RESEARCH ARTICLE

Dosimetric Comparison and Feasibility of Simultaneous Integrated Boost (SIB) in Treatment of Malignant Gliomas Using Intensity Modulated Radiotherapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT)

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Abstract

Objective: To evaluate the dosimetric parameters of Simultaneous Integrated Boost in the treatment of malignant gliomas and compare the SIB plans of VMAT and IMRT. **Methodology:** CT and MRI of 28 patients were used for generating SIB plans with VMAT and IMRT. A dose of 2Gy per fraction was prescribed to the CPTV and 2.4Gy to the GPTV for a total of 25 fractions. The plans were accepted only if they met the set of planning objectives defined in the protocol. **Results:** We could achieve the planning objectives in all the SIB plans. Although GPTV coverage was statistically better in VMAT (98.67% vs 98.19% ;p=0.024) the difference is not clinically meaningful. The conformity index for GPTV was higher in IMRT (0.83 vs 0.76; p=0.001). The coverage of CPTV was better in IMRT (97.88% vs 96.87%; p=0.021). But the conformity index of CPTVannulus was higher in VMAT (0.72 vs 0.67; p=0.01). There was no difference in homogeneity index of GPTV and CPTV annulus between the plans. The mean dose received by normal brain was higher in IMRT (28Gy vs 24.2Gy; p<0.001). Ipsilateral optic nerve has received lesser Dmax in IMRT (44.2Gy vs 46.95Gy; p=0.02). No difference was seen in Dmax of brainstem, optic chiasm, contralateral optic nerve. The treatment times and monitor units were significantly less in VMAT. **Conclusion:** SIB is dosimetrically feasible for hypofractionation in malignant gliomas using IMRT and VMAT. IMRT plans had better boost conformity, lower ipsilateral optic nerve and brainstem maximum doses compared to VMAT. Whereas, VMAT had better coverage, better overall PTV conformity, lower normal brain mean dose, lower monitor units and lesser treatment times. Although planning of VMAT is cumbersome and time consuming, the advantage of reducing treatment time is beneficial to the patients' comfort and better managing of patient load in high volume centres.

Keywords: Dosimetry- gliomas- IMRT- VMAT- SIB

Introduction

The standard of care in the treatment of high-grade gliomas is maximal surgical resection followed by adjuvant radiotherapy. The prognosis of high-grade gliomas especially that of Glioblastoma is very poor. Combining of radiotherapy and chemotherapy (concomitant and adjuvant temozolomide) has shown a significant survival benefit and minimal additional toxicity in patients with glioblastoma multiforme. However there is a high chance of tumor recurrence and this is considered the most common cause of treatment failure. So different strategies of dose prescription and planning techniques have been tried to achieve better tumor control and better sparing of organs at risk (OARs) (Cha et al., 2014; Nakamatsu et al., 2008; Narayana et al., 2006).

IMRT techniques employ variable intensity with multiple radiation beams resulting in greatly improved target volume conformity and improved sparing of normal tissues and organs at risk (OARs) (Veldeman et al., 2008). IMRT also has the ability to produce inhomogeneous dose distributions, which allows the simultaneous delivery of different doses per fraction to separate areas within the target volume. This is the basis behind simultaneous integrated boost (SIB) delivery. VMAT allows simultaneous variation of three parameters during treatment delivery, i.e. gantry rotation speed, treatment aperture shape via movement of MLC leaves and dose rate. This results in further improvement in target volume conformity and OAR sparing (Teoh et al., 2011).

In our study, we wanted to test the feasibility of SIB planning while achieving the set dosimetric objectives and compare the dosimetric parameters between SIB-VMAT and SIB- IMRT.

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Materials and Methods

Simulation images of 28 sequential patients were used for generating SIB plans. Our method of target volume delineation was adapted from the one used by Cho et al., (2010) in their SIB study. We have modified the Cho et al., (2010) protocol to include tumor edema in the high-risk PTV and a 2cm margin was given to this and designated as low-risk volume. This modification is based on RTOG-0825 contouring protocol for the sequential method of treatment for malignant gliomas. Target volumes were delineated based on postoperative-enhanced MRI. The FLAIR abnormality is identified as the Gross Tumor Volume (GTV), and it is ensured to include the surgical cavity and contrast enhancing lesion seen in the T1-contrast MRI. To this GTV, a 2 cm margin is given to draw Clinical Target Volume (CTV) which is reduced to 0.5 cm along the natural boundaries to the tumor growth like the skull, ventricles, falx, etc. In the event of overlap of CTV with the critical structures like brainstem, optic nerves or optic chiasm, the CTV is cropped along the structures. Two Planning Target Volumes (PTV) were created. GPTV is the high-risk boost volume which is created by giving a 0.5 cm margin to the GTV. A 0.5 cm margin is given to the CTV and labeled as CPTV. The GPTV is subtracted from CPTV and the resulting circumferential area around GPTV is labeled as CPTVannulus, and this was the low-risk volume for treatment planning. Organs at risk (OARs) are contoured, and a margin of 3 mm is given to create a planning risk volume (PRV). PRVs are created for optic nerves, optic chiasm, and brainstem in our study. In the event of overlap of CPTVannulus or GPTV with any of the PRVs of organs at risk (OARs) and the dose to the OARs cannot be constrained within the set limits, another PTV (PTVoverlap) is created, and a different prescription is given such that the dose received by PTVoverlap is the maximum possible prescription dose that can be received without compromising the OAR tolerance limits.

Dose Prescription

GPTV was prescribed a dose of 2.4 Gy per fraction to a total dose of 60Gy in 25 fractions (EQD2=62.4Gy and BED=78Gy) and CPTV was prescribed a dose of 2 Gy per fraction to a total dose of 50Gy in 25 fractions. Dose constraints were used for organs at risk based on the report by Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) (Marks et al., 2010).

Critical Structure	Maximum Dose (Dmax)
Lenses	10 Gy
Eyes	50 Gy
Optic Nerves	55 Gy
Optic Chiasm	55 Gy
Brainstem	60 Gy
Brain	72 Gy
Cochlea	45 Gy

For the purpose of the study the Dmax is defined as D0.03cc (Dose received by 0.03cc volume) as used in the RTOG-0825 protocol. Eyes were used as a surrogate for Retinae. Brainstem Dmax limit is kept at 60Gy and D1-10cc can receive up to 59Gy. Full organ of brainstem can receive up to 54Gy.

Treatment Planning

After target volume delineation, each contour was evaluated and verified by the Consultant. After contour verification, the SIB-IMRT and SIB-VMAT plans were generated for each patient by the Medical Physicist. To maintain the uniformity among the plans, a template was created based on an ideal plan meeting all the PTV and OAR objectives and used for generating rest of the plans. Planning was done using Varian Eclipse Treatment Planning System (TPS) ver.10.1. for treatment on Varian Clinac-iX linear accelerator (Varian Medical Systems, Inc.,Palo Alto, CA) with Millennium MLC-120 leaves.

SIB-IMRT: For generating IMRT plans, an indigenous method of manually placing multiple beams was used for beam arrangement in 18 of the 28 patients. For rest of the patients, software based beam angle optimization was done using Plan Geometry Optimizer ver.10.0.28 included in the Varian Eclipse TPS. The energy used was 6MV, and a fixed dose rate of 300MU/min was used for each field. The optimization of dose distribution in IMRT was done using Dose Volume Optimizer ver.10.0.28 based on the created template. No collimator angle was given in the fields used in IMRT when manually placed.

SIB-VMAT: For generating VMAT plans, the arc geometry was decided depending on the location and size of the tumor. For smaller peripherally locate tumors, one isocentre-two half rotations were used and for rest of the tumors, one isocentre-two full rotations were used. For tumors which were not adequately covered with two full rotations, an additional non-coplanar semi-arc was used to ensure adequate coverage. A collimator rotation of 30º was used for the VMAT fields and of the two arcs, one is placed clockwise and another counterclockwise. Energy used was 6MV, and a variable dose rate was used with a maximum of 600MU/min. The dose distribution in VMAT plans was optimized using Progressive Resolution Optimizer ver.10.0.28.

For maintaining the uniformity of the plans, same constrains and weightages were used for optimization of all the plans. No adjustments are made to the plan to improve the conformity indices once they meet the planning objectives. Instead, conformity index is measured as an outcome variable.

Planning Objectives

• 98% of GPTV should receive 5700 cGy, and 98% of CPTVannulus should receive 4750 cGy.

• The minimum dose to the target volume should be kept within 10% of the dose at the center of the volume.

• The near Dmax (D1%) for GPTV should be less than 6600cGy and for CPTVannulus, it should be less than 6000cGy.

• Reduce OAR mean doses as much as possible without violating the above-stated objectives.

Compliance Criteria

• 95% of GPTV is covered by 6000cGy,and 99% of GPTV is covered by 5400 cGy. 95% of CPTVannulus is covered by 5000cGy,and 99% of CPTVannulus is covered by 4500 cGy.

• Variation Acceptable: 90% of GPTV, is covered by 6000cGy, 97% of GPTV is covered by 5400cGy,and 90% of CPTV is covered by 5000cGy, and 97% of CPTV is covered by 4500cGy.

• Deviation Unacceptable:<90% of GPTV is covered by 6000cGy,<97% of GPTV is covered by 5400cGy. And <90% of CPTV is covered by 5000cGy <97% of CPTV is covered by 4500cGy.

Results

All the plans met the planning objectives as mentioned in the protocol. The dosimetric data was obtained from the Dose Volume Histograms(DVHs) generated in the Varian Eclipse Treatment Planning System(TPS). Dosimetric parameters were tested for normal distribution using Kolmogorov–Smirnov test (K–S test). Since two different plans were generated in the CT image set of every individual patient, the data is considered matched pair and paired tests are used to compare the two plans. For normally distributed variables, paired t-test is used and for non-normally distributed variables, a corresponding non-parametric test Wilcoxon signed rank test is used. All the dosimetric values are reported in mean (±SD) and median (minimum-maximum) values. All statistical analyses were carried out with 5% level of significance, and p<0.05 was considered as significant. We have used IBM-SPSS v19 for statistical analysis and Microsoft Excel

for generation of graphs.

The results of dosimetric comparison are given in the Table 1.

The mean GPTV volume was 255.5cc (± 127.1cc) and mean volume of CPTV annulus was 330.5cc (± 104.4cc). Most of the patients had at least one overlapping OAR with the CPTV. The median number of overlapping OARs is 3 (0-4) with 71.5% of patients having at least 3 overlapping OARs. For achieving the stated planning objectives, the number of fields used for optimization in IMRT ranges from a minimum of 5 to a maximum of 11. The median number of fields used for IMRT are 9. Most of the VMAT plans (67.9%) were optimized using one isocentre – two complete rotations. In others, a complimentary non-coplanar semi-arc was used in 5 patients, two semi-arcs were used in 2 patients who had awell-lateralized tumor, three full rotations were used in one patient, and three semi-arcs were used in one patient.

All the plans in our study have met the planning objectives that were described in the protocol. This indicates that Simultaneous Integrated Boost using Intensity Modulated Radiotherapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT) is dosimetrically feasible in the treatment of malignant gliomas. In our study, we found that, when comparing the dosimetric parameters of GPTV, the SIB-VMAT plans had slightly better coverage [98.67% (±1.06) vs 98.19% (±1.36); p=0.024], D98% (57.87Gy vs. 57.53Gy; p=0.024), and

Table 1. Summary of the Results of the Study

Variable	SIB-IMRT	SIB-VMAT	Relative diff. [%]	p-value
Conformality index of GPTV	0.83 (0.73-0.97)	0.76 (0.57-0.96)	-8.43	0.001†
Conformality index of CPTV	0.67 (0.56-0.82)	0.72 (0.55-0.84)	7.46	0.01†
Homogeneity index GPTV	0.13 (0.08-0.18)	0.12 (0.07-0.18)	-7.69	0.108
Homogeneity index CPTV	0.19 (0.13-0.25)	0.19 (0.13-0.25)	0	0.346
Near maximum dose [D1%] (Gy)	65.5 (61.6-67)	65.84 (64-67)	0.52	0.21
Brainstem max dose (Gy)*	53.07 (0.7-60)	58 (3.4-61)	9.29	0.003†
Brainstem mean dose (Gy)*	26.9 (1.4-41.5)	26.52 (1.2-43.4)	-1.41	0.061
Optic chiasm max dose (Gy)*	49.4 (1.5-56.5)	50.2 (1.5-56.5)	1.62	0.064
Optic chiasm mean dose (Gy)*	39.37 (1.2-51.6)	39.62 (1.2-54.7)	0.63	0.665
Ipsilateral optic nerve max dose (Gy)*	46.6 (1.5-56.8)	53.5 (1.4-58)	14.8	0.056
Ipsilateral optic nerve mean dose (Gy)*	30.2 (1-45.5)	31.1 (1-50.8)	2.98	0.136
Contralateral optic nerve max dose (Gy)*	36.9 (1.4-53.1)	36.47 (1.2-57)	-1.16	0.676
Contralateral optic nerve mean dose (Gy)*	21.1 (1-42.1)	21.4 (0.9-42)	1.42	0.767
Ipsilateral lens max dose (Gy)	7.28 (0.8-10.7)	7.78 (0.8-12.5)	6.86	0.158
Contralateral lens max dose (Gy)	6.3 (0.7-10.9)	7.34 (0.8-10.6)	16.5	0.002†
Ipsilateral eye max dose (Gy)	28.02 (1.3-45.3)	26.13 (1.1-41.6)	-6.74	0.349
Ipsilateral eye mean dose (Gy)	12.63 (0.7-39.4)	13.04 (0.8-19.9)	3.24	0.119
Contralateral eye max dose (Gy)	21.6 (1-45.5)	19.37 (1-32.8)	-10.32	0.262
Contralateral eye mean dose (Gy)	10.25 (0.7-32.5)	10.84 (0.7-18.9)	5.75	0.509
Normal brain max dose (Gy)	58.62 (52.8-62)	57.73 (53.1-63.1)	-1.52	0.088
Normal brain mean dose (Gy)	28 (49-57.5)	25.12 (11.2-36.5)	-10.28	<0.001†
MUs to treat single fraction	1681.5 (771-2696)	620.86 (319-1610)	-63.07	<0.001†
Time to treat single fraction (min)	5.29 (2.57-8.98)	2.62 (1.66-3.92)	-50.47	<0.001†

Relative difference (%), [(VMAT-IMRT)/IMRT] x 100. The negative value indicates that the VMAT had lower values. For Conformality index and Homogeneity index, lower values are better. *indicates that PRV values are used.†indicates significant p-value (<0.05).

Table 2. Comparison of Dosimetric Parameters of Our Study with Other Studies

|	Cases	Dose [Gy/fr]	BED	annulus volume (cc)	Boost volume (cc)	Coverage annulus [%]	Coverage boost [%]	mean dose for normal brain [Gy]	D95% for annulus [Gy]	D95% for boost [Gy]	Max Brainstem dose [Gy]	Max Optic Chiasm dose [Gy]	Max Ipsi Optic nerve dose [Gy]
Chan et al (2003)	5	GTV: 70/33; GTV + 25mm: 59.4/33	88.55	361	58	98	98	27	-	-	58	43	43
Hermanto et al (2007)	20	GTV + 25 mm: 50/30, GTV + 5 mm: 60/30	75	347	90	99.7	99.4	19.1	-	-	45.8	27.6	14.6
Thilmann et al (2001)	20	GTV + 1 mm margin: 75/30; Edema + 15 mm margin: 60/30	98.44	-	-	88.4	87.5		-	-	-	-	-
Sultanem et al (2004)	25	GTV: 60/20, GTV+15-mm margin: 40/20	82.5	207	40	-	-	-	43.8	58.5	-	-	-
Nakamatsu et al (2008)	13	GTV + 5 mm: 70/28; Edema: 56/28	91.88	240.9	106.2	99.9	99.9	25.7	57.1	69.9	42.9	21.6#	
Suzuki et al (2003)	6	GTV + 5 mm: 70/28, Edema + 25 mm: 56/28	91.88	263.3	104.6	-	90	25.22	55.92	69	-	-	-
Farzin et al (2015)	20	PTV: 54/30; BV: 60/30	75	-	-	-	-	-	-	-	-	24.7	7
Shaffer, IMRT (2010)	10	GTV + 25 mm: 60/30	75	-	343	-	98.3	22.68	-	-	55.6	52.2	51.9
Shaffer, VMAT (2010)	10	GTV + 25 mm: 60/30	75	-	343	-	98.3	24.72	-	-	55.6	52.5	51.3
Current study, SIB-IMRT	28	GTV + 5 mm: 60/25; GTV + 25mm: 50/25	78	330.53	255.55	97.88	98.2	28	49.5	58.85	50.29	43.86	37.7
Current study, SIB- VMAT	28	GTV + 5 mm: 60/25, GTV + 25mm: 50/25	78	330.53	255.55	96.87	98.67	25.12	49.72	59.25	51.06	44.19	39.93
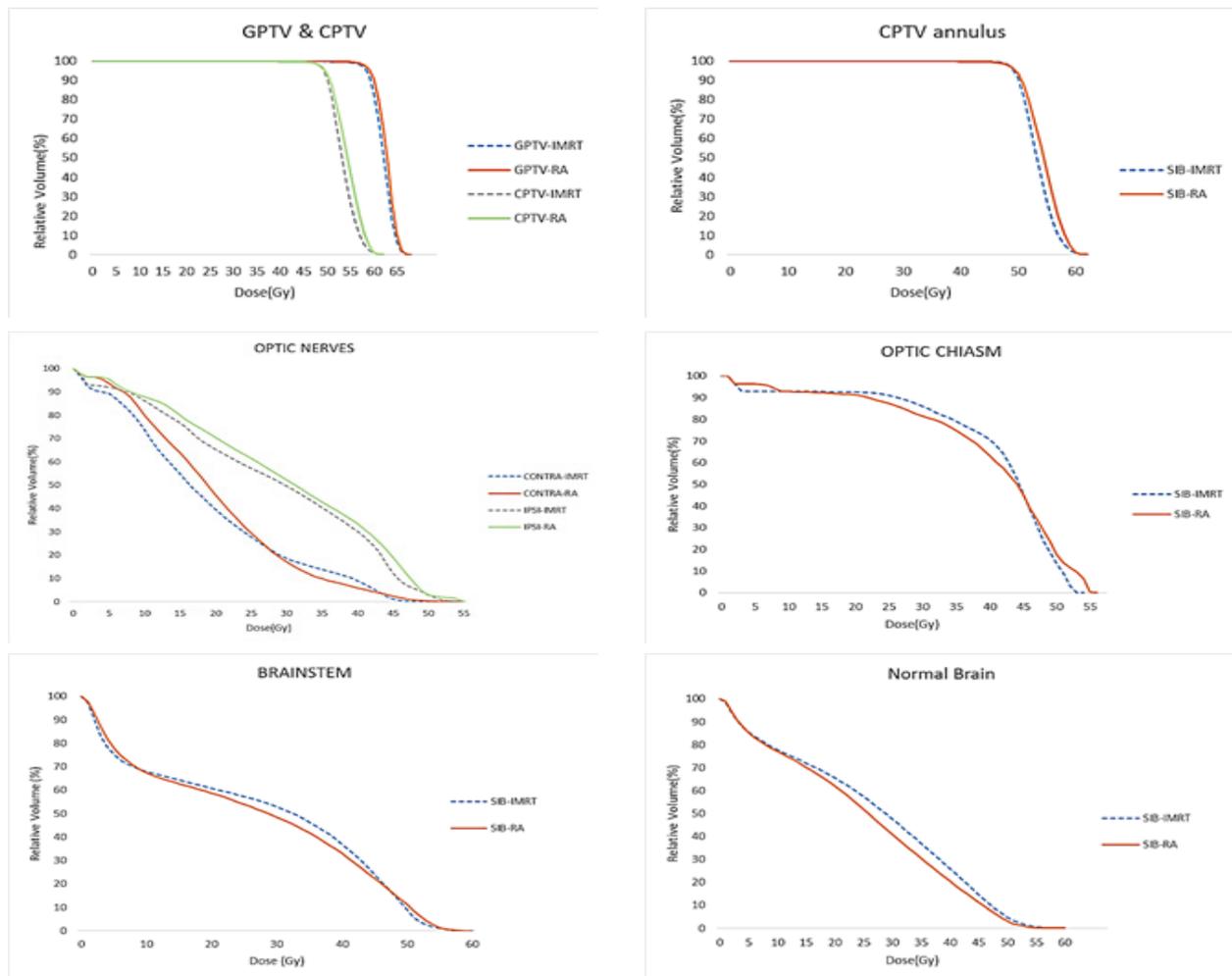
Figure 1. Mean Cumulative Dose Volume Histogram (DVH), Generated from the Mean of all the Medians of Dosimetric Parameters of Different Structures in all the Patients. A) The median doses of GPTV and CPTV in VMAT are slightly higher than in IMRT. B) The median dose received by CPTVannulus is slightly higher in VMAT than in IMRT. C) VMAT plans gave higher Dmax to ipsilateral optic nerve than IMRT plans. D) There was no difference between the plans with respect to optic chiasm dose. E) IMRT plans had lower median Dmax and D1cc than VMAT plans in Brainstem. F) IMRT plans gave higher mean doses to normal brain than VMAT.

near minimum dose (D99% - 57.65Gy vs. 56.4Gy; p<0.001) compared to SIB-IMRT. Although the numbers show statistical significance, the difference may not be clinically meaningful. This better coverage was obtained at the expense of conformity index in the VMAT plans which had significantly lower conformality compared to IMRT plans. The VMAT plans had 8.4% lower conformity index than IMRT plans (0.83 vs. 0.76; p=0.001). While VMAT had relatively uniform conformity for both GPTV and CPTV, IMRT concentrated dose to the boost volume more than the low risk PTV. There was no difference seen in the homogeneity index and near maximum dose.

When CPTV parameters were evaluated, converse to what we have seen in GPTV, SIB-IMRT had better coverage and lower near maximum dose compared to SIB-VMAT (97.88% vs. 96.87%; p=0.021). However, the conformity index for CPTV annulus was better with VMAT plans than IMRT plans (0.72 vs. 0.67; p=0.01). There was no difference seen in homogeneity index and D98%. The normal brain received a significantly lower mean dose in VMAT plans compared to IMRT plans (28Gy vs. 24.2Gy; p<0.001), which is in contrast to what was seen in other dosimetric studies done between IMRT and VMAT sequential plans.

When OAR doses are evaluated, we found that the IMRT plans delivered significantly lower Dmax (0.03cc) doses to ipsilateral optic nerves (median Dmax of 46.95Gy in VMAT and 44.2Gy in IMRT; p=0.02)., contralateral lens and contralateratl cochleae and PRV brainstem (median Dmax of 58Gy in IMRT and 57.3 in VMAT; p=0.003). There was no difference seen in maximum doses delivered to contralateral optic nerves, optic chiasm, ipsilateral lens, ipsilateral cochleae and both eyes between the plans.

Consistent with the other dosimetric studies (Wagner et al., 2009; Cozzi et al., 2008; Shaffer et al., 2010; Nguyen et al., 2013; Holt et al., 2013; Farzin et al., 2015) the VMAT plans required significantly lesser monitor units compared to IMRT plans (520 vs 1618). There was a 68% reduction in the median number of monitor units required to deliver a single fraction in VMAT compared to IMRT and thus lesser low dose radiation is delivered to the rest of the body.

The treatment times were also significantly less in VMAT plans (2.48 min) which require only a 47% of the time required to deliver a single fraction compared

with what an IMRT plan (5.29 min) needs.

Discussion

The major cause for the failure of treatment and thus poor prognosis in malignant gliomas is the local recurrence. So several attempts have been made (Cha et al., 2014; Nakamatsu et al., 2008; Cho et al., 2010; Iuchi et al., 2014) to improve local control by dose escalation like altered fractionation and brain brachytherapy. One such strategy is the use of simultaneous integrated boost where higher doses are given to the high-risk area (GTV) while giving conventional doses to the low-risk area (PTV). Feasibility studies done in SIB-IMRT showed the safety as well as reduced treatment times in the use of SIB with improvement in progression-free survival although overall survival remains unchanged. There are phase III trials under way using SIB-IMRT in the treatment of gliomas. Although survival is dismal and rarely long-term survival is expected concerns regarding late toxicities remain. The use of IMRT showed significant improvement in conformity, PTV coverage and better sparing of OAR when compared to 3DCRT. Dosimetric studies done comparing IMRT with VMAT stated that the latter achieved equal or better PTV coverage and OAR sparing while having lesser monitoring units and shorter treatment times when compared to IMRT (Wagner et al., 2009; Shaffer et al., 2010). Lesser number of monitoring units result in a decrease in the amount of low dose radiation to the non-target areas. Reduced treatment times will result in an increase in the number of patients treated per day and better usage of departmental resources. And reduced overall duration of treatment from 6 weeks in conventional sequential technique to 5 weeks in simultaneous integrated boost will have the radiobiologic advantage of reducing accelerated repopulation of tumor cell clonogens (Mohan et al., 2000). The simultaneous integrated boost with IMRT also helps in reducing the normal tissue doses compared to sequential RT as the total number of fractions can be reduced. This benefit of reducing the normal tissue doses by SIB-IMRT compared to sequential RT was shown by Chan et al., (2003) in their dosimetric study.

We have attempted to make the plans as uniform as possible in our study. Rather than using previously generated plans, each plan was freshly generated for every patient in the study based on a template designed to achieve the stated planning objectives. We have used PTV coverage planning objectives to make the plans comparable, and conformity indices were not adjusted to compare the plans after they meet the planning objectives. Instead, the conformity index is labeled as an outcome variable and used to compare the ability of both the plans to maintain conformity in Simultaneous Integrated Boost.

Inconsistency in our study is that we have used two different methods of beam arrangement in IMRT plans, one being the manual placement of the beams in few patients and using a computerized beam angle optimization in other patients. In VMAT plans, most of the plans were generated using two complete rotations. In a few patients, it was not possible to achieve the planning objectives with two complete rotations where we had to use an additional non-

coplanar semi-arc placing sagitally to achieve the planning objectives. In two well-lateralized patients, we have used two semi-arcs to reduce the dose to the normal brain on the opposite side. However, as these are the situations we face in the clinical application also and as we have used planning objectives as a tool to make the plans comparable, we have included all such plans for the study to make an overall comparison between the techniques when the planning objectives are met.

Since we have used rigid planning constraints and the PTV objectives were used to make the plans comparable, the tolerance doses to optic nerves and chiasm has exceeded in two patients. But we have included them in the study anyway since these were the doses received by PRV and not the actual OAR and attempt to reduce the doses resulted in the compromise of the PTV coverage. This also helps in comparing both the techniques as their ability to reduce the OAR doses without compromising the PTV coverage. Because of these strict optimization rules, we had to reject few plans, and re-optimization was done which otherwise might have been clinically acceptable.

Most of the plans had at least two overlapping OARs. So we have measured mean doses of the OARs also which might not be clinically relevant for the serial organs. It is sometimes not possible to find the significant difference in the maximum dose received by the OARs between the plans when they overlap with the PTV. So we have used mean doses received by the OARs to challenge both the plans SIB-IMRT and SIB-VMAT. A similar method was also used by Shaffer et al. in their planning comparison study of VMAT and IMRT.

Unlike other dosimetric studies, we have given dose constraints to the PRV of the OARs and optimization was done such that the PRV should not receive the doses more than the tolerance limits of that particular OAR. This will help in further reducing the doses to the OARs and also PRV acts as a reserve volume through which the dose fall off can be observed. This also helps in protecting the OARs during the inter-fraction and intra-fraction variations in the setup that might occur during day-to-day treatment. This is especially important for the closely located critical structures like brainstem, optic chiasm, and ipsilateral optic nerves which often overlap with PTV.

The low-risk volume and boost volume coverage in our study compared favorably with the other studies in SIB. But the comparison with the other studies with our study is difficult because most of the studies in SIB have used IMRT only but not VMAT, and different volumes and different dose prescriptions were used. We have prescribed a BED of 78Gy to the boost volume similar to what was used in Cho et al. (2010) There are other studies which have used much higher BED beyond 90Gy. Compared to other studies in SIB our study had larger boost volumes as we have included tumor edema into the boost volume whereas most of the other studies have included edema into the low-risk volume. We have included edema in the boost volume as it might contain microscopic tumor cell deposits (Kelly et al., 1987), and also this makes the boost volume more irregular and the ability of the IMRT and VMAT plans to boost the irregular volume can be challenged.

The OAR doses in our study are also comparable to the other studies, but our OAR doses are less than the other studies as we have given constraints to the PRV of the OARs. As seen in most of the dosimetric studies comparing IMRT and VMAT, the monitor units used in VMAT are significantly lesser compared to IMRT. In a comparison made between single phase IMRT and VMAT, Shaffer et al., (2010) have reported monitor units as 789 and 363 respectively. But we found in our study that the IMRT had mean monitor units of 1681 and VMAT used 620 monitor units. This difference might because of the higher dose per fraction used in our study, the SIB technique, higher number of fields used in IMRT, double the number of arcs used in VMAT. However, the percentage difference between IMRT and VMAT is similar in both the studies, Shaffer showing 54% difference and our study showing 63% difference. Similarly, treatment times were also less in VMAT compared to IMRT as seen in other studies. Shaffer et al., (2010) have reported 65% reduction in treatment times using VMAT and our study showed a reduction of 50.5% reduction in VMAT plans. We have used a minimum of 2 arcs for VMAT planning, but studies have shown that a single arc also gives a decent coverage and a good OAR sparing which would further reduce the treatment times. This reduction in treatment time owes to the ability of VMAT to continuously change the fluence rate and MLC beam aperture shapes delivering the dose in a continuous arc like gantry movement. Whereas IMRT needs to deliver the dose in placing the gantry in different fixed beam angles and adjusting the MLCs to the match the tumor shape in that particular beam position. The reduction in treatment time is beneficial to the patients increasing their comfort as less time is spent in the immobilization mask and also that the intra-fraction variations in position can also be reduced thereby increasing the accuracy of the treatment time. The decrease in treatment time also increases the efficiency of a department especially in high volume centers as more number of patients can be treated per day.

In conclusion, with the stated planning objectives, Simultaneous integrated boost is dosimetrically feasible for hypofractionation in malignant gliomas using Intensity Modulated Radiotherapy and Volumetric Modulated Arc Therapy. Both IMRT and VMAT are comparable in their dosimetric properties with both having advantages and disadvantages over one another. IMRT had advantage of having better boost conformity, lower ipsilateral optic nerve and brainstem maximum doses compared to VMAT. Whereas, VMAT had better coverage, better overall PTV conformity, lower normal brain mean dose, lower monitor units and lesser treatment times. By giving dose constraints to the PRV rather than for OAR itself, the OAR doses can be further reduced while maintaining the PTV coverage. Although planning VMAT is cumbersome and time consuming, the advantage of reducing treatment time is beneficial to the patients' comfort and better managing of patient load in high volume centers. The clinical benefit of SIB in reducing the overall treatment time and reduced OAR doses while giving higher BED to the tumor should be evaluated in further studies.

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