

# Arteriovenous Malformation (AVM) Treated with Robotic Radiosurgery: Impact of Beam Reduction in 12 Gy Normal Brain Volume and It's Clinical Implication

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## Abstract

**Purpose:** Dosimetric study to evaluate impact of “beam” reduction in AVM radiosurgery on normal brain dose parameters and it's clinical implications.

**Materials and Methods:** Five small volume AVMs (nidus volume 0.31 - 1.94 cc) planned for single fraction SRS with robotic radiosurgery system. Planning scans done with CT scan brain, CT & MR angiography, then nidus volume and organ at risk (OARs) were contoured. Planning was done with multiplan planning system. Plan evaluated as per Flickenger model parameters of 12 Gy normal brain vol & marginal dose. 7.5 mm and 10 mm cons used, optimization done with sequential algorithm. 20 Gy was prescribed to isodose with appropriate nidus coverage (>98%). Total beams of five plans were 85 - 250, monitor unit 17,259 - 24,602 MU. 12 Gy normal brain volume is 0.9 - 7.6 cc. Then beam reduction is done by reducing beams with minimum MU in steps of 50, 100, 150, 200, 250 MU and after beam reduction, re-optimization done. Prescription isodose was changed to keep the nidus coverage > 98%. Impacts of beam reduction on 12 Gy normal brain vol and conformity/homogeneity index were analyzed. **Results:** Optimal plans of five patients with 20 Gy prescribed to 88% - 90% isodose, nidus coverage more than 98%. In dosimetric parameters, mean CI was 1.36 - 1.51, nCI 1.41 - 1.51, HI 1.1 - 1.4 and mean 12 Gy normal brain volume 0.17, 1.44, 5.3, 5.5 and 7.6cc respectively. After beam reduction of less than 50 MU contribution (in case#1), prescribing at suitable isodose (85%) beam reduces to 79 and 12 Gy volume marginally increases to 26.4 cc. Beam reduction of less than 100 MU reduces to 53 - 92 beamlets. Reduction of beams with less than 150 MU con-

tribution did not significantly change the 12Gy normal brain volume. However, reduction of beamlets with more than 200 MU, 250 MU, 300 MU, 450 MU and 550 MU significantly affects the 12 Gy normal brain volume. Prescription-isodose modified from 83% to 50% to have >98% coverage. CI and HI increased from 1.36 - 1.51 to 2.51 - 2.63 and 1.1 - 1.4 to 1.52 - 1.54 respectively. There was exponential increase in 12 Gy volume with reduction of beams with higher proportion in larger nidus. **Conclusions:** In robotic radiosurgery system, beam reduction even after re-optimization impairs the conformity index and increase 12 Gy normal brain volume, hence long-term toxicity. Optimal beam numbers are required for optimal plan generation.

### Keywords

AVM, Robotic Radiosurgery, CK-Cyberknife, 12 Gy Volume, Beam Reduction

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## 1. Introduction

Arteriovenous malformations (AVMs) of the brain are genetically determined abnormal formation of vasculature in the development which in turn may lead to a focal arterio-venous shunt and hence higher probability of rupture and bleeding [1] [2]. Patients usually present with symptoms like neurological deficits, seizures or headache. Life-time risk of hemorrhage in AVM is around 40% and the risk of haemorrhage increases annually by 2% - 3% [1] [2]. Surgical excision is the treatment of choice in “safe” non-eloquent, superficial AVMs with high cure rate. Single fraction radio surgery (SRS) is an effective alternative especially in deep seated and AVMs located in eloquent areas of brain [3] [4] [5]. Obliteration with SRS depending upon the size of the nidus, it’s location and “marginal” dose delivered [4] [5]. Usually complete obliteration rate (cure) in suitable cases varies between 70% - 90% [5] [6] [7]. The side effect (persistent neurological deficit) depends upon the 12 Gy normal brain volume and site of the nidus [4]. Modern precise techniques such as multiple arcs or multiple beams (robotic radiosurgery) promise higher conformity, lesser dose to normal brain (lesser 12 Gy volume) and hence are supposed to be more effective in “border line” size nidus. However, with increase in number of beams, there is increase in monitor unit and treatment time [8] [9].

In the present study, we are analyzing the impact of reduction of beams on dosimetric parameters in optimal AVM nidus (<2.5 cm nidus) planned optimally with robotic radiosurgery system. The main objective of the present study is to evaluate the impact of beam reduction on an optimal plan after re-optimization.

## 2. Materials and Methods

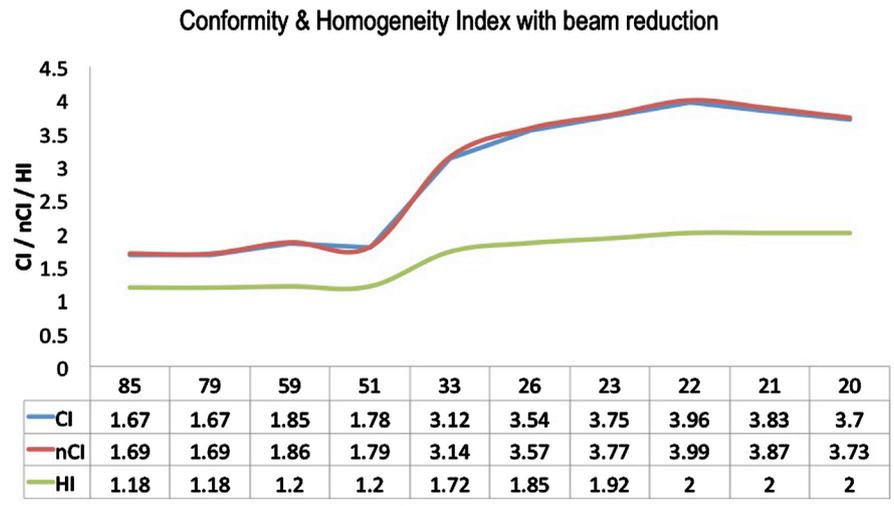
Five AVM patients with small volume in different part of the brain were considered for the study. All these symptomatic AVM patients (presented mostly with

occasional episodes of convulsion or headache without any obvious bleeding) were confirmed by digital subtraction angiography (DSA) and were planned for SRS with robotic radiosurgery system. Planning scans done as per the protocol with plain CT scan brain, CT angiography and MR angiography. After fusion of the images in “Multiplan” system and assessment of diagnostic DSA images, the nidus volume and organ at risk (OARs) were contoured. No PTV margin was generated in the nidus (target) and normal brain volume contoured without excluding the nidus volume. Robotic Radiosurgery (CyberKnife®) treatment plans were generated in Multiplan treatment planning algorithm. Computed tomography images of the patients acquired with 1 mm spacing were used to create treatment plans. Treatment plans are generated using the sequential optimization method. Radiosurgery plans were generated with treatment paths that control the beam orientations specific to different anatomical sites. Treatment plans for patients with AVM were generated using the head path with 6D skull tracking method to deliver a dose of 20 Gy marginal dose in a single treatment session. Multiple shells with asymmetric margins around the target were used to limit the dose to critical structures near the target. The dose distribution in the computed tomography images of the patient’s head was calculated using the “Raytracing” algorithm. Collimator sizes of 7.5 and 10 mm were used in the treatment plan. Number of beams, monitor unit (MU), nodes, CI, nCI, HI and 12 Gy normal brain volumes in all the plans were documented in **Table 1**. Approved plan had nidus coverage more than 98%, optimal number of beams, acceptable CI, nCI and HI values and adjacent critical structure dose within normal limits. The nidus volumes were small, ranging from 0.32 cc to 9.4 cc [**Table 1**]. As the nidus volumes were very small and irregular in shape; approved plan CI and HI values were on the higher side (CI range 1.36 - 1.51). Plan evaluation was done as per the Flickenger model parameters of 12 Gy normal brain volume, appropriate marginal dose with nidus coverage more than 98%. 12 Gy volume considered without subtraction of nidus volume. As per the flickenger model, probability of persistent neurological deficits were less than 5% in all the cases. Marginal dose of 20 Gy provides complete obliteration rate of 85% at 2 year. Subsequently for this study, treatment plans were generated by removing the beams with certain number of monitor units and optimized once again to meet the dose volume objectives of the treatment plan. After approval of the plan, beam reduction done in steps by reducing beams with contribution less than MU of 50, 100, 150, 200 and 250 respectively. The collimator size was not changed to keep uniformity and evaluate the impact of beam reduction with re-optimization. Prescription of the isodose was changed to keep nidus coverage > 98%. Impact of beam reduction on the 12 Gy normal brain volume and conformity/homogeneity index was analyzed [**Figure 1**]. The formulae used to calculate the conformity index and the homogeneity index are given as follows. Conformity Index (CI) =  $(V_{RI} \times TV)/(TV_{RI})^2$ . Where  $V_{RI}$  is the overall volume including the target volume, receiving the prescription isodose or more, TV is

**Table 1.** Dosimetric parameters of plans with “beam reduction” from optimal plan of five different patients with AVM in different location of brain.

Beam Sr cut No. off (MU)	Beam					Coverage %					Prescription %					CI					nodes					12 Gy Vol in cc								
	Pt1	Pt2	Pt3	Pt4	Pt5	Pt1	Pt2	Pt3	Pt4	Pt5	Pt1	Pt2	Pt3	Pt4	Pt5	Pt1	Pt2	Pt3	Pt4	Pt5	Pt1	Pt2	Pt3	Pt4	Pt5	Pt1	Pt2	Pt3	Pt4	Pt5	Pt1	Pt2	Pt3	Pt4
1	0	250	145	127	135	85	98.2	98.1	98.5	98.2	98.5	88	88	90	88	98	1.51	1.37	1.41	1.36	1.41	105	78	85	88	64	1.75	5.3	6	7.6	0.9			
2	50	126	92	100	160	63	98.2	98.1	98.9	98.1	98.9	89	88	90	87	87	1.52	1.32	1.43	1.43	1.53	80	58	77	75	63	1.78	5.6	6.5	7.9	1.2			
3	100	92	69	85	87	53	98.2	98.1	98.5	98.1	98.5	87	86	90	87	87	1.51	1.4	1.41	1.42	1.52	63	46	64	65	46	1.81	6.2	5.9	8.3	1.5			
4	150	76	58	65	69	47	98.1	98.2	98.9	98.1	98.5	84	84	89	86	85	1.61	1.42	1.47	1.49	1.7	55	39	52	55	42	1.93	6.5	7.3	8.8	1.9			
5	200	61	47	58	57	40	98.2	98	98.2	98.2	97.8	82	84	89	83	83	1.72	1.41	1.46	1.58	1.72	46	33	48	49	37	2.6	7.2	7.6	9.5	2.2			
6	250	52	42	54	49	33	98.3	98	98	98.1	98	80	79	88	80	79	1.81	1.61	1.44	1.74	1.91	38	31	45	42	31	2.9	7.9	8.2	10.3	2.6			
7	300	47	33	50	46	29	98.1	98.3	98.1	98	98.1	77	74	85	77	73	1.83	1.67	1.58	1.94	2.26	34	27	41	39	28	3.3	8.5	8.7	10.9	2.9			
8	350	42	31	43	40	28	98	98.4	98.1	98	98.1	74	64	78	73	68	1.96	2.15	1.75	2.3	2.66	31	26	43	35	27	3.8	9.3	9.7	11.6	3.4			
9	400	38	29	43	36	26	98	98.2	98.3	98.1	98.1	71	63	76	67	66	2.13	2.2	1.89	2.46	2.8	30	25	34	32	26	4.4	9.7	10.6	12.2	3.8			
10	500	36	28	39	35	24	98	98.3	98.1	98.1	98.1	66	63	66	65	65	2.39	2.4	2.9	2.54	3.1	28	24	32	32	23	5.2	10.4	11.2	13.1	4.6			

Beam reduction done with reduction of beam from optimal plan with cutoff of beam less than 50 MU, then 100 MU and similar pattern. Re-optimization of plans were done after each beam reduction. Plan considered optimal after beam reduction and optimization with change in prescription iso-dose. Acceptable plan need to have more than 98% nidus coverage. Change in number of beamlets, nodes and 12 Gy normal brain volume was considered for analysis and correlation. Pt: Patient; Nidus volume: Pt1: 1.53 cc, Pt2: 1.94 cc, Pt3: 1.54 cc, Pt4: 1.86 cc, Pt5: 0.32 cc. Site: Pt1: Left Frontal lobe, Pt2: Left Frontal lobe, Pt3: Right Temporo-parietal lobe, Pt4: Left Frontal lobe, Pt5: Left Temporal lobe.



Impact of beam reduction on conformity index parameters of patient no 1. With reduction of beam & re-optimization, there is impairment of CI & HI. CI & HI impairment was dramatic after gross reduction of beams suggest that there is a threshold of beam reduction. After the threshold, gross impairment of conformity index in evident

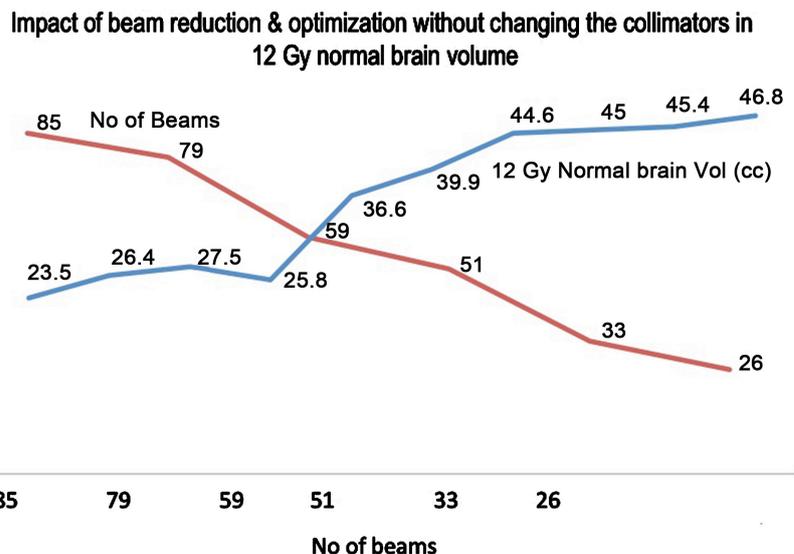
**Figure 1.** Correlation of number of beamlets and 12Gy normal brain volume.

the volume of the nidus, and  $TV_{RI}$  is the volume of the target which receives the prescription isodose or more. Homogeneity index (HI) =  $D_{max}/D_{RI}$  where  $D_{max}$  is the maximum dose in the target and  $D_{RI}$  is the reference/prescription isodose [10] [11] [12].

### 3. Results

Optimal plans with 20 Gy marginal dose prescribed to appropriate isodose with nidus coverage more than 98% and optimal beams were described in **Table 1**. After reduction of beams with less than 50 MU contribution, optimization and prescribing at suitable isodose to have nidus coverage more than 98% and then 12 Gy normal brain volumes were calculated in all the plans. Similarly further reduction of beams with contribution more than 100 MU, then 150, 200, 250 and whereon were evaluated, re-optimization done; prescription isodose changed to have nidus coverage more than 98% and then 12 Gy volumes were calculated. In all the plans, after reduction of beams more than 200 MU, 250 MU, 300 MU, 350 MU, 450 MU and 550 MU there was significant increase in 12 Gy normal brain volumes. In order to have nidus coverage more than 98%, prescription isodose was modified from 83% to 50%. CI and HI were increased respectively [**Figure 2**].

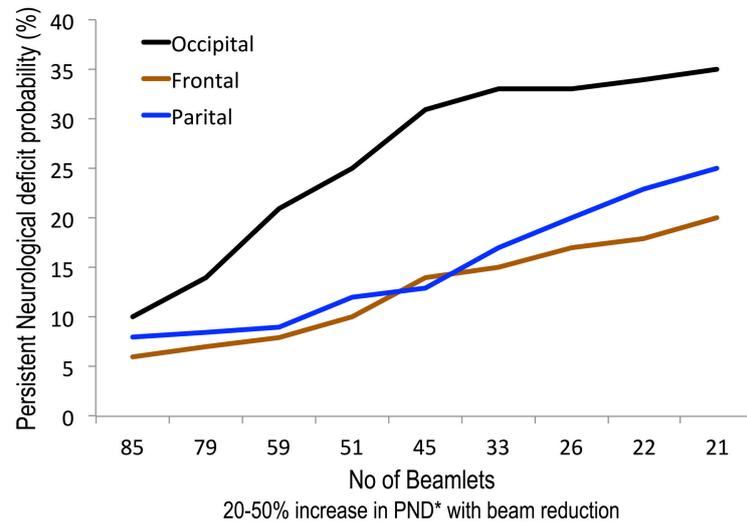
Correlation between the reduction of beams and increase in 12 Gy normal brain volume was done by Pearsons Correlation test (correlation 95.6%, p-value = 0.003) [**Figure 1** and **Figure 2**]. There was no increase in 12 Gy volume despite reduction of beams till a threshold was reached. After that there was exponential increase in 12 Gy normal brain volume with reduction of beams. It does suggest that there is a optimal scope of reduction of beams in optimal plans without increasing 12 Gy volume and other (HI, CI) dosimetric parameters [**Figure 3**]. Hence, after planning the optimal plan, prior to approval there may be an option to consider beam reduction upto an extent without compromising on the dosimetric parameters.



Impact of beam reduction on 12 Gy normal brain volume in patient no 1. With reduction of beam & re-optimization, there is increase in 12 Gy normal brain volume. 12 Gy normal brain volume increase was dramatic after gross reduction of beams suggesting that there is a threshold of beam reduction. After the threshold, there is significant & gross increase in 12 Gy normal brain volume. Threshold depends upon the nidus volume, collimators used, output factors and dose prescription

**Figure 2.** Changes in conformity with beamlet reduction.

### Beam reduction effect: Neurodeficit probability



\*PND: Persistent Neurological deficit

Prediction done according to Flickinger et al. Rad Onc 2002; 63:347-354.

**Figure 3.** Effect of beamlet reduction on persistent neurological deficit.

## 4. Discussion

Arteriovenous malformation (AVM) is relatively uncommon but a unique lesion in brain. The outcome is excellent with surgery and radiosurgery [5] [6] [7] [8] [9]. Outcome (complete obliteration) depends upon the nidus volume, dose delivered, site of lesion, supplying and draining vessels and previous treatment. In suitable cases complete obliteration rate varies between 70% - 90% depending upon various factors [10]. Majority of the patients present at young age or at adolescent. Rarely we do see elderly patients presenting with AVM. It is assumed that a proportion of “sudden death” with “unknown” etiology in adults may be related with bleeding from “occult” AVMs. Hence, though AVM is a benign condition, the implications are more serious and need interventions. Treatment with radiosurgery is not devoid of long-term complications. In a large series with long-term follow up, serious long term toxicities such as persistent neurological deficits are upto 9% [5] [6] [7]. Toxicities after radiosurgery depend upon 12 Gy normal brain volume and site of lesion, as described by the Flickenger’s model [5]. Nidus in eloquent areas of brain (thalamus, pons) has higher probability of long-term toxicity [6].

AVM radiosurgery was traditionally done with “gold standard” gammaknife radiosurgery system with invasive frame and multiple Co60 sources [13]. Usually from the available 201 non-coplanar cone source positions, suitable positions are selected to deliver dose to the nidus and prescription isodose was usually 50%. Hence, there was inhomogeneity to the target and “hot spot” in the centre of the nidus with possibility of necrosis. In standard LA-based SRS systems [BrainLAB system], 5 to 9 fixed fields or limited number of arcs (2 to 6 arcs) were used with micro-MLC [14] [15]. There was significant improvement

in target coverage and conformity with micro-MLCs; however some region of normal brain also received high dose especially in smaller targets [15]. Then, the “non-coplanar arc” based systems (arc based treatment delivery such as BrainLAB®, RapidArc®) came into practice [16]. “Arc” treatment basically consists of multiple beams in different coplanar or non-coplanar planes. Multiple beams in arc format improved conformity, and homogeneity and reduce dose spillage to normal brain region. Robotic radiosurgery with CyberKnife uses multiple nodes and beams to deliver the dose. Usually from available 1200 nodes, 100 to 200 nodal points are used to deliver dose in a non-coplanar manner [17] [18] [19]. Small cones used to deliver dosage ensure high conformity and minimal dose spillage. There is “intra-fraction” tracking and usually no or minimal PTV (ITV) margin with robotic radiosurgery system; hence the target volume (PTV) is relatively smaller compared with other systems required to give 1 to 2 mm PTV margin [11] [17]. “Multiple isocentres” do have advantage of reducing high dose region and improving homogeneity.

Delivery accuracy with robotic radiosurgery system is implicable. Also as there is no or minimal PTV margin required, target volume is smaller, but there are issues with compliance because of longer treatment time [12]. In Multiplan system, plan evaluation usually consists of target coverage, OAR dose parameters, prescription isodose and total monitor units. There is a need to evaluate the plan in respect of number of beams and treatment time as well [20]. Reduction of beams by reducing beams with lesser monitor unit contributions may alter the dose distribution parameters and reduce coverage. On the other hand, with reduction of beams with minimal contribution may not have significant changes in dosimetric parameters until a threshold is reached. Robotic radiosurgery plan may be optimized in terms of number of beams and treatment time, apart from the standard parameters. In the present study, when beam reduction protocol was applied without compromising the target coverage, there was no significant influence on HI, CI and also 12 Gy volume till a threshold was reached. After the threshold, with minimal reduction of beams, there was significant increase in 12 Gy normal brain volume and deterioration in both conformity and homogeneity indices.

In initial reduction of beams, there was only moderate increase in delivered monitor unit. Hence, initially even though there was reduction of beams, there was not significant deterioration in plan dosimetric parameters. Further reduction of beams with lesser monitor unit contribution, there was significant deterioration in dosimetric parameters. Beam reduction in multiple non-coplanar systems has a threshold for beam reduction. Any attempt to reduce further beamlets will impair the plan dosimetry.

This phenomenon may be considered with another perspective as well. Fixed beams planned in earlier systems (eg. BrainLAB®) and there are possibilities for improvement of coverage and reduction of 12 Gy normal brain volumes if planned with multiple non-coplanar beams. It can be assumed that multiple beams with robotic radiosurgery system or arc radiation therapy delivery sys-

tems do have an advantage of reduction of 12 Gy normal brain volume and hence long-term toxicities. Reduction of beams in robotic radiosurgery system increase 12 Gy volume and there are proportional increase in the probability of late toxicities (persistent neurological deficits) [Figure 3] [10] [17]. Probability of increase in late toxicity with increase in 12 Gy normal brain volume was calculated as per the Flickenger's model. Probability of increase in late toxicity with increase in 12 Gy normal brain volume is higher in occipital region lesions than in parital or frontal lobe lesion.

It may be assumed that, with modern arc treatment or multiple beams there is a possibility of treatment of larger volume nidus without increasing 12 Gy volume and hence late toxicity. In the present study, analysis was done in 2.5 cm, 3.5 cm and 4.5 cm diameter nidus in same region of brain; planned with similar marginal dose (20 Gy/1fr), coverage (98%) and planning algorithm [17]. There were significant increases in 12 Gy volumes with increase in nidus volumes. Hence, even with modern multiple beam robotic radiosurgery system we are not able to treat larger volume nidus without increasing late toxicities. Modern radiosurgery delivery systems with arc or multiple non-coplanar beams are safer in small nidus compared with fixed field radiosurgery systems, however it may not be beneficial in larger volume nidus to reduce toxicity [7] [17].

In summary, multiple beam robotic radiosurgery systems with non-coplanar beams may have dosimetric superiority compared with conventional fixed field radiosurgery systems. In robotic radiosurgery systems, there is a threshold for beam reduction. There is a need for adequate number of beams (threshold) to achieve optimal plan. The threshold depends upon the nidus volume, site of lesion and planning indices such as number of cons used, optimization algorithm and output parameters.

## Study Presented

Present data was present at the Annual meeting of Indian Society of Neurooncology (ISNOCON), Lucknow India.

## Disclaimer

None.

## Conflicts of Interest

None.

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