].

Being a noninvasive, more comfortable & outpatient procedure, nowadays Linac based SRS has gained more acceptance. In our report, we intend to report our experience of treating an AVM patient with Linac-based SRS, procedure, technique, and outcomes in terms of symptomology and complications, along with the review of the literature.

Case illustration:

A 25-Year-old male presented in radiation oncology OPD in March'2019, with complaints of headache for two years in the left side. Headache was sudden in onset & had no triggering factor. Initially, he used to have this headache once a month and was often associated with vertigo and dizziness, which afterward increased in frequency. There was no associated nausea, vomiting, visual disturbance, photophobia, neck stiffness, fever, weight loss, or neurologic. No significant family history. He had no previous history of trauma. He visited a nearby physician, started on symptomatic treatment, and was advised for radiological Assessment. Contrast CT scan with CT Angiogram revealed a large irregular mixed density area measuring 4.6 x 4.4 cm at the left parieto-occipital lobe showing serpiginous enhancement with IV contrast. The lesion had no perifocal oedema, calcification, or midline shifting (Figure-1). Subsequently underwent MRI at our hospital, which showed a mass lesion containing multiple flow voids in the left parietal lobe measuring 3.8 cm x 4.0 cm with no perilesional edema. The lesion was supplied by the left posterior cerebral artery and via the cortical branches of the left middle cerebral and pericallosal artery. Venous drainage of the lesion is to the superior sagittal sinus, transverse sinus, and deep venous sinuses.

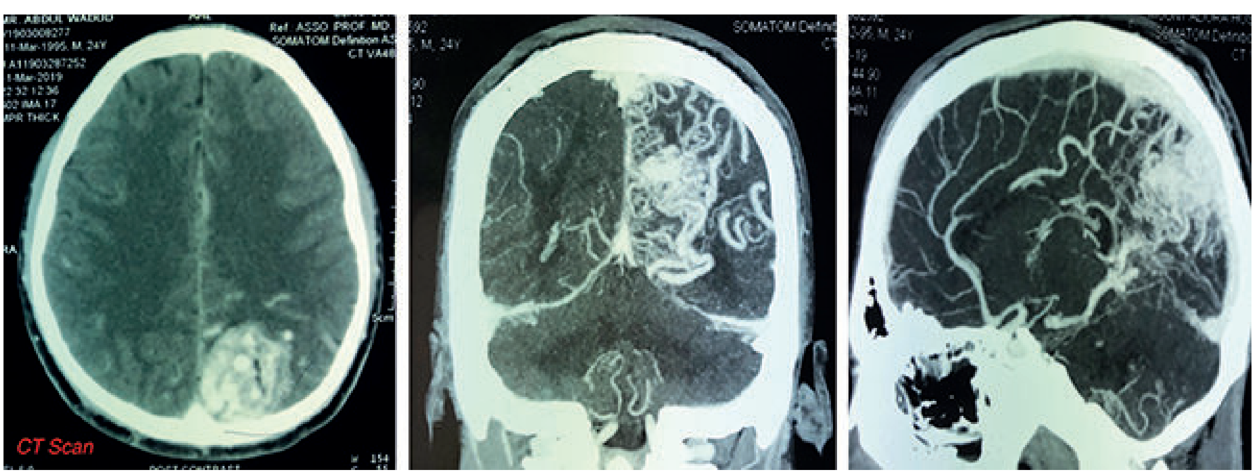

Fig.-1: *CT scan & Angiography of Brain showing serpiginous enhancement of the malformed lesion.*

A multidisciplinary board was constituted to discuss the treatment options involving Radiation oncologists, Neurosurgeon & Neuroradiologist. In view of the non-eloquent area with superficial & deep venous drainage (SM grade-III), the Patient was offered surgical resection with adjuvant SRS. However, the Patient did not want any surgical intervention. Hence, He was planned for SRS.

Therefore, after taking informed written consent explaining the nature of the disease, possible treatment outcome in terms of Nidus obliteration, acute & Late complications of SRS. He underwent Stereotactic Radiosurgery with a dose of 23 Gy in two sessions on 18th & 19th March 2019.

Stereotactic Radiosurgery (SRS) Procedure

For setup & RT Simulation, the Patient was positioned on special head support (Elekta Fraxion). Later a three-clamped double-layered specialized thermoplastic mask was used to position the Patient in an easily reproducible supine & neutral position. A contrast-enhanced thin sliced CT-angiography and planning CT scan of 1.25 mm with contrast having stereotactic localizer box in situ (Figure-2) was acquired. The localizer box has “Z” shaped markers around the patients (laterals and anterior) to give nine localizing markers in each axial slice, which helps us to locate the stereotactic coordinates of the tumor with reference to the Isocentre of the treatment plan. A high-resolution T2-weighted magnetic resonance imaging (MRI) with IV contrast of similar thin slices(1-1.25mm) were acquired in the same setup for treatment position. Both the MRI and planning CT images were transferred to the Monaco treatment planning system and were co-registered before defining the target & critical structures.

Radiation oncologist along with neuro-radiologist delineated the treatment target, which included all the nidus. A margin of 2 mm was added to finalize the planning target volume (PTV) (Figure-2). The organ at risk (OAR) such as epidermis, midbrain, optic chiasma, pituitary gland, Eye lens, Eyeball, optic nerve, and normal brain was contoured. In view of the large size, a total dose of 23 Gy was prescribed in two fractions. The SRS treatment plan was generated with the help of the Monaco (Elekta, Version 5.3) treatment planning system with the intention to deliver the maximum Dose to the target and minimizing the Dose to all organs at risk (OAR’s). For this planning, the VMAT inverse treatment technique is used with three non-coplanar partial arcs. Optimization of the dose planning was achieved by ensuring sharp Dose fall-off outside the target (80% isodose at the edge) (Figure-3).

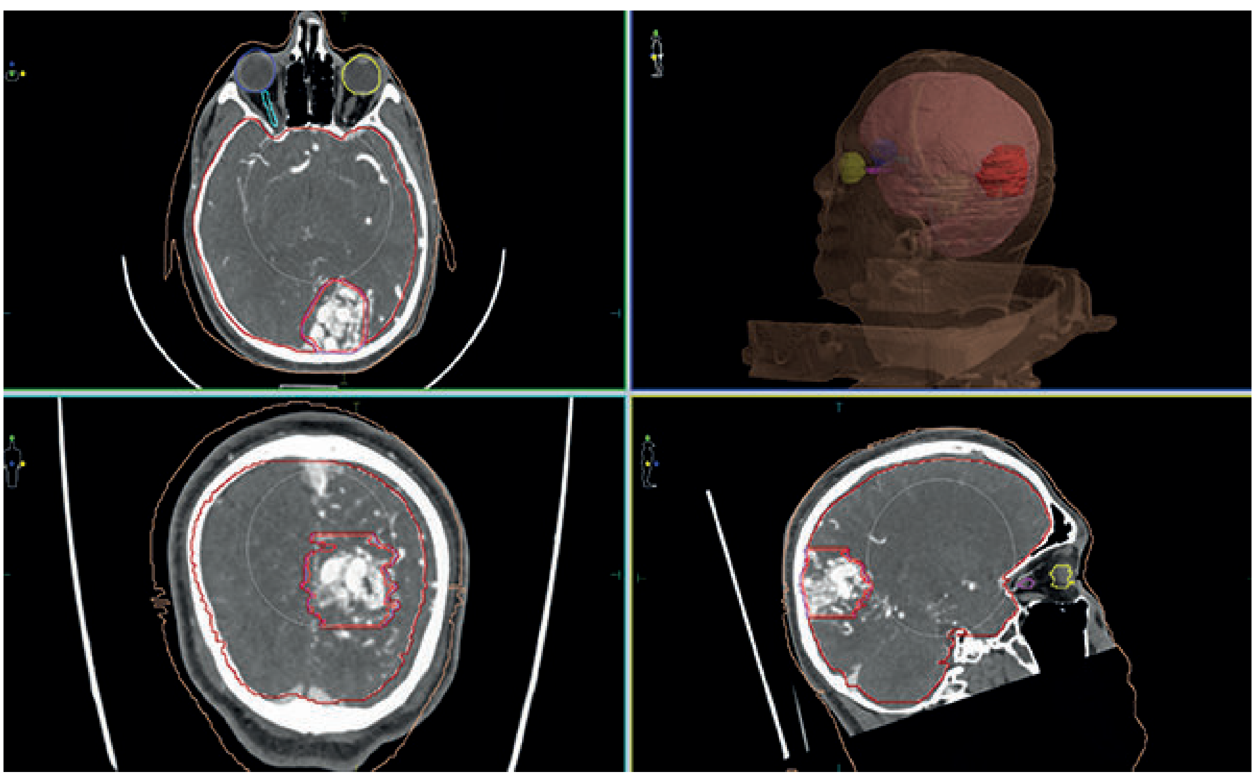

Fig.-2: 3D display of Contouring and defining the target including all nidus

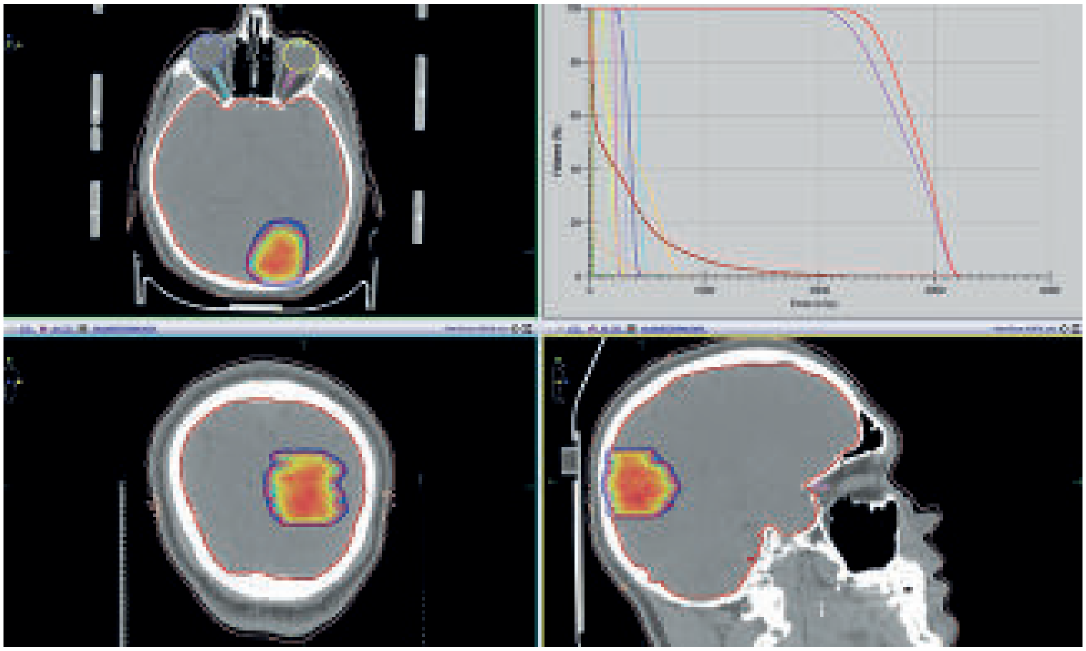

Fig.-3: *Treatment Planning System (TPS) showing 80% Isodose display of the Prescribed Dose*

The treatment plan was evaluated carefully against RTOG OARs constraints for Stereotactic Radiosurgery by radiation oncologists and medical physicists. Dose Volume Histogram (DVH) (Figure-3) and color wash display of Dose in each slice were carefully evaluated to ensure high conformity and reduce the low dose spill outside the target. In addition, a comprehensive patient-specific Quality Assurance (QA) was carried out upon plan approval to reassure that the planned Dose would be delivered precisely within standard limits. Collision check, dummy run, and dosimetric fluence verification were checked during QA with the help of Matrix (IBA, Germany) array detectors.

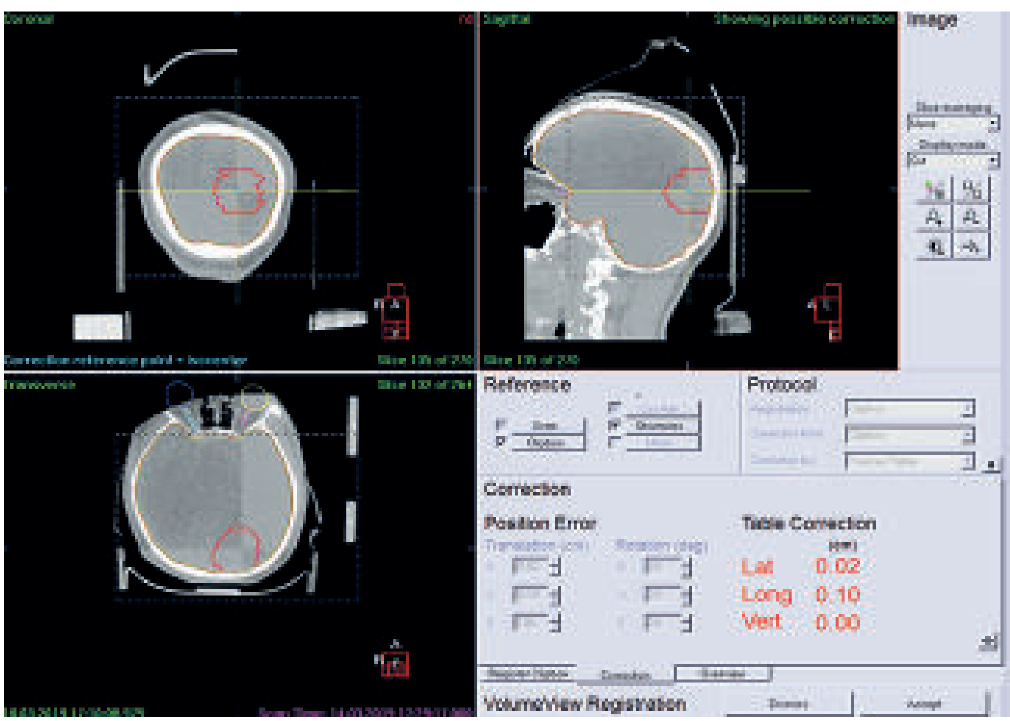

Fig.-4: *Verification of the patient treatment setup by Cone Beam CT to ensure sub-millimetric accuracy*

After the patient-specific QA, the Patient was scheduled for treatment. During the treatment, reproducibility of the patient position was verified using Kilovoltage Cone Beam CT (CBCT) & hexapod 6D couch prior to the radiation delivery to ensure accuracy to the level of submillimetre (Figure-4). The treatment execution was done by Versa HD Treatment unit using VMAT Technique using 6.0 MV Flattening Filter Free (FFF) photon beam.

Complication:

The patient was kept under observation for 24-hours post-procedure to see side effects, if any, because of high dose radiation-induced edema. He was essentially free of any such immediate radiation-induced complication. He was called for clinical Assessment after four weeks. The patient developed strip-shaped hair loss over the radiated area, which was transient, and he had regained complete hair within six months (Figure-5)

Follow-up:

After the SRS patient was called for clinical Assessment at four weeks and three months, subsequently the patient was called for clinical and radiological assessment at 6 months, 16 months, and 28 months. Radiological Assessment was done with CT Angiogram. Because of the non-availability of DSA, he could not undergo DSA evaluation

Outcome:

Radiological assessment was done at Six (06), Sixteen (16) & Twenty Eight (28) months post SRS. At six months, the lesion had a stable appearance with no significant interval change (3.5x3.2cm). Subsequent Radiological assessment at 16 months revealed complete obliteration of the nidus. He had his last follow-up done in June'2021 that is 28-months post-procedure. Clinically he was asymptomatic without any neurological deficit. The radiological assessment showed persistence of complete obliteration of nidus. However, this time patient developed mild surrounding edema around the radiated area in the left parieto-occipital white. On MR Spectroscopy, there was minimum edema in left parieto occipital white matter and cystic encephalomalacia matter (Figure-6).

Fig.-5: *Post SRS temporary hair loss (on the left) showing completely regained hair within 6 months.*

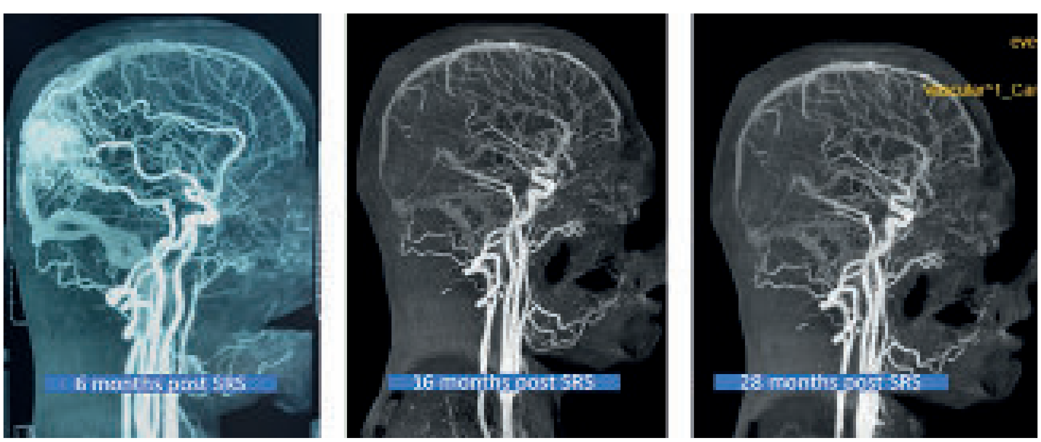

Fig.-6: *Comparative analysis of nidus obliteration showing complete obliteration of all niduses at 16-month post SRS with no partial revascularization of nidus on subsequent imaging in 28 months.*

Discussion:

Arteriovenous malformation is a vascularanomalies containing atypical blood vessels that are abnormally constructed, directly shunting the arterial and venous system without intervening capillary network[1]. The annual incidence is as low as 1.3 per 100,000 populations having more predominance in male and positive family history[2,3]. With few exceptions, AVM is commonly diagnosed in the 2nd or 3rd decade of life. Stroke-like 'symptoms, i.e., headache, difficulty in speaking, weakness, visual difficulties, are the common presentation for AVM[11,12]. This presentation is explained by the chronic ischemic effect of brain tissue in the vicinity of AVM due to the inability to absorb sufficient oxygen from the high-flow arteriovenous shunt. In this case report, our patient was 25 years young. His primary complaint was the headache of different intensities for about two years. However, he had no such positive family history of Brain AVM.

The standard for diagnosing AVM is Comprehensive history taking, clinical examination & radiological imaging (CT, MRI), and arteriography to better understand the vascular aberration[13]. For example, after the initial consultation, our Patient had a CT scan of the brain done, which suggested serpiginous contrast enhancement in the left parieto-occipital lobe in a 4.6x4.4 cm irregular mixed density area. Later, a CT angiogram & MRI brain was done to fetch more details to confirm and grade AVM.

Spitzer-Martin's (SM)[14] Grading system categorizes different features to give a grade between 1 to 5. This score has been widely practiced, mainly correlates the feasibility of surgery and its outcome. The grading is as shown in table 1.

Our Patient has had a medium-sized lesion in a non-eloquent area having both superficial and deep venous drainage. His AVM was graded SM Grade III (measured 3.8 cm x 4.0 cm, in a non-eloquent area with venous drainage to both superficial and deep veins).

Several factors are considered before treating AVM. i.e., Patients age, associated medical History, Location, size & morphology of AVM, The overall angioarchitecture of AVM (Compact vs. Diffuse), Patient's clinical presentation, History of the prior hemorrhagic event, History of prior management. Options of treatments are to be individually tailored considering the natural History, contributing factors, and not the least available facilities & expertise available in that particular center alongside the Patient's priority. These include Observation, Endovascular embolization, microsurgery alone or as an adjunct with other treatments, surgical removal by an open approach, Stereotactic Radiosurgery[15].

ARUBA, a randomized trial of Unruptured Brain Arteriovenous Malformation, compared the risk of medical management & observation-only versus prophylactic intervention for patients with cerebral AVM with no prior event of hemorrhage[22]. After an interim analysis, this prospective randomized study had statistically significant morbidity in the treatment arm. So, this study was prematurely discontinued due to poor study design and profound criticism. Nevertheless, this trial reinforced investigators to understand better the indication and ultimate safety of intervention weighing against the risk of Hemorrhage and the Patient's lifetime outcome. Pollock et al. conducted a retrospective study of 171 ARUBA eligible Patients of SM Grade I & II (48.9%), SM Grade III (31.6%), and SM Grade IV & V (19.5%). In addition, the authors investigated the risk of stroke or clinical impairment after SRS. They finally concluded that Radiosurgery is a relatively safe modality for Unruptured AVM[23]. Similarly, many more evidence

Table -I

Spetzler-Martin[14] Grading System

Feature		Points assigned
Size of AVM	Small (< 3cm)	1
	Medium (3-6cm)	2
	Large (>6 cm)	3
Eloquence of adjacent brain	Non-eloquent	0
	Eloquent	1
Venous Drainage	Superficial vein only	0
	Deep veins	1

supports the treatment of unruptured AVM instead of generalized observation and medical therapy approach[24, 25, 26, 27]. The general consensus to date supports that SM Grade I & II has superior benefit from treatment. SM grade IV & V do best with the conservative approach. SM Grade-III is a heterogeneous group. For this group, multimodality management yields the best outcome with lowered complication[28, 29].

In our case report, he was having SM Grade-III AMV which was a large-sized AVM in a non-eloquent area having both superficial and deep venous drainage. Although he had no history of Hemorrhage/event of any rapture. It was difficult to evaluate whether or not patient was having any angiographic weak points, as at the time of diagnosis DSA could not be done, only CT angiography was done. However, the Patient was symptomatic, and his complaint of headache was hampering his social and personal life. For our case, first and the most effective window of treatment would have been surgery. With this intention, he was seen by a neurosurgeon first and offered surgery. But he was not willing to undergo surgery at all. Then a joined discussion was held among Radiation Oncologists, Neurosurgeon & Neuroradiologist. Surgical resection with adjuvant SRS was a recommended option for him. But He preferred a noninvasive approach and was unwilling to go for any kind of surgical intervention. Hence, he was finally treated with SRS.

In the last decade, the practice of doing SRS in a dedicated GKRS unit having a Co-60 radioisotope has shifted to Linac-based SRS systems. Numerous reports are favoring the feasibility in clinical, technical, and dosimetry aspects. The recent development of micro-multi leaf collimator (MMLC) and intensity modulation with dynamic or static arc added freedom to generate and optimize plans with non-coplanar arcs, dynamic conformal arcs, static conformal fields, and intensity-modulated fields. Linac system has the advantage of reducing treatment time with better conformity and dose homogeneity across the target volume and better healthy tissue sparing than a GKRS unit for larger or irregularly shaped lesions requiring multiple isocenter[30]. The modern treatment planning system is capable of planning inversely with simultaneous optimization of multileaf collimator (MLC) position, dose rate, and gantry rotation speed to achieve desired dose distribution, better conformity, and dose homogeneity. Volume Modulated Arc Therapy (VMAT) is a modern radiotherapy technique using a rotational arc where leaves move continuously across the treatment field while the gantry is rotating to dynamically adapt the shape of the treatment beam to the planned target volume with improvement in conformity and OAR sparing and create an intensity-modulated beam. This VMAT modality has improved treatment quality, reduce treatment time with dose delivery accurate and actual measurements[31]Bottom of Form. The classic invasive frame-based approach for patient setup in GKRS was focused for a precise setup. These immobilization systems have been translated into a noninvasive and more patient-friendly Linac-based SRS supplanting invasive head ring i.e. specialized thermoplastic mask, a bite-block fixation mechanism, and/or relocatable frame. These immobilization devices give freedom to change the treatment plan from single fraction SRS into Hypo-fractionated or multiple session treatment schedules when appropriate[32]. In this case report, we have treated the Patient with Linac based system in VMAT based inverse planning technique using the noninvasive double-layered thermoplastic mask with a Z-shape localizer box. This technique eased us to plan the treatment in two days, keeping patients comfortable without compromising the setup accuracy to the submillimeter level.

As discussed earlier, larger AVM where surgery is not possible and those located in eloquent areas or patients have personal or medical limitations to undergo surgery; SRS has a significant role. Conventionally, SRS is considered a single session procedure, but certain features i.e., the proximity of AVM to the eloquent area or vital structure, become critical during the dose selection in such cases. Prescribing a high dose to a large volume AVM in a single session keeping the toxicity minimum to the neighboring brain parenchyma is challenging. The α/β ratio of endothelial cells of larger AVM has higher value (>3 Gy) than the ratio of adjacent normal brain tissue(2Gy). So, fractionated radiotherapy instead of a single session can potentially reduce normal brain tissue toxicity & produce desired obliteration. Several studies support altered fractionation, or regimen i.e., Dose fractionated SRS, hypo-fractionated, or Volume staged SRS. Literature published by Kano, Kondziolka et al. suggests larger lesions may be planned for staged Radiosurgery so that there shall be less chance of radiation-related complications but with an amplified chance obliteration[33,34]. In 2017, Mukherjee et al.

described Dose Fractionated Gamma Knife Radiosurgery as a substitute of Volume fractionated SRS in Large AVM. Their study population had AVM median volume of 26.5cc & received radiation on 2-3 fractions. Their marginal Dose ranged from 8.9 Gy-11.5 Gy and 11.3 Gy-15 Gy in three and two fraction regimens. They had rational nidus obliteration with acceptable toxicity. The authors reinforced that a high prescription dose accelerates the nidus obliteration process, i.e., a cumulative dose of 29- 30 Gy[35]. Karlsson et al. also shared their experience of risk-reducing and protective role of high Dose SRS (marginal dose 25Gy) in Unruptured AVM instead of Observation only [36]. In Our report, the large sized AVM was 40cc, though in a non-eloquent area with superficial venous drainage. So, he was decided for fractionated stereotactic Radiosurgery with a total Dose of 23Gy in two fractions.

The outcome of Radiosurgery is determined on nidus obliteration after SRS, radiation-related acute and late toxicities, development of neurologic deficit, or Hemorrhage. The obliteration rate (OR) following SRS is also not static and has a long latency period. This period is generally 2 to 3 years or more [37, 38]. There have been several factors identified impacting on obliteration rate as well obliteration failure, i.e., proper patient selection, optimal determination of target volume in an embolized nidus to avoid any geographical miss, Homogenous dose distribution and minimum dose, size of the nidus, prescribed Dose, peripheral Dose at lesion margin, nidus topography &angioarchitecture, male sex etc. Arteriovenous fistula, partial revascularization following SRS, contributes to obliteration failure[39]. Smaller nidus with high Dose is positively related to nidus obliteration. Friedman et al., in their study of outcome for AVM by Linac-based SRS described the relation of nidus volume and obliteration rate (OR), a nidus volume of 1 to 4 cm3 had OR 81%, next to which 4 to 10 cm3 and >10 cm3 had nidus OR 89% and 69% respectively [40]. Engelhart et al. & Karlsson et al. emphasized the importance of the direct relation of Dose to the extent of obliteration. Engenhart et al. also reinforced the fact of positive correlation of OR with homogenous Dose within the target volume[41]. Alike prescribed Dose & Homogeneity inside PTV, many authors have stressed the positive correlation of marginal Dose on OR. Schlienger et al., in their report of 169 patients belonging to SALT group, have said about their statistically significant OR by maintaining 60-70% peripheral Dose for 24-26Gy. They have also described about the situation of a compromise in Dose and peripheral isodose for larger nidus or proximity of critical structure[42]. Meder et al. detailed that the nidus of plexiform angioarchitecture and location within the deep brain tissue has more obliteration rate than one having ventricular, paraventricular or cerebellar location[43]. The study of Masahiro et al. at the University of Tokyo for Analysis of Nidus obliteration following Gamma Knife SRS described a similar experience of obliteration rate was 72% at 3year and 87.5% at 5year. The authors also mentioned about smaller nidus, previous Hemorrhage, the higher radiation dose to the lesion's margin, and male sex as positive predictive indices for better obliteration[44]. Our Patient had a relatively more significant lesion having plexiform vessels located deep into the cerebral cortex with no previous history of Hemorrhage. He had a smaller nidus. During the procedure, Contouring was done with reference from the Cerebral angiogram to include all possible nidus. Planning optimization was done in such a way that 80% isodose of the prescribed Dose was maintained along the lesion margin. After SRS, he was found to have a stable-sized AVM at six months follow-up. Late had complete obliteration of nidus at 16 months with no radiological evidence of obliteration failure or recanalization on subsequent follow-up imaging at 28 months. He had early obliteration through but ties with the studies mentioned above.

The frequently mentioned Complication following SRS of AVM mentioned in literature can be early and delayed. Early adverse radiation effect (AREs) is including headache, nausea, seizure, permanent neurologic deficit, Hemorrhage. Late AREs include cyst formation, persistent Oedema, necrosis, and secondary neoplasm (i.e., Meningioma, Glioblastoma)[45, 46]. We cannot make a complete comment on the delayed sequelae report in this case report as a longer follow-up is needed. Our Patient was on an adequate coverage of high dose steroid and prophylactic anticonvulsant. So, he neither experienced any significant periprocedural adverse effects nor early adverse effects as described above. At the presentation, he had no sign of neurologic deficit or Hemorrhage. So, there was no new seizure or Hemorrhage. However, he experienced the loss of hair over the part of the scalp over the irradiation field. His hair loss started within two weeks post-procedure. The skin was normal and devoid of erythema, desquamation, or any reaction. The new hair started growing about 04-week post-procedure and completed regrowth with the same texture and length over the same area by 6month. Tripathi et al., in their case series reporting and analyzing the pattern and factors associated with temporary no cicatricial focal alopecia in post-GKRS patients. They described a radiation exposure to scalp 3Gy result in temporary and reversible hair loss. This Dose-dependent phenomenon can even lead to permanent hair loss in higher radiation exposure. The authors also mentioned that purposive dose spillage for Arteriovenous malformation situated over the cortical surface causes an inevitable temporary assault to hair growth. Their report hair loss started 2-3 weeks after SRS, and regrow starts within 2-3 months[47]. He had a single seizure event after 28months of the procedure, for which he has been prescribed anticonvulsant medications. He was also found to have mild Oedema and cystic encephalomalacia in MRS Brain. This is a late sequel of SRS, which is likely and requires conservative management only.

Hemorrhage critical for AVM. An event of prior Hemorrhage, single draining vein, diffuse AVM nidus is considered high-risk factors for bleeding. Pollock et al. described the estimated annual risk of Hemorrhage is approximately 2-4% for all AVM. However, this risk almost triples for the high-risk individual, which is as high as 8.94% for the chance of the second Hemorrhage in diffuse & compact nidus AVMs. Pollock et al., in their study of evaluation of the risk of stroke in ARUBA eligible Patients, described of ultimate benefit of SRS by reducing the risk of Hemorrhage instead of remaining untreated. They stated that the risk of Hemorrhage remains the same in the first five years to that of natural History of unruptured AVM, but has been significantly declined to 0.2% per from 6 to 10-year post-procedure. This is due to the fact that it takes almost 1 to 5 years to produce nidus obliteration and safeguard future risk of bleeding following SRS[48]. In this case report, the patient has a low risk of Hemorrhage due to the nature of presentation (superficially located having multiple venous drainages with no prior bleeds). However, a one-year post-procedural follow-up revealed complete nidus obliteration. Eventually, we are expecting a very low risk of Hemorrhage for him in future days as well.

Conclusion:

Linac-based SRS for Arteriovenous Malformation (AVM) is an established and equally effective single modality treatment for carefully selected patients. This procedure ensured complete obliteration of the nidus within a treatment period of one year. Moreover, he had no major immediate or late complications. So, the citizen of Bangladesh can avail Linac-based Stereotactic Radiosurgery facility at their doorstep.

References:

1. Fleetwood IG, Steinber GK. Arteriovenous malformations. Lancet 2002; 359:863-73.
2. Gabriel RA, Kim H, Sidney S, McCulloch CE, Singh V, Jhonston SC,Ko NU, Archrol AS , Zaroff JG and Young WL: Ten-year detection rate of brain arteriovenous malformation in large , multiethnic, defined population. Stroke.41:21-26.2010
3. Mayo clinic staff. Disease and condition. Arteriovenous malformations. Risk factors. Available at: https://www.mayoclinic.org/diseases-conditions/brain-avm/symptoms-causes/syc-20350260
4. Mullan S, Mojtahedi MJ, Johnson DL, et al. Embryological basis of some aspect of cerebral vascular fistulas and malformations. J Neurosurgery 1996:85;1-8.
5. Yasargil MG.Pathological considerations. In Yasargil MG, ed. Microneurosurgery: AVM of the Brain, Histology, Embryology, Pathological considerations, Hemodynamics, Diagnostic studies, Microsurgical Anatomy. New York: Thieme Verlag; 1987:49-211
6. Sandalcioglu IE, Wende D, Eggert A, et al. Vascular endothelial growth factor plasma levels are significantly elevated in patients with cerebral arteriovenous malformations. Cerebrovasc Dis 2006; 21: 154-58.
7. Sure U, Butz N, Schlegel J, et al. Endothelial proliferation, neoangiogenesis, and potential de novo generation of cerebrovascular malformations. J neurosurgery 2001; 94:972-77
8. Stevens, J & Leach, J & Abruzzo, Todd & Jones, Blaise. (2008). De Novo Cerebral Arteriovenous Malformation: Case Report and Literature Review. AJNR. American journal of neuroradiology. 30. 111-2. 10.3174/ajnr. A1255.
9. Bulsara KR, Alexander MJ, Villvicencio AT, Graffagnino C. De novo cerebral arteriovenous malformation: case report. Neurosurgery 2002; 50: 1137-1140, discussion1140-1141.
10. Du R, Hashimoto T, Tihan T, Young WL, Perry V, Lawton MT. Growth and regression of arteriovenous malformation in a patient with hereditary hemorrhagic telangiectasia: case report. J Neurosurgery 2007;106: 470-477.
11. Hofmeister C, Stapf C, Hartmann A, Sciacca RR, Mansmann U, Ter Brugge K, Lasjaunias P, Mohr JP, Mast H, Meisel J. Demographic, morphological, and clinical characteristics of 1289 patients with brain arteriovenous malformation. Stroke. 2000; 31:1307–1310.

12. Choi JH, Mohr JP. Brain arteriovenous malformations in adults. Lancet Neurol. 2005; 4:299 –308.

13. Mayo clinic staff. Disease and condition. Arteriovenous malformations. Test and diagnosis. Available at: https://www.mayoclinic.org/diseases-,conditions/brain-avm/diagnosis-treatment/drc-20350265

14. Spetzler RF, Martin NA . A proposed grading system for arteriovenous malformations. J Neurosurgery. 1986 Oct;65(4): 476-83

15. Deruty R, Pelissou-Guyotat I, Mottolese C, Bascoulergue Y, Amat D. The combined management of cerebral arteriovenous malformations. Experience with 100 cases and review of the literature. Acta Neurochir (Wien). 1993;123(3-4):101-12

16. Lunsford LD, Kondziolka D, Flickinger JC, et al. Stereotactic Radiosurgery for arteriovenous malformations of the brain. J Neurosurg 1991; 75:512–24

17. Steiner L, Lekshell L, Greitz T, Forest DM, Backlund EO. Stereotaxic Radiosurgery for cerebral arteriovenous malformation. Report of a cese. Acta Chir Scand 1972; 138: 459-464

18. Kjelberg RN, Hanamura T, Davis KR, Lyons SL, Adams RD. Bragg peak Proton beam therapy for arteriovenous malformation of the brain. N Engl J Med 1983;309: 269-274

19. Fabrikant JI, Levy RP, Steinberg GK et al. Heavy-charged-particle radiosurgery for intracranial arteriovenous malformation. Stereotact Funct Neurosurg 1991; 57:50-63

20. Betti 00, Munari C, Rosier R (1989) Stereotactic Radiosurgery with the linear accelerator: treatment of arteriovenous malformations. Neurosurgery 24: 311- 321

21. Orio, P., Stelzer, K. J., Goodkin, R., & Douglas, J. G. (2006). Treatment of arteriovenous malformations with linear accelerator-based Radiosurgery compared with Gamma Knife surgery, Journal of Neurosurgery JNS, 105(Supplement), 58-63.

22. Mohr JP, Parides MK, Stapf C, Moquete E, Moy CS, Overbey JR, *et al*. International ARUBA investigators. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): A multicentre, non blinded, randomized trial. Lancet 2014; 383:614 21.

23. Pollock BE, Link MJ, Brown RD. The risk of stroke or clinical impairment after stereotactic Radiosurgery for ARUBA-eligible patients. Stroke. 2013 Feb;44(2):437-41.

24. Feghali J, Huang J. Updates in arteriovenous malformation management: the post-ARUBA era. Stroke Vasc Neurol. 2019 Sep 21;5(1):34-39

25. Wong J, Slomovic A, Ibrahim G, Radovanovic I, Tymianski M. Microsurgery for ARUBA Trial (A Randomized Trial of Unruptured Brain Arteriovenous Malformation)-Eligible Unruptured Brain Arteriovenous Malformations. Stroke. 2017 Jan;48(1):136-144.

26. Elhammady MS, Heros RC. Editorial: The ARUBA study: where do we go from here? J Neurosurg. 2017 Feb;126(2):481-485. Bervini D, Morgan MK, Ritson EA, Heller G. Surgery for unruptured arteriovenous malformations of the brain is better than conservative management for selected cases: A prospective cohort study. J Neurosurg 2014; 121:878 90. 41.

27. Rutledge WC, Abla AA, Nelson J, Halbach VV, Kim H, Lawton MT. Treatment and outcomes of ARUBA eligible patients with unruptured brain arteriovenous malformations at a single institution. Neurosurg Focus 2014;37: E8

28. Pandey P, Marks MP, Harraher CD, Westbroek EM, Chang SD, Do HM, Levy RP, Dodd RL, Steinberg GK. Multimodality management of Spetzler-Martin Grade III arteriovenous malformations. J Neurosurg. 2012 Jun;116(6):1279-88.

29. Kano H, Flickinger JC, Yang HC, Flannery TJ, Tonetti D, Niranjan A, *et al*. Stereotactic Radiosurgery for Spetzler Martin Grade III arteriovenous malformations. J Neurosurg 2014; 120:973 81

30. lark B, McKenzie M, Robar J, Vollans E, Candish C, Toyota B, Lee A, Ma R, Goddard K, Erridge S. Does intensity modulation improve healthy tissue sparing in stereotactic Radiosurgery of complex arteriovenous malformations? Med Dosim. 2007 Fall;32(3):172-80.

31. Subramanian S, Srinivas C, Ramalingam K, Babaiah M, Swamy ST, Arun G, Kathirvel M, Ashok S, Clivio A, Fogliata A, Nicolini G, Rao KS, Reddy TP, Amit J, Vanetti E, Cozzi L. Volumetric modulated arc-based hypofractionated stereotactic radiotherapy for the treatment of selected intracranial arteriovenous malformations: dosimetric report and early clinical experience. Int J Radiat Oncol Biol Phys. 2012 Mar 1;82(3):1278-84

32. Gevaert T, Verellen D, Tournel K, et al. Setup accuracy of the Novalis ExacTrac 6DOF system for frameless Radiosurgery. Int J Radiat Oncol Biol Phys 2012; 82:1627–35.

33. Kano H, Kondziolka D, Flikinger JC, et al. Stereotactic Radiosurgery for arteriovenous malformation VI: Multistage volumetric management of large Arteriovenous malformation. J Neurosurgery 2012: 116: 54-65

34. Sirin s, Kondziolka D, Niranjan A, Flickinger JC, Maitz AH, Lunsford LD. Prospective staged volume radiosurgery for large arteriovenous malformation: indication and outcomes in otherwise untreatable Patient. Neurosurgery 2008; 62(suppl 2): 744-754.

35. Mukherjee KK, Kumar N, Tripathi M, Oinam AS, Ahuja CK, Dhandapani S, *et al*. Dose fractionated gamma knife radiosurgery for large arteriovenous malformations on daily or alternate day schedule outside the linear quadratic model: Proof of concept and early results. A substitute to volume fractionation. Neurol India 2017; 65:826-35.

36. Karlsson B, Lax I, Söderman M. Risk for Hemorrhage during the 2-year latency period following gamma knife radiosurgery for arteriovenous malformations. Int J Radiat Oncol Biol Phys. 2001 Mar 15;49(4):1045-51.

37. Pollock BE, Gorman DA, CoffeyRJ. Patient outcomes after arteriovenous malformation radiosurgical management: result based on a 5- to14-years follow-up study. Neurosurgery 2003;52: 1291-1296, discussion 1296-1297,

38. Lisak R, Vladyka V, Simonova G et al. Artereovenous malformation after lekshell gamma knife radiosurgery: rate of obliteration and complications. Neurosurgery 2007; 60: 1005-1014, discussion1016-1016

39. pollock BE, Kondziolka D, Lunsford LD, et al. Repeat stereotactic radiosurgery of arteriovenous malformations: Factors associated with incomplete obliteration. Neurosurgery 1996;38: 318-324

40. Friedman W, Bova F, Mendenhall W. Linear accelerator radiosurgery for arteriovenous malformations: the relationship of size to outcome. J Neurosurgery 1995:82:180-189

41. Engenhart R, Wowra B, Debus J et al. The role of high dose single fraction irradiation in small and large intracranial arteriovenous malformation. Int J Radiat Oncol Biol Phys 1994; 3:521-529, klarsson B, Linqiust C, Steiner L,et al . Prediction of Obliteration after gamma-knife surgery for cerebral arteriovenous malformation: Neurosurgery 1997; 40:425-431

42. Schlienger M, Atlan D, Lefkopoulos D, Merienne L, Touboul E, Missir O, Nataf F, Mammar H, Platoni K, Grandjean P, Foulquier JN, Huart J, Oppenheim C, Meder JF, Houdart E, Merland JJ. Linac radiosurgery for cerebral arteriovenous malformations: results in 169 patients. Int J Radiat Oncol Biol Phys. 2000 Mar 15;46(5):1135-42.

43. Meder JF, Oppenhiem C, Blustajn J, et al. Cerebral arteriovenous malformations: the value of Radiologic parameter in predicting response to Radiosurgery. Am J Neuroradiology 1997; 18:1473-1483

44. Shin M, Maruyama K, Kurita H, et al. Analysis of nidus obliteration after Gamma Knife surgery for arteriovenous malformation based on long-term follow up data: the University of Tokyo experience. J Neurosurg. 2004 Jul;101(1):18-24.

45. Pollock BE, Gorman DA, Coffey RJ. Patient outcome after arteriovenous malformation radiosurgical management: result based on a 5- to 14-year follow up study. Neurosurgery 2003; 52:1291-1296, discussion 1296-1297

46. Flickering JC, Kondziolka D, Pollock BE, Maitz AH, Lunsford LD. Complications from arteriovenous malformation radiosurgery: multivariate Analysis and risk modelling. Int. J Radiat Oncolo Biol Phys 1997; 38: 485-490.

47. Tripathi M, Buddhiraja M, Kumar N, Batish A, Ahuja CK, Kamboj P, Kaur R, Kaur A. Temporary noncicatricial focal alopecia following Gamma knife radiosurgery: Case series and review of literature.Neurol India 2018;66:1469-1474

48. Pollock BE, Flickinger JC, Lunsford LD, Bissonette DJ, Kondziolka D. Factors that predict the bleeding risk of cerebral arteriovenous malformatioyear ns. Stroke. 1996 Jan;27(1):1-6.