Dosimetric Comparison of Robotic and Linear Accelerator Multi-Leaf Collimator-Based Stereotactic Radiosurgery for Arteriovenous Malformation

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Abstract

Purpose: To investigate the dosimetric comparison of different collimators which are used in robotic radiosurgery (cyberknife-CK) and linear accelerator (LINAC) for stereotactic radiosurgery (SRS) in arteriovenous malformation (AVM). **Materials and Methods:** Twenty-five AVM patients were planned in CK using FIXED cone, IRIS collimator, and multi-leaf collimator (MLC) based in LINAC. Dosimetric comparison was performed using Paddick conformity index ($CI_{Paddick}$) and International Commission on Radiation Units and measurements (ICRU) homogeneity index (HI_{ICRU}), gradient score (GS), normal brain dose received by 10cc (D_{10cc}) and critical structure (brain stem, optic chiasma, optic nerves) doses. Paired sample *t*-test was used for statistical analysis. **Results:** Mean treatment volume was 3.16cc (standard deviation ± 4.91cc). No significant deviation ($P =0.45$, 0.237 for FIXED vs. IRIS and FIXED vs. MLC, respectively) was found in target coverage. For $CI_{Paddick}$, the mean difference (MD) between FIXED- and MLC-based plans was $0.16(P = 0.001)$; For HI_{ICRU}, difference between FIXED and IRIS was insignificant (0.5, $P = 0.823$); but, when FIXED versus MLC, the deviation was 7.99% ($P = 0.002$). In FIXED- and MLC-based plans, significant difference was found in GS70 and GS40 ($P < 0.041$ and 0.005, respectively). MD between FIXED- and MLC-based plans for normal brain for 5Gy, 10Gy, 12Gy, and 20Gy were 36.08cc ($P = 0.009$), 7.12cc ($P = 0.000$), 5.84cc ($P = 0.000$) and 1.56cc ($P = 0.000$), respectively. AVM volume <0.7cc should be treated with CK FIXED and >0.7cc were treated by using FIXED or IRIS collimators. AVM volume > 1.4cc can be treated by either LINAC MLC-based SRS or CK. **Conclusion:** Our study shows CK collimator (IRIS and FIXED) could be able to treat brain AVMs in any size. Linac MLC-based SRS has some limitations in terms of conformity and low-dose spillage, and advantages like reduced treatment time and MU.

Keywords: Arteriovenous malformation, collimator, stereotactic radiosurgery

Introduction

Arteriovenous malformation (AVM) is a congenital vascular abnormality with abnormal communication between arteries and veins, resulting in arteriovenous shunting. This intervening network of abnormal vessels is called nidus. Curative AVM embolization achieves high obliteration rates with a low complication rate for carefully selected lesions.[1] Stereotactic radiosurgery (SRS) is preferred for AVMs located in eloquent locations or for smaller AVMs without any history of hemorrhage, or sometimes in combination with surgical interventions. SRS can be frame-based or frameless and can be delivered using Gamma Knife® (GK), Cyberknife (Accuray Incorporated,

Sunnyvale, CA, USA) or by linear accelerators (LINAC). Most literature report results by using GK SRS (Elekta AB, Stockholm, Sweden).[2,3]

CK-based frameless SRS is a safe and effective measure providing equal outcomes to traditional frame-based methods without stereotaxic frame.[4] Over time, LINAC-based radiation treatment has been modified in such a way that it is now being

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used more frequently for radiosurgery.[5,6] Dose plans that have higher conformity index (CI) and gradient index (GI) produce a low local progression and minimal complication for brain metastasis SRS.[7] High conformity is required in SRS plans, which emphasize the steep dose gradient and the reduction of the normal structure dose.[8]

Uniformity of dose distribution inside the target volume is analyzed by using homogeneity index (HI); however, there is no consensus for the acceptable criteria.[9] This plan quality metrics are needed for comparing the different modalities of SRS and its dose calculation algorithm.[10] An earlier study, which compared CK and LINAC plans, was performed with a large volume AVM.[11] The present study evaluated the dosimetric impact of three different collimators used in SRS. A comparison was made between FIXED cone (FIXED) and IRIS® collimator in CK and multi-leaf collimator (MLC) beam modulator in Elekta LINAC. AVM volume and its dosimetric significance with these collimators were analyzed.

MATERIALS AND METHODS

Patient selection and target delineation

Twenty-five patients, who were treated with single fraction radiosurgery between April 2014 and July 2020, were analyzed. Patient demography, prescription dose, and prescription isodose line are shown in Table 1. All the patients were treated with Cyberknife. After obtaining an informed consent, the patients were simulated with brain thermoplastic cast in chin neutral position. Planning computed tomography (CT) scan was performed with 1 mm slice thickness in Siemens Somatum® 64 slice CT scanner without any contrast enhancing agent. Magnetic resonance imaging (MRI) sequences were acquired with 1 mm axial slice thickness in T1 sequence (with contrast) in same planning simulation set up. CT angiography was done with digital subtraction angiography (CTDSA) and two-dimensional (2D) images were reconstructed volumetrically with the axial slice thickness of 1 mm. Planning CT was taken as the primary image in treatment planning system (TPS), MRI, and CTDSA was used as secondary imaging modality. Image fusion was done with rigid image registration algorithm for each imaging modality. AVM was delineated by a team of neuroradiologist, neurosurgeon, and radiation oncologist in MRI and CTDSA [Figure 1]. Normal structures such as brain, optic chiasma, optic nerves, and brainstem were delineated. Optimization was performed using Multiplan system and treatment delivery were done by Cyberknife VSI (Accuray, Sunnyvale, CA, USA). MLC-based SRS plans were generated in Monaco planning station.

CK treatment planning

CK has variable IRIS and FIXED collimators system which can change between 5 mm and 60 mm at SSD of 80 cm. IRIS has two stacked banks of 6 tungsten segments that create a 12-sided variable aperture, which approximates a circular aperture and produces beam profiles similar to the FIXED collimators. The use of IRIS collimator can reduce overall treatment time and

Table 1: Patient characteristics, prescription dose and isodose lines

	n (%)
Age (year)	
10-20	6 (24)
21-30	8 (32)
31-40	8 (32)
40-55	3 (12)
Location	
Brain stem	2 (8)
Cerebellum	1 (4)
Corpus callosum	3 (12)
Left fronto temporal	2 (8)
Left occipital	2 (8)
Left parieto occipital	2 (8)
Left temporal parietal	1 (4)
Para vestibular	3 (12)
Parietal	2 (8)
Prepornsium	1 (4)
Right fronto temporal	2 (8)
Right parietal	1 (4)
Right temporal	3 (12)
Volume (cc)	
0.124-0.986	12 (48)
1.49-4.56	9 (36)
6.17-22.19	4 (16)
Prescription dose (Gy)	
15-16	2 (8)
18	4 (16)
20	8 (32)
21	1 (4)
22	6 (24)
23-25	4 (16)
Isodose line (%)	
70-75	6 (24)
76-80	9 (36)
81-83	8 (32)
90-92	2 (8)

monitor units.[12] FIXED collimator has 12 variable cones (5 mm, 7.5 mm, 10 mm, 12.5 mm, 15 mm, 20 mm, 25 mm, 30 mm, 35 mm, 40 mm, 50 mm, 60 mm defined at 80 cm source to axis distance (SAD)), which can be interchanged. Six-dimensional skull tracking is the intra-fractional imaging method of correcting the rotational and translational errors from generated DRRs from projection of orthogonal X-ray's imaging systems. The treatment planning was performed by using Multiplan® (Accuray Incversion 4.3). Collimators were selected according to the size of AVM and the number of collimators was limited to three for FIXED. In IRIS, it can be chosen from 7.5 mm to 60 mm, but three to four apertures are preferably chosen. 6MV flattening filter free (FFF) beam was used with non-isocentric beam placements for planning. Planning parameters for the CK (FIXED and IRIS collimator) are shown in Table 2. Brain subtracted AVM was taken as the critical structure. Sequential optimization algorithm was used
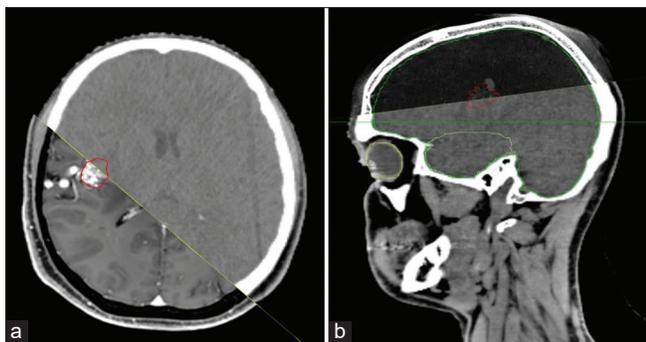
Figure 1: Axial (a) and sagittal(b) visualization of arteriovenous malformation delineation; noncontrast computed tomography co-registered with contrast enhanced computed tomography, t1 contrast magnetic resonance imaging and three-dimensional-computed tomography angiography images

to reduce the MU and obtain an optimal one. After desired dose distribution was achieved, the final dose calculation was performed using the ray-tracing algorithm [Figure 2]. Quality assurance was performed by using BB16-SDVP (Stereotactic Dose Verification Phantom-Standard Imaging, Madison WI, USA) was used for patient-specific quality assurance (PSQA) in CK for a specific plan to verify all the parameters such as robot position, MU delivery, and dose accuracy. Dimension of the phantom is 20 cm (length) × 20 cm (breath) × 10 cm (height) and it is made up of two 4 cm build-up slabs on top and bottom, as well as two interchangeable 2 cm test inserts in the middle. Density of the slab is 1.09 g/cc with nominal CT density is 70 and relative electron density to water is 1.055. Gold and lead fiducial markers were placed inside the phantom which provides further orientation and positional accuracy when performing PSQA. A16 Exradin microchamber (Standard Imaging, Madison WI, USA) was used for PSQA which has the volume of 0.007 cc and collecting diameter is 0.33 mm.

Multi-leaf collimator-based linear accelerator treatment planning

Volumetric modulated arc therapy (VMAT) planning was done in Monaco (Version 5.11, Elekta Instruments AB, Stockholm, Sweden) TPS. VMAT planning was done by using 4 Full/ Semi/Partial arcs which includes coplanar and noncoplanar beams (for all plans) [Table 2]. Previously published papers were proposed that multiple noncoplanar and coplanar arc plans are superior plan quality compared to single coplanar arc plans.[13,14] Based on this, number of arcs including coplanar and non-coplanar arc angle was chosen and the overlap in the skin surface was avoided. Elekta synergy® (beam modulator) had the 6MV flattening filter (FF) beam and a 4 mm MLC leaf width at the isocenter with a dose rate of 600MU/min. Shell structures were created around the AVM for achieving high conformity and dose constraints were provided to the TPS for reducing the brain-AVM dose. Two-stage optimizations were performed by using the inverse planning optimization algorithm the inverse planning algorithm was used for the most
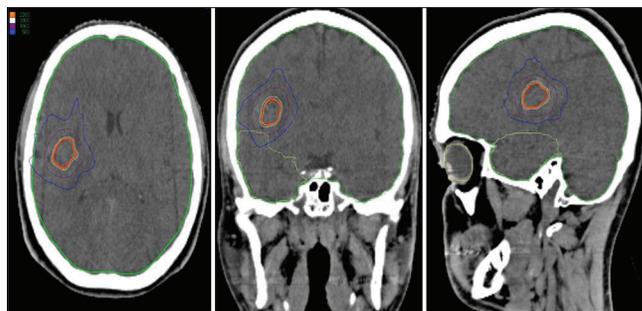
Figure 2: Isodose lines shown in axial, coronal and sagittal CT images of the robotic radiosurgery plan; Red- arteriovenous malformation (target); 22 Gy-Orange (Prescription dose); 20 Gy-White; 10 Gy-Purple; 5 Gy-Blue

Table 2: Volumetric modulated arc therapy and cyberknife planning parameters

VMAT planning parameters	
Arc specification	**Angles**
Arc1 (coplanar) partial/semi arc	
Start angle	270°-300°
Stop angle	90°-120°
Arc2 (coplanar) (full arc)	
Start angle	179°
Stop angle	181°
Arc 3 (noncoplanar) couch-270°-320°	
Start angle	180°
Stop angle	100°
Arc 4 (noncoplanar) couch-45°-90°	
Start angle	270°-300°
Stop angle	90°-120°
Minimum segment width (cm)	0.5
Fluence smoothing	Medium
Target margin	Tight (2 mm)
Number of segments	Mean=606 (range 293-997)
Avoidance margin	Normal (8 mm)

Cyberknife planning parameters		
Collimator	**FIXED**	**IRIS**
Number of node, mean (range)	84 (50-106)	77 (34-99)
Number of beam, mean (range)	161 (61-240)	150 (46-226)
Minimum MU, mean (range)	18.05 (3.7-82)	8.4 (4.9-16)
Maximum MU, mean (range)	127.7 (89.5-205)	127.8 (91-204)

VMAT: Volumetric modulated arc therapy, MU: Monitor units

feasible solution to achieve the target coverage and reducing the critical structure (e.g., brainstem and optic chiasma) doses. The separation of the arcs was determined using the stage 1 optimization process. Once the desired fluence (high and low dose distribution) achieved then the segmentation process initiated. After the final dose calculation, the dose distribution around the target was evaluated. The above process was repeated for achieving the deliverable plan which satisfies the target conformity and normal structure doses. Finally, the Monte Carlo algorithm was used to perform the final dose calculation with 1.5 mm grid size and 1% statistical

uncertainty [Figure 3]. RW3 plates® was used for plan specific quality assurance.

Plan analysis

Target coverage

Volume of AVM, which received 98% of prescription dose, was taken as target coverage.

Paddick conformity index

Radiation Therapy Oncology Group (RTOG) CI[15] is defined as the ratio between the volume of reference dose (V_{RI}) and the target volume (TV). CI_{RTOG} does not quantify the reference dose that is going outside the target volume. It could lead to an acceptable CI, but reduced target dose coverage or prescription isodose going outside the target volume. Due to the above-mentioned issue in CI_{RTOG}, Paddick developed the CI that includes a target coverage and volume outside the target, which is receiving the prescription dose.[16]

- $CI_{paddick} = TV_{PIV} \times TV_{PIV}/(TV \times V_{RI})$
- TV_{PIV} = volume of target which is receiving prescription isodose volume (PIV)
- TV = volume of target
- V_{RI} = volume of PIV

In the above equation, target coverage and plan selectivity has been included. If the target coverage is adequate and the dose spillage is observed outside the target volume, then the indices will decrease. The dose spillage is less outside the target volume; at the same time, if the dose coverage is reduced inside the target volume, then the $CI_{paddick}$ value is reduced. Ideally, the $CI_{paddick}$ value is 1, if the target coverage is 100% prescription dose and the volume received outside the target is zero.

International Commission on Radiation Units homogeneity index

International Commission on Radiation Units (ICRU) homogeneity index (HI) defines the overdose and it cannot indicate the underdosage to the target. Therefore, ICRU 83[17] recommends for the ratio of difference between the near minimum and the near maximum to the median dose of target.
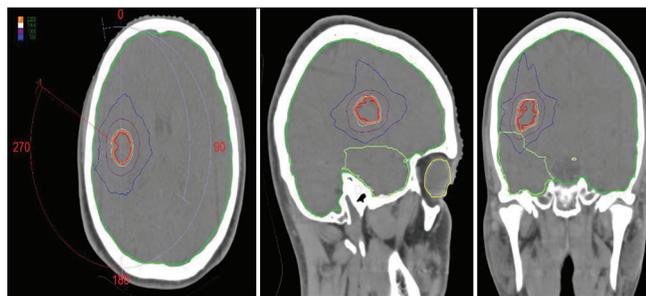
Figure 3: Isodose lines shown in axial, coronal and sagittal computed tomography images of the multi-leaf collimator-based linear accelerator plan; 2 coplanar and 2 noncoplanar arc beam geometry also shown. Red-arteriovenous malformation (target); 22 Gy-orange (prescription dose); 20 Gy-white; 10 Gy-purple; 5 Gy-blue

$HI_{ICRU} = (D2\%-D98\%)/D50\%$

Clinical perspective in SRS is a higher dose in the center of the target and a lower dose (which is usually the prescription dose) in the edges of the target. Therefore, the HI is generally a description of the minimum isodose line (which encompasses the target) and the isodose line ranging from 60% to 85%, depending on clinical acceptance.

Gradient score

In single fraction stereotactic treatments, low-dose region is also important to analyze normal tissue complication. In order to analyze the low dose, the GI is defined as the ratio of the volume of 50% isodose to the volume of prescription isodose.[18]

Gradient Score $(GS)_{50} = PIV_{half}/PIV$

PIV_{half}- volume of 50% prescription isodose; PIV.

The quality of the plan could be analyzed using further low doses (e.g., 40%, 30%) also. Although a GS of 40% was followed for the present study, 30% gradients were also extracted.

- $GradientScore_{70} = PIV_{70\%}/PIV$
- $GradientScore_{40} = PIV_{40\%}/PIV$
- $GradientScore_{30} = PIV_{30\%}/PIV$
- $PIV_{70\%}$- volume of 70% prescription isodose;
- $PIV_{40\%}$- volume of 40% prescription isodose
- $PIV_{30\%}$- volume of 30% prescription isodose
- Normal structure dose and image guidance.

The normal brains receiving 5Gy (V_{5Gy}), 10Gy (V_{10Gy}), 12Gy (V_{12Gy}), and 20Gy (V_{20Gy}) were derived and compared among FIXED, IRIS and MLC-based plans. The dose received by normal brain volume of 10cc (D_{10cc}), Brainstem, Optic chiasma, and Optic nerves were compared for three different collimators. In Cyberknife, the intra-fractional motion is taken care by orthogonal 2D-kilo voltage imaging system. In LINAC frameless SRS, pretreatment volumetric CBCT was used for patient positioning verification. In this study, we evaluated the patient setup uncertainties in both Cyberknife and LINAC.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics for planning parameters (Target volume, treatment time, etc.), dosimetric data (target conformity, target homogeneity, etc.), and normal structure doses were analyzed. Paired sample *t*-test (dependent sample *t*-test) was used to analyze the mean difference (MD) among the sets of data and its significance. In the above test, FIXED collimator was taken as a reference and its parameters were compared with IRIS and MLC-based planning parameters.

RESULTS

The median age of the study cohort was 27 years (range 13–52 years). The mean treatment volume of AVM was

3.16cc (standard deviation [SD] 4.91cc) (range 0.124cc–22.19cc). The mean short axis and the long axis diameter was 13.7 mm (range 3–34.5 mm; SD ± 8.68 mm) and 21.1 mm (range 7–45 mm; SD ± 10.71 mm), respectively [Table 1]. The prescription isodose line was ranging from 70% to 92% with a mean value of 79% (SD ± 5.2%). No significant deviation was found in AVM dose coverage (P = 0.45 and 0.237 for FIXED vs. IRISs and FIXED vs. MLC, respectively) between the collimators. Dose conformity was better for CK plans, and the mean CI was comparable for FIXED and IRIS plans. When comparing $CI_{Paddick}$, no significant (P = 0.188) deviation was found between FIXED and IRIS. Mean $CI_{Paddick}$ was 0.67 (range 0.41–0.91, SD=±0.14) for FIXED plan and it was 0.51 (range 0.31–0.85, SD = ±0.18) in MLC-based plan (excluding the two smallest targets), and it was found statistically significant (P = 0.001). The mean $CI_{Paddick}$ for IRIS collimator was 0.63 (range 0.4-0.86, SD ± 0.12 and it was statistically insignificant (P = 0.231) when comparing FIXED collimator-based plans [Tables 3 and Figure 4].

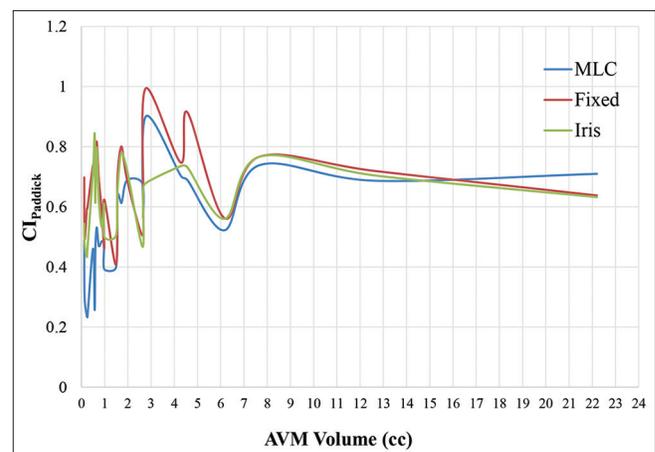The difference of HI_{ICRU} between FIXED and IRIS was insignificant (MD = 0.5, P = 0.823), however, the deviation was 7.99% (P = 0.002) when the FIXED plan was compared with the MLC-based plan. The analysis of lowdose spillage was done by generating different gradient indices such as GS_{70}, GS_{50}, GS_{40}, and GS_{30}. CK plans showed lower GI values [Table 3] owing to appreciable sparing of normal brain volume receiving high doses. Comparing GSs (GS_{70}, GS_{50}, GS_{40}, and GS_{30}), an insignificant difference was found between FIXED and IRIS plans; however, a significant difference was found between GS_{70} and GS_{40} (P = 0.041 and 0.005, respectively) in FIXED and MLCbased plans. The mean GS_{70} for the CK plan (Fixed) was 3.8, whereas a higher index of mean value of Linac plan is 7.3 resulting in statistical significance.

The MD between FIXED and MLCbased plans of D_{10cc} received by normal brain was 3.5Gy and it was found to be significant (P = 0.000) [Table 4] in favor of CK. MD of D_{10cc} of brain-AVM between FIXED and MLCbased plans were 36.08cc (P = 0.009), 7.12cc (P = 0.000), 5.84cc (P = 0.000), and 1.56cc (P = 0.000) for 5Gy, 10Gy, 12Gy, and 20Gy, respectively. Doses to brainstem, optic chiasma, and optic nerves were acceptable for both CK and MLCbased plans [Table 5]. Plans generated in CK using FIXED and IRIS collimators had comparable dosimetric quantities and MU values but significantly higher treatment time for FIXED collimator. The distance between 100% prescription dose to 80% and 50% was compared for anterior, posterior, lateral-medial and superior-inferior directions for all three collimators [Table 6]. In all the targets, the distance between these two isodose line was lesser and comparable between FIXED and IRIS collimator when comparing MLC-based plans in all directions (except superior-inferior for some targets). Mean MU for delivering 15Gy to 22Gy to AVM was 11582 (SD ± 3649), 9999.4 (SD ± 3126.2), and 5870 (SD ± 1171.5) for FIXED, IRIS and MLC-based plans, respectively [Table 4]. Analysis of the LINAC plan shows a significantly lesser MU and shorter treatment times with respect to the CK plans. However, patient positional error during the delivery is a concern. In $CI_{Paddick}$, the maximum

Table 3: Mean, standard deviation, *t* and *P* value of the Target coverage, Paddick conformity index, International Commission on Radiation Units and Measurements homogeneity index, gradient score 70%, gradient score 50%, gradient score 40% and gradient score 30% for FIXED, IRIS and multi-leaf collimator-based plans

Parameter	Collimator	Mean±SD	*t*	*P*
Target coverage (%)	FIXED	99.68±3.92		
	IRIS	99.8±6.28	−0.765	0.452
	MLC	98.57±4.91	−1.212	0.237
$CI_{Paddick}$	FIXED	0.67±0.14		
	IRIS	0.63±0.12	1.212	0.231
	MLC	0.51±0.18	−3.542	0.001
HI_{ICRU} (%)	FIXED	22.58±7.97		
	IRIS	22.02±9.48	0.225	0.823
	MLC	14.59±9.27	−3.266	0.002
GS 70	FIXED	3.8±1.2		
	IRIS	4.4±2.03	0.421	0.675
	MLC	7.3±4.66	2.103	0.041
GS 50	FIXED	6.5±2.41		
	IRIS	7.5±3.88	0.432	0.668
	MLC	8.52±5.83	0.681	0.499
GS 40	FIXED	9.1±3.5		
	IRIS	10.3±5.39	0.471	0.640
	MLC	21.84±16.24	2.981	0.005
GS 30	FIXED	13.0±6.62		
	IRIS	14.70±7.34	0.518	0.607
	MLC	25.74±18.4	1.843	0.071

HI_{ICRU}: International Commission on Radiation Units and Measurements homogeneity index, $CI_{Paddick}$: Paddick conformity index, GS 70: Gradient score 70%, GS 50: Gradient score 50%, GS 40: Gradient score-40%, GS 30: Gradient score 30%, SD: Standard deviation, MLC: Multi-leaf collimator

Figure 4: Arteriovenous malformation volume versus Paddick CI for multi-leaf collimator, FIXED and IRIS collimator-based plans. Above 1.5cc arteriovenous malformation volume, multi-leaf collimator and CK plans shows the small deviaition

Table 4: Mean, standard deviation, *t* and *P* value of normal brain D_{10cc}, V_{5Gy}, V_{10Gy}, V_{12Gy} and V_{20Gy}

Brain-AVM	Collimator	Mean±SD	*t*	*P*
D_{10cc} (Gy)	FIXED	8.51±4.23		
	IRIS	8.61±3.97	−0.085	0.743
	MLC	12.04±3.52	−3.204	0.000
V_{5Gy} (cc)	FIXED	34.83±44.44		
	IRIS	33.09±40.58	0.144	0.886
	MLC	70.91±73.43	−2.846	0.009
V_{10Gy} (cc)	FIXED	10.38±14.09		
	IRIS	11.92±12.63	−0.409	0.684
	MLC	17.50±15.56	−11.324	0.000
V_{12Gy} (cc)	FIXED	6.75±9.5		
	IRIS	7.24±8.63	−0.191	0.850
	MLC	12.59±12.20	−7.242	0.000
V_{20Gy} (cc)	FIXED	0.46±0.72		
	IRIS	0.54±0.78	−0.42	0.676
	MLC	2.02±2.38	−3.958	0.001

D_{10cc}: Dose received by 10cc volume of normal brain, V_{5Gy}: Volume of normal brain receiving 5Gy, V_{10Gy}: Volume of normal brain receiving 10Gy, V_{12Gy}: Volume of normal brain receiving 12Gyy, V_{20Gy}: Volume of normal brain receiving 20Gy, AVM: Arteriovenous malformation, SD: Standard deviation, MLC: Multi-leaf collimator

Table 5: Mean, standard deviation, *t* and *P* value of brainstem, optic chiasma, optic nerve left, optic nerve right, monitor units and treatment time for FIXED, IRIS and multi-leaf collimator-based plan

Critical structure	Collimator	Mean ± SD (Gy)	*t*	*P*
Brain stem	FIXED	5.28 ± 4.35		
	IRIS	5.71 ± 4.75	−0.906	0.374
	MLC	4.75 ± 4.25	1.125	0.272
Optic chiasma	FIXED	2.23 ± 2.14		
	IRIS	1.89 ± 1.84	2.45	0.022
	MLC	3.21 ± 3.07	−3.94	0.001
Optic nerve left	FIXED	1.25 ± 1.64		
	IRIS	1.22 ± 1.75	0.203	0.841
	MLC	1.84 ± 2.00	−3.024	0.006
Optic nerve right	FIXED	0.98 ± 1.10		
	IRIS	1.00 ± 1.09	−0.156	0.878
	MLC	1.61 ± 1.15	−3.471	0.002
MU	FIXED	11,583 ± 3650		
	IRIS	9999 ± 3126	1.648	0.106
	MLC	5871 ± 1172	−7.451	0.000
Delivery time (min)	FIXED	50.56 ± 9.69		
	IRIS	37.12 ± 8.33	5.259	0.000
	MLC	26.08 ± 3.19	−12.002	0.000

MU: Monitor units, MLC: Multi-leaf collimator, SD: Standard deviation

difference was found in volume lesser than 1.5cc. Above 1.5cc volume, no significant difference was found between FIXED CK plans and MLC-based plans for $CI_{paddick}$ ($P = 0.116$). If the AVM volume was less than 0.7cc, the FIXED CK plan shows a significant ($CI_{Paddick}$ MD = 0.06, $P = 0.032$) advantage in terms of conformity when compared to the IRIS CK plan [Figure 5].

The absolute mean dose difference between planned and measured doses in phantoms were 1.66% (SD = 0.77%), 1.95% (SD=±0.87%), and ± 1.83% (SD=±1.02%) for Fixed, IRIS and MLC based plans, respectively.

DISCUSSION

This study evaluated the plan quality comparison of FIXED and IRIS collimators in CK plans and MLC-based collimator in LINAC plans for SRS. Target coverage for the AVM was above 98% for all three collimator-based plans. Blamek *et al*.[11] studied the dosimetric comparison for large or critically located AVM plans, which were generated by CK and LINAC mMLC with a mean volume of 21.7cc (1.02cc to 146.45cc) for 15 patients. The mean $CI_{Paddick}$ (it was denoted as conformation number-CN[19]) was 0.68, 0.58 for CK based and L-mMLC plans, respectively. They found, all the CK plans has the superior conformity over mMLC based linac plans and the conformity has been worsened if the volume was < 1cc. Stanley *et al*.[20] compared the various indices for MLCbased SRS in brain metastases patients and stated that the mean $CI_{Paddick}$ value was 0.556 and the maximum CI value was observed at 0.12 cc. In our study, the same pattern was observed with above study but in single large volume target ($CI_{Paddick}$ = 0.505 for 2.627 cc) has the worst conformity. It shows the conformity is not always depends on the volume, but it is also depending on the shape of target which is the scope of future research especially in vast irregular (nidus volume) targets like AVM. In single largest target (22.19cc), the $CI_{Paddick}$ value shows the better conformity in MLC based plan and it was due to number of arcs and high intensity modulation were provided the better conformity than cyberknife-based plan.

Conformity and gradient (high dose and low dose spillage) are also depending on coplanar and non-coplanar arrangements of the beam. Clark *et al*.[13] studied the single-isocenter VMAT plan feasibility for multiple brain metastasis and stated that moderate dose spill (GS) is reduced when multiple non co-planar arcs are used. Multiple noncoplanar arcs could provide a better GS where the targets are close to the critical structures. Hanna *et al*.,[21] evaluated VMAT based image guided radiosurgery for multiple (range 2–9) brain metastasis with the volume in the range of 0.89-–65.05 cc. They have used multiple noncoplanar which has 3–4 couch angles (~0°, 60°, and 300°) with co-planar arcs for all the patients and elucidated the multiple nonplanar arcs could provide more conformity and sparing of normal brain than co-planar arcs. In our study, all the patients were planned with coplanar and noncoplanar arcs (at least two noncoplanar) for achieving less normal brain dose. The clinical advantage of high dose inside the target is preferable for SRS and it could lead to excellent local control of the tumor and reduces the radio necrosis in brain. Due to this, the prescription isodose kept at the periphery is 60%–80% (relative to maximum dose) range.[22]

In this study, the HI_{ICRU} for CK-based plans were in the range of 18%–32% except one AVM which was inside the

Table 6: Distance between prescription isodose to 80% and 50% isodose for anterior, posterior, right, left, superior and inferior directions-FIXED, IRIS and multi-leaf collimators for small, medium, large volume targets

| | Small volume (0.134cc) | | | | | | Medium volume (1.5556cc) | | | | | | Large volume (22.194cc) | | | | | | Mean | | | | | |
| | Distance (100%-50% dose) (mm) | | | Distance (100%-80% dose) (mm) | | | Distance (100%-50% dose) (mm) | | | Distance (100%-80% dose) (mm) | | | Distance (100%-50% dose) (mm) | | | Distance (100%-80% dose) (mm) | | | Distance (100%-50% dose) (mm) | | | Distance (100%-80% dose) (mm) | | |
	FIXED	IRIS	MLC	FIXED	IRIS	MLC	FIXED	IRIS	MLC	FIXED	IRIS	MLC	FIXED	IRIS	MLC	FIXED	IRIS	MLC	FIXED	IRIS	MLC	FIXED	IRIS	MLC
Anterior	2.75	5.1	5.8	1.15	1.21	2.2	4.6	5.05	7.3	1.8	2.1	1.9	8.2	7.58	11.2	5.45	6.11	8.3	3.9	6.36	7.62	1.6	1.735	2.7
Posterior	3.66	4.5	5.4	1.82	1.92	2.7	4.56	5.54	6.4	1.7	2	2	7.82	8.58	10.5	6.41	6.45	7.8	4.8	5.88	7	2.25	2.42	3.2
Right	2.74	3.58	1.07	1.12	1.87	4	4.7	6.42	7.5	1.65	1.92	2.6	8.35	9.52	11.5	6.15	5.89	8.1	3.91	5.18	2.94	1.53	2.35	4.7
Left	3.1	3.74	1	1.15	1.65	5	4.58	4.92	6.4	1.85	1.96	2	7.42	7.87	12.6	5.89	4.58	8.7	4.24	4.97	2.6	1.61	2.14	5.5
Superior	2.8	4.58	2.5	1.4	1.45	1.2	4.5	5.86	3.4	1.55	2.15	0.8	6.98	8.88	11.4	5.33	5.78	7.4	3.92	6.04	3.35	1.79	1.98	1.4
Inferior	2.77	3.5	5.4	1.1	1.31	2.9	3.5	4.39	2.8	1.65	2.25	1.1	5.82	6.66	15.3	5.24	7.35	7.8	3.64	4.598	6.1	1.51	1.87	3.2

Mean distance was estimated based on all the planned AVMs. AVM: Arteriovenous malformation, MLC: Multi-leaf collimator

brainstem (it needs homogeneous dose and its HI_{ICRU} was 11.9% and PD was 15Gy) but in MLC based plans the HI_{ICRU} was in the range of 7.4%–24.8%. Increasing the dose inside the target (in Linac MLC plans) which has <1cc volume has also increasing the dose at the target edges (due to smaller AVM volumes) which lead to reduce the conformity of the MLC based plans. If the volume of the AVM is large, then the high dose dummy structures were drawn (with high dose constraints during optimization) to increase the dose at center of the target. HI_{ICRU} was comparatively higher in CK plans, which emphasize that the increasing of the high dose inside the target volume is more feasible if small circular cones or collimators are used. Lowdose spillage is a crucial parameter for predicting and reducing the risk of radio necrosis in the brain. V_{8Gy}–V_{16Gy} to the normal brain is a crucial dose for analyzing the radio necrosis.[23,24] High GS observed in MLC-based plans were due to coplanar arcs which were overlapping each other in the target segment. It could be avoided, if the VMAT plans were performed with a greater number of noncoplanar arcs.[25]

The mean GS_{70} of MLCbased plan was 1.92 times higher than that of the FIXED CK plan. The above-mentioned effect was observed for GS_{50} (1.31 times), GS_{40} (2.42 times), and GS_{30} (1.98 times) also (excluding the smallest volume target). Above 1.5cc volume, GS_{70} and GS_{50} were comparatively less (GS_{70} MD = 0.39 [$P = 0.140$], GS_{50} MD = 0.27 [$P = 0.368$]) and they were insignificant when compared with the FIXED- and MLCbased plans [Figure 6]. It was observed in MLCbased plans that the irregularity of the AVM could increase the D_{10cc}, V_{12Gy} to the brain. Below 0.7cc volume, GS_{70} and GS_{50} were comparatively less (GS_{70} MD = 1.49 [$P < 0.006$], GS_{50} MD = 2.77 [$P < 0.002$], GS_{30} MD = 4.9 [$P < 0.015$]) and they were significant when compared to the FIXED and the IRIS plans [Figure 7]. Han *et al.*[26] studied dosimetric comparison of fractionated radiosurgery using Gamma knife, CK and linac based plans for multiple large brain metastases. They stated the average sparing of normal brain volume receiving 12Gy and 20Gy has been reduced by ~20% for GK and CK based plans when comparing linac plans. In CK, the collimator resolution is ranging from 2.5 to 10 mm and it could provide the steeper dose gradient and increased conformity. However, in linac based MLC has the resolution of 4 mm in longitudinal axis has the limitation for improving the conformity and dose gradient even with the increasing the number of coplanar/ noncoplanar arcs in linac-based plans. Decreasing trend was observed when increasing the AVM volume for all three collimators [Figure 8]. FFF beam could provide increased clinical efficiency.[27] Penumbral width for the FFF beam and the FF beam is also a factor for dose gradient and the FFF beam requires a less modulation when compared to the FF beam.[28] FFF beam requires more MU when compared to the FF beam because of the conical shape profile, which crosses a steep dose gradient between the central and the peripheral areas of the target. It increases better conformity and steep dose gradient. Furthermore, leaf width and modulation of the
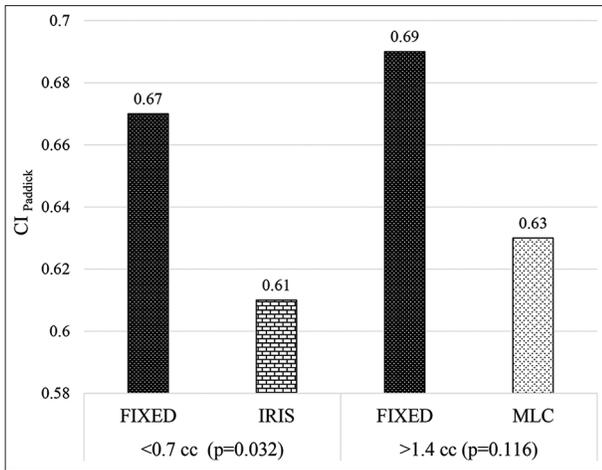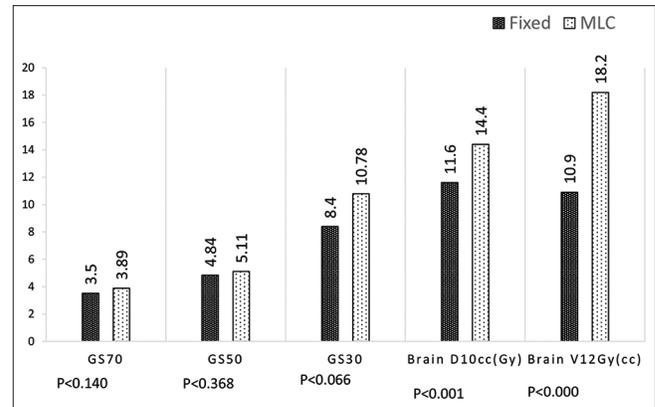
Figure 5: Paddick conformiity index for the arteriovenous malformation volume below 0.7cc for FIXED versus IRIS plans and above 1.4cc for FIXED Vs multi-leaf collimator-based plans
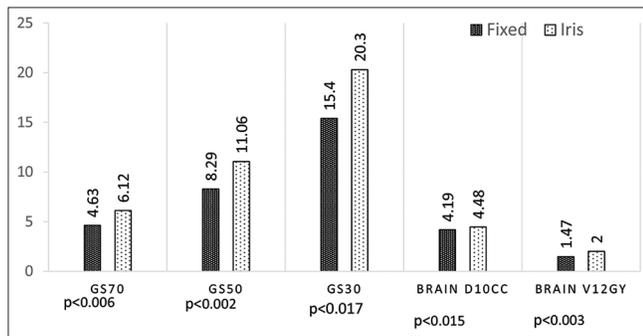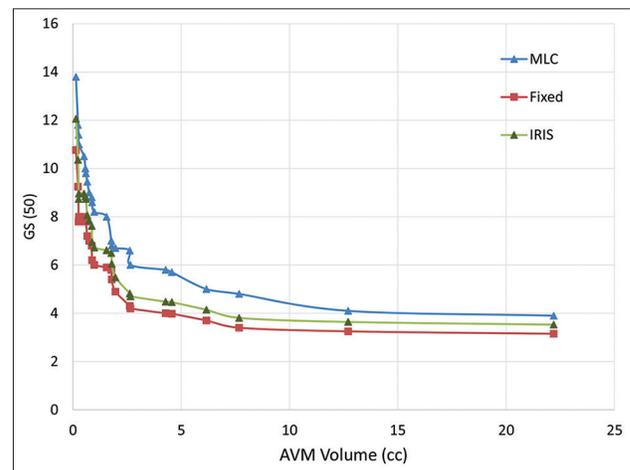

Figure 7: GS70, GS50, GS30, D10cc and V12 Gy of normal brain dose for arteriovenous malformation volume below 0.7ccfor FIXED cone and IRIS collimator-based CK plans

Figure 6: GS70, GS50, GS30, D10cc and V12 Gy of normal brain dose for arteriovenous malformation volume above 1.5cc for FIXED CK plans and multi-leaf collimator plans

Figure 8: Comparison of Gradient score (50) between multi-leaf collimator, Fixed and IRIS collimator-based plans

beam are the crucial factors to conform the dose within the target while reducing the highdose spillage.

In CK, the SSD was changed to target and the collimator size was changed for performing the modulation. The advantage of CK beam delivery is that FFF beams with conical shaped collimators provide a sharper dose fall-off. In our results, the target conformity is more in CK-based plans for both FIXED and IRIS collimators, and it was superior in the FIXED collimator where a 5 mm cone was used. A 5 mm cone is not recommended in IRIS,[12] due to the dosimetric straggling effect and the poor reproducibility of shape. In this study, VMAT was showing lesser delivery time due to the minimum segment size being comparatively bigger than the CK collimator size (e.g., 5 mm). In CK, a higher degree of freedom to manipulator movement provides better conformity, which leads to more treatment time. Increased MU in CK is due to the higher number of positions for the manipulator and the changing of collimator for the same position. Where available FFF beam delivery could reduce the treatment time further in VMAT plans, when compared to FF beams used by us. Kang *et al*.[29] studied dosimetric characteristics of small MU settings and

observed 10% of error when a small MU segment was used. In LINACbased cranial SRS, a small segment, and a low MU could lead to dosimetric uncertainty in beam delivery. If dose delivery uncertainty was <1% in <5MU and it is considered dosimetrically acceptable.[30] In our study, the mean MU per segment is 4.2 (SD ± 2.8) and it is dosimetrically feasible to deliver (acceptable tolerance <1%). Podder *et al*.[31] studied the leakage measurement for synergy beam modulator and the mean and maximum leakage was found to be 0.9% ±0.014% and 1.6% ±0.07%, respectively. The maximum leakage of FIXED and IRIS is 0.05% and 0.12%, respectively. The two-bank tungsten design in this collimator could reduce the leakage, which is less than that of the FIXED collimator.[12] The brain-PTV dose is less in CKbased plans due to less leakage and small pencil beams.

Studies previously published from our institution show that it is possible to achieve an intra-fractional variation <1 mm in translational shift and an intra-fractional variation <1° in rotational shift.[32,33] Some studies show that in LINACbased SRS, the comparison between online CBCT (pre-treatment

and post-treatment) and Exact track® (Brainlab) demonstrated that orthogonal 2D-imaging verification (something missing) was <1.01 mm and translational shift was < 0.95°, and the deviation should not be avoided. Mechanical accuracy is an important parameter to provide the margin around the gross target. Isocenter tolerance in synergy is <2 mm diameter and 1 mm for CK. Margin is needed for LINAC SRS, which leads to an increase in normal brain dose. Jhaveri *et al*.[34] studied the impact of margin with local recurrence and symptomatic radiation necrosis. They found that expanding the PTV margin more than 1 mm could increase the risk of symptomatic necrosis and not associated with recurrence. In our study GS (GS50) was inverse to target volume and in small volume it has more statistical uncertainty [Figure 8].

CONCLUSION

In cranial SRS, volume of normal brain and surrounding critical structures are crucial if the volume of target is small. Suitable collimators of choice could provide a better conformity and a steep dose gradient to the target, without increasing the dose to the critical structures. In our study, small volume (<0.7cc) targets should be treated with CK FIXED and volumes > 0.7cc could be treated by using either FIXED collimator or IRIS collimator. AVM volume >1.4 cc can be treated with either LINAC MLC-based SRS (with stringent plan analysis with volumetric image guidance) or CK. Linac MLC-based SRS has some limitations when compared to CK in terms of conformity and low-dose spillage, and it shows some advantages like reduced treatment time and MU that could reduce the setup uncertainty. If the tolerances are achieved for the organs-at-risk in MLC-based LINAC plan, it could be delivered with volumetric image guidance.

Conflicts of interest

There are no conflicts of interest.

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