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Quantitative Estimation of Integral Doses and Skin Entry Exit Doses during Different Radiation Treatment Delivery Techniques for Craniospinal Irradiation Patients

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ABSTRACT

Introduction: The present study includes a qualitative analysis of skin entry exit doses and Integral doses (ID) utilizing various treatment planning strategies.

Material and Methods: For this study, we have taken 20 patients suffering from medulloblastoma and planned for Craniospinal irradiation (CSI) with Helical Intensity Modulated radiation therapy HIMRT, Helical three dimensional conformal radiation therapy H3DCRT, and Volumetric modulated arc therapy VMAT treatment planning techniques on Accuray Radixact X9 and Elekta Synergy (Agility) linear accelerator.

Results: Various dosimetric parameters like D_{max}, D_{mean}, $D_{80\%}$, $D_{50\%}$, $D_{30\%}$, and D10% have been calculated for skin and skin_ring. Integral doses have been calculated for PTV-Brain and PTV-Spine, taking into consideration at least V95% (target coverage by 95% of the prescribed dose). Statistical analysis was done using SPS software version 22. Mean skin entry and exit doses were [HIMRT=7.07±0.703, H3DCRT = 7.87±0.958 VMAT=4.09±0.706]. For Phase-1mean integral dose for PTV_Brain and PTV_Spine was [HIMRT=11.37±4.458, H3DCRT=12.30±5.00, VMAT=7.21±2.990] and Phase-2 mean integral doses for GTV_Boost was [HIMRT=0.10±0.10 H3DCRT = 0.11±0.117 VMAT=0.03±0.067]. Skin entry exit doses and integral doses were observed to be highest in H3DCRT and then HIMRT. Meanwhile, VMAT plans show minimum entry exit doses and integral doses for Phase 1 and Phase 2.

Conclusion: This study concludes that VMAT treatment planning techniques showing less skin entry exit doses and integral doses compared with helical treatment planning techniques. Taking care of these factors can give better clinical outcomes in terms of less late side effects.

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Introduction

Arc-based radiation treatment deliveries include helical intensity modulated radiation therapy [HIMRT], Helical three dimensional conformal radiation therapy [H3DCRT], and Volumetric modulated arc therapy [VMAT]. Advancement technologies have enhanced treatment delivery and ensured the target coverage with prescribed doses while simultaneously reducing volumetric doses to Organs at risk [OAR]. However, during helical treatment delivery, through full 360-gantry rotation, there is the possibility that a large volume of patients will get low doses, too. Radio biologically low doses cause cell injury, which can result in late side effects [1].During treatment planning, the skin is considered a type of critical organ that is at risk if it gets out of tolerance doses. Integrative doses to Planning Target Volume (PTV) and Organs at Risk (OAR) have been delivered during treatment delivery. Patients with medulloblastoma were treated using two-dimensional (2D) junction techniques in the prone position and bilateral fields to the whole brain with required collimator rotations and one or more anterior fields to cover the spinal cord. Earlier2D techniques get more skin doses, integral doses, and entry and exit doses. Developments in treatment delivery and treatment planning techniques currently make it feasible to reduce volumetric skin doses through the optimization of treatment plans. Nowadays, advanced techniques like Intensity intensity-modulated radiation Therapy (IMRT), Tomotherapy, and Volumetric Modulated Arc Therapy (VMAT) are available, which help in reducing doses to organs at risk and simultaneously conformal and homogenous dose distribution to the target volumes. These techniques use varying dose rates, small multileaf collimator sizes at the isocenter, beam energy, gantry speed, and algorithm [2,3]The amount of dose received by OAR and cells that come in the path of the

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beam from scattered radiation results in cytotoxic damage. Later, these radiations have side effects on OAR, which can result in secondary malignancies in any part of the body. Skin entry, exit dose, and integral doses totally depend upon which type of treatment planning techniques, modulation factors, grid size, gantry speed, and algorithm used during patient treatment planning [4]If the same patient is planned using different planning techniques, the resultant integral dose and entry-exit doses will be different [5]. Our aim in this study is to investigate how integral and skin entry exit doses vary for the same patient when planned with HIMRT, H3DCRT, and VMAT. The aim of this study is to quantitatively estimate integral doses (ID) and skin entry exit doses in different radiation treatment delivery techniques for craniospinal irradiation patients. This is a unique study that compared advanced helical intensity modulated radiation therapy, helical three-dimensional radiation therapy, and volumetric arc therapy on the latest model of Accuray Radixact X9 LINAC for craniospinal irradiation patients. The new version of Radixact is a unique smart radiation therapy system and fully integrated system that is designed to provide treatment delivery more efficiently and effectively, imaging capabilities, treatment flexibility, higher dose rate, and less treatment time compared to the old version. There are studies present for an old version of Accuray Radixact X7, static three-dimensional conformal radiation therapy, and rapid arc treatment modalities, but Helical radiation therapy is a new type of radiation treatment technique that is especially beneficial for CSI patients in terms of better homogenous and uniform dose distribution and without any junctions (No hot and cold spots)[6]. CSI patients have large target sizes, including the whole brain and spinal cord. However, there are chances of getting higher skin doses due to beam entry through 360º around the patient. Therefore, it is very important to get to know about skin doses as they play a very important role in making clinical decisions for better clinical outcomes.

Materials and Methods

This is a retrospective type of study**.** For this study, 20 patients from CSI were taken. The patient's CT scan was done on a Philips Gamine GXL 16-slice CT machine with 3mm of slice thickness. CT images were transferred through Digital Imaging and Communication in Medicine (DICOM) to Accuracy Precision version-2.0.1.1[5].) and Monacoversion 5.51.10 Treatment Planning Systems (TPS). A radiation oncologist delineated the target and OAR according to the RTOG protocol (Radiation Therapy Oncology Group-0319) guidelines for Cranialmedulloblastomacancer [7]. The skin ring was created by giving a 3mm negative margin to the skin. The purpose of making a skin ring is to evaluate the actual dose delivered to the skin at 3 mm on the inner side. Point dose has been calculated for five dose points at the forehead, chin level, chest level, abdomen, and pelvic region to calculate average entry-exit doses. The mean volume for PTV_Brain was 1601.401cc, PTV_Spine was 147.662cc, and Boost_GTVwas 200.10cc. Treatment plans were created for Helical-Intensity Modulated Radiation Therapy (HIMRT), Helical Three-Dimensional Conformal Radiation Therapy (3DCRT) and Volumetric Modulated Arc Therapy (VMAT) with Accuray Precision version 2.0.1.1(5) software Accuray, Morison USA and Elekta Monaco software version 5.51.10. In the first phase, a total dose of 36Gy/20#, 1.8Gy/# was given to the PTV-Brain and PTV-Spine. In phase-2, 18 Gy dose in 10 fractions was given to Boost_GTV. In all treatment planning required target coverage for PTV_Brain and PTV_Spine was checked with $V_{95\%}$ (Target coverage with minimum 95% of the prescribed dose), and OAR tolerance doses were checked according to QUANTEC data -2010 (Quantitative Analysis of Normal Tissue Effect in the Clinic) [8]. Treatment was delivered using the helical intensity modulated radiation therapy technique, which is beneficial in terms of no hot spot or cold spot compared to other techniques.

Treatment planning Techniques

Helical-Intensity Modulated Radiation Therapy (HIMRT) & Helical Three-Dimensional Conformal Radiation Therapy (H3DCRT)

HIMRT & 3DCRT plans were created for Accuray Radixact X9 Tomotherapy machine with Accuray Precision Version 2.0.1.1 [5] Accuracy Madison USA treatment planning software. All treatment plans were created in IMRT and 3DCRT Mode; The Pitch was 0.293, the Modulation factor was between 2-3, the Convolution-superposition algorithm for dose calculation, and the field width of 2.5 x 40 cm^2 was used with 64 numbers of binary MLCs and 6MV Flattening Filter Free (FFF) photon beam.

Volumetric Modulated Arc Therapy

VMAT plans were generated with Elekta Synergy (Agility) LINAC with Elekta Monaco version 5.5.1.10 treatment planning software. To generate the patient treatment plans, a 6 MV Flattening filter photon beam and 80 pairs of MLCs with 0.5 cm width at the isocenter were used. To cover the whole target area, three arcs were inserted with two to three rotations per arc according to requirement. The first arc was inserted at the head and neck region, the second arc was at the thoracic region, and the third arc at the abdomen region was inserted. The Monte Carlo algorithm was used to optimize the plan. The grid spacing was 0.30 cm with 3% statistical uncertainty per control point, the minimum segment width was 0.5 cm, and the medium fluence smoothing method was adopted. The aim of this study is to quantify the various volumetric doses for Skin and Skin Ring (D_{max}, D_{mean}, $D_{80\%}$, $D_{50\%}$, $D30_{\%}$, and D10%), Skin entry-exit point doses, and integral dose to target volumes.

Treatment plan evaluation

Treatment plans were evaluated by the Medical Physicist and Radiation Oncologist as per guidelines of quantitative analysis of normal tissue effects in the clinic (QUANTEC – 2010). Cumulated Dose Volume Histograms (DVH) were used to evaluate various OARs volumetric doses (D_{max}, D_{mean}, $D_{80\%}$, $D_{50\%}$, $D_{30\%}$, and $D_{10\%}$) and target doses ($D_{1\%}$ and $D_{95\%}$). The minimum target coverage criteria were V95% (Target coverage with at least 95% of the prescribed isodose curve) and considering the hotspot region more than 110% of the prescribed dose. Integral Dose (ID) to target volumes and the whole body is defined as the product of absorbed dose D (Gy) and target volume. Integral dose was calculated with this mathematical equation, Integral Dose (ID) = D (Gy) x Vol (L)**,** Where D (Gy) is the mean absorbed dose to target (Gy), Vol (L) is the target volume (L is liter) [9, 10]. In this study, the mathematical equation used for integral dose calculation is the same as that used in the Aoyama et al. study.

Statistical analysis

Data was collected for all patients and entered into Microsoft Excel software, which was then analyzed in the Statistical Package for the Social Science (SPSS V.22) software. Mean and standard deviations were calculated. Repeated measure ANOVA Wilks's Lambda Test and Friedman's ANOVA tests, as appropriate, were performed to assess significant differences for various dosimetric parameters. The normality of dosimetric parameters was checked using the Shapiro-Wilk test. If the P-value is less than 0.05, then it will be considered significant. Repeated measure ANOVA Wilks's Lambda test was performed for normal distribution, and Friedman's ANOVA test was performed for non-normal distribution.

Results

From Table 1, for skin, Dmax (maximum dose) is highest in HIMRT at 59.70 Gy (110.55%), Dmean is highest in H3DCRT at 7.67Gy whereas VMAT plans show minimum Dmax 55.75 Gy and minimum Dmean 4.13 Gy. For skin_ring, Dmax is highest in H3DCRT at 50.90 Gy, and Dmean is high in H3DCRT at 5.23 Gy. The skin entry exit doses are highest in H3DCRT 7.87Gy, and VMAT plans show minimum doses of 4.09Gy. The result shows that VMAT plans show minimum skin entry exit doses, whereas there is a minor difference in skin entry exit doses for HIMRT and H3DCRT treatment planning techniques.
Dosimetric comparison of volumetric doses to Skin and Skin_ring (Dmax, Dmean, Dmin, D80%, D50%, D30%, D10%) , entry exit doses and p-values for HIMRT, H3DCRT and VMAT treatment planning techniques. Where * represents repeated measure ANOVA Wilks's Lambda Test and # represents Friedman's ANOVA Test.

Table 1. Effect of HIMRT, H3DCRT and VMAT treatment planning techniques on skin and skin-ring

OARs	Dosimetric parameters	HIMRT	H3DCRT	VMAT	P- VALUES HIMRT VS. H3DCRT VS. VMAT
Skin	Dmax	59.70±1.741	58.59±2.334	55.75±2.573	0.000*
	Dmean	7.07±3.421	7.67±3.798	4.13±1.595	0.000#
	Dmin	0.10±0.243	0.13±0.300	0.11±0.271	0.000#
	$D_{80\%}$	0.61±1.014	1.47±3.277	0.73±1.273	0.000#
	$D_{50\%}$	3.46±1.753	4.06±2.141	3.33±1.502	0.001#
	$D_{30\%}$	4.74±1.348	7.11±6.651	5.11±2.377	0.003#
	D10%	15.21±5.979	18.73±11.760	9.75±4.321	0.000*
	Entry & exit dose	7.07±.703	7.87±0.958	4.09±0.706	0.000*
Skin_ring	Dmax	48.83±3.493	50.90±2.606	48.55±2.472	0.000*
	Dmean	4.62±2.253	5.23±3.055	4.33±2.128	0.000#
	Dmin	0.10±0.246	0.12±0.300	0.03±0.091	0.000#
	$D_{80\%}$	0.50±0.828	0.6±1.050	0.35±0.752	0.000#
	$D_{50\%}$	2.36±1.352	2.75±1.512	2.12±1.226	0.000#
	$D_{30\%}$	4.46±3.879	4.92±4.905	3.81±2.426	0.000#
	$D_{10\%}$	9.61±2.793	9.99±3.270	10.40±6.791	0.573*

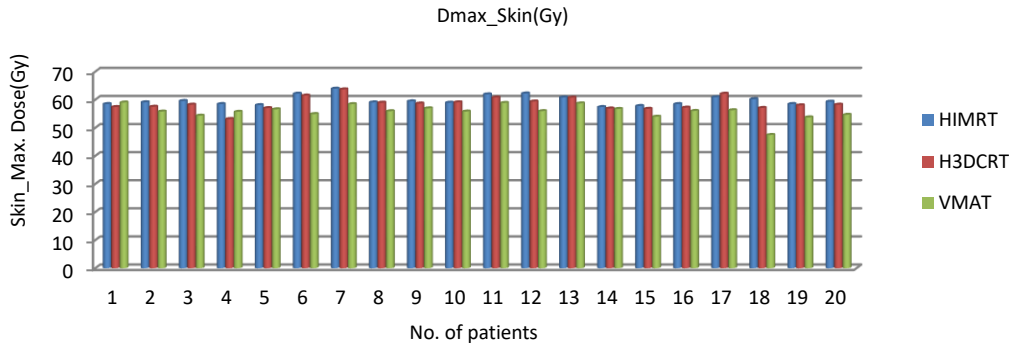

Figure 1. Dosimetric comparison of skin maximum doses (Dmax) in HIMRT, H3DCRT, and VMAT treatment planning techniques.

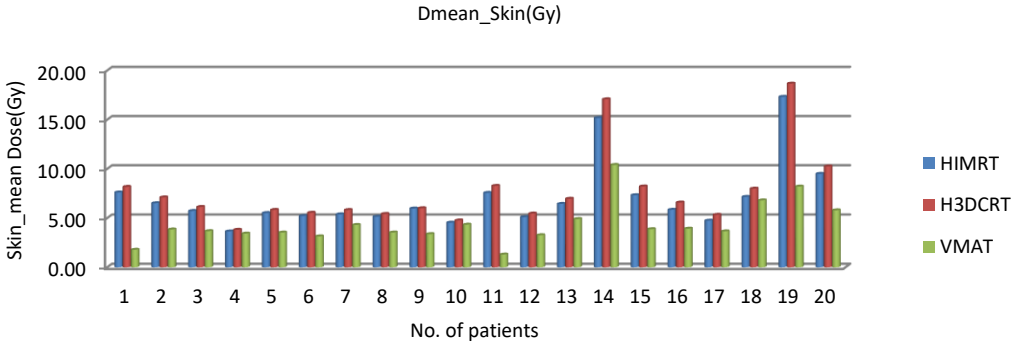

Figure 2. Dosimetric comparison of skin mean doses (Dmean) in HIMRT, H3DCRT, and VMAT treatment planning techniques

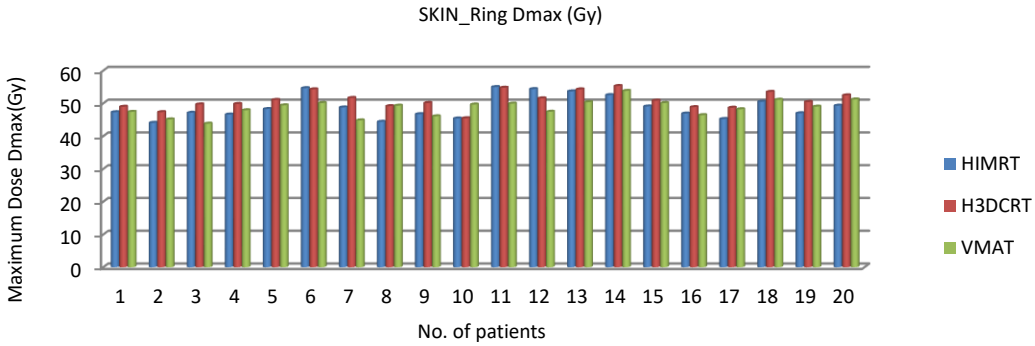

Figure 3. Dosimetric comparison of skin_ring maximum doses (Dmax) in HIMRT, H3DCRT, and VMAT treatment planning techniques

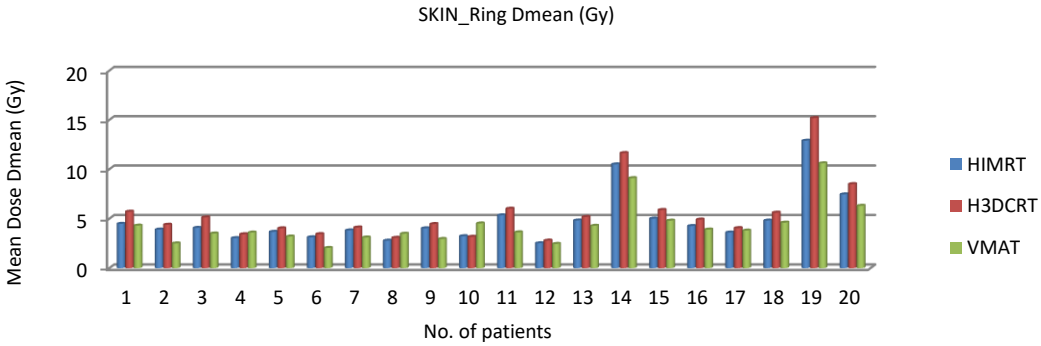

Figure 4. Dosimetric comparison of skin_ring mean doses (Dmean) in HIMRT, H3DCRT, and VMAT treatment planning techniques

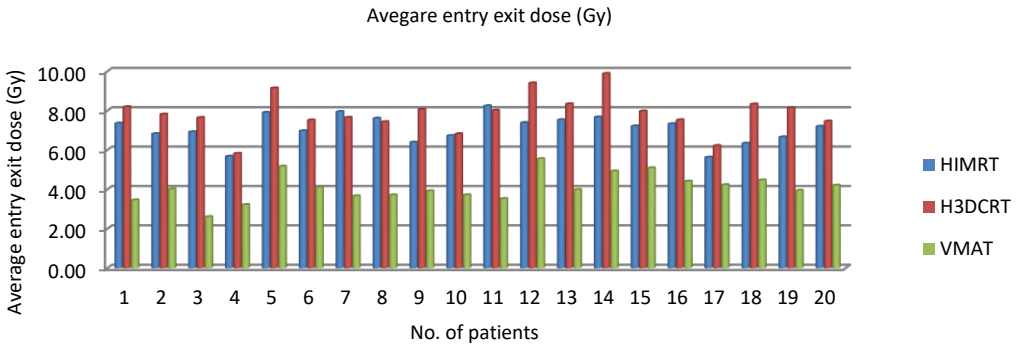

Figure 5. Dosimetric comparison of skin average entry exit doses in HIMRT, H3DCRT, and VMAT treatment planning techniques

Table 2. Effect of HIMRT, H3DCRT and VMAT treatment planning techniques on integral doses in Phase-1 and Phase-2

Target Volume	Dosimetric parameters	HIMRT	H3DCRT	VMAT	P- VALUES
					HIMRT Vs. H3DCRT Vs. VMAT
PTV_Brain & PTV_Spine	ID_Phase_1	11.37±4.458	12.30±5.007	7.21±2.990	0.000#
	ID_Phase_2	0.10±0.109	0.11±0.117	0.03±0.067	0.000#

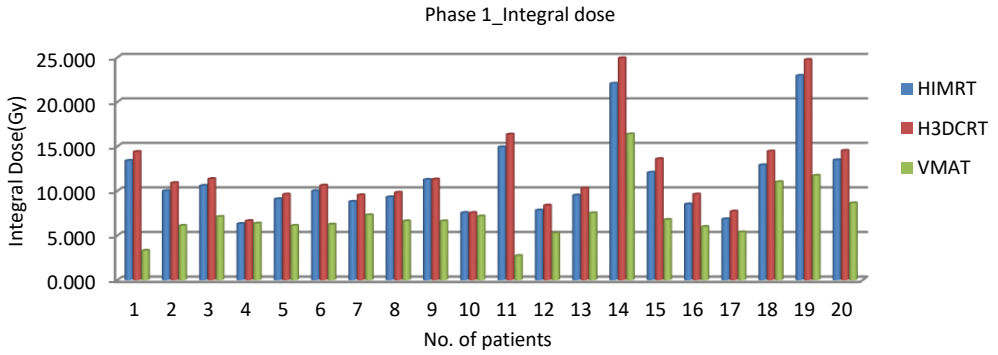

Figure 6. Dosimetric comparison of integral doses for Phase-2 in HIMRT, H3DCRT, and VMAT treatment planning techniques

From figure 1 dosimetric comparison of maximum doses (D_{max}) has been done for skin structure in HIMRT, 3DCRT and VMAT treatment planning. HIMRT and H3DCRT treatment plans showing high maximum doses, whereas minimum doses in VMAT treatment planning.

From Figure 2, mean doses (Dmean) have been evaluated for skin in HIMRT, 3DCRT, and VMAT treatment planning techniques. Maximum D_{mean} is showing in HIMRT and H3DCRT, whereas VMAT plans show fewer mean doses.

FromFigure 3, maximum doses (Dmax) have been compared for skin_ring structure in HIMRT, 3DCRT, and VMAT treatment planning techniques. Results show that H3DCRT plans show high Dmax, and there is a minor difference in HIMRT and VMAT results.

From Figure 4, dosimetric comparisons of mean doses (D_{mean}) have been made for skin _ring structure in HIMRT, 3DCRT, and VMAT treatment planning techniques. It was found that H3DCRT plans showthe highest Dmean. Whereas HIMRT and VMAT treatment plans are with less doses and approximately same results.

From Figure 5, dosimetric comparisons of average entry exit doses (Gy) have been done in HIMRT, 3DCRT, and VMAT treatment planning techniques. Results showed that maximum average entry exit doses are in H3DCRT and then HIMRT treatment planning techniques. Whereas VMAT plans show minimum average entry-exit doses.

From Table 2, Integral doses for target volume in Phase-1 and Phase-2 are highest in H3DCRT and VMAT treatment plans, showing comparatively fewer doses. The difference in the results is due to the treatment planning technique, collimation, dose rate, gantry speed, dose calculation sequencing parameter, and algorithm. The differences were statistically significant with p value less than 0.005 (significance level). The p-value, HIMRT Vs. H3DCRT Vs. VMAT for Phase-1, was 0.000, and for Phase-2 was 0.000.

Comparative analysis of integral doses for Phase-1 and Phase-2 with p-values for PTV_Brain and PTV_Spine in HIMRT, H3DCRT and VMAT treatment planning techniques.Where # represents Friedman's ANOVA Test.

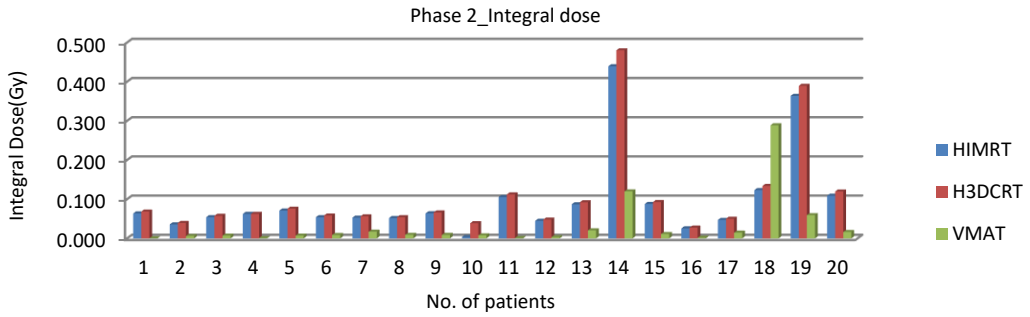

Figure 7. Dosimetric comparison of integral doses for Phase-2in HIMRT, H3DCRT, and VMAT treatment planning techniques

From Figure 6, dosimetric comparison of integral doses (ID) for Phase-1 treatment planning has been done in HIMRT, 3DCRT and VMAT treatment planning techniques. Treatment plans with H3DCRT and HIMRT techniques showing high integral doses. Whereas VMAT plan showing minimum integral doses.

From Figure 7, a dosimetric comparison of integral doses (ID) for the boost plan has been made in HIMRT, 3DCRT, and VMAT treatment planning techniques. Maximum integral doses are shown in H3DCRT treatment plans and then HIMRT techniques. Whereas VMAT treatment plans showing minimum integral doses for all patients except patient number 14 and 18.

Discussion

In the present study, a comparative evaluation of various dosimetric parameters has been done for skin entry exit doses and integral doses for target volumes in HIMRT, H3CDRT, and VMAT treatment planning techniques. Skin entry exit doses strongly depend upon the type of treatment technique, beam energy, dose calculation algorithm, grid size, beam collimation, and modulation factor. Helical treatment delivery in IMRT and 3DCRT mode showed higher skin entry-exit doses because of 360-degree beam entry-exit and lack of secondary collimators [11,12]. Statistical analysis showed that p-values are significant for all treatment techniques. Integral doses are higher in helical treatment planning techniques compared to VMAT treatment planning techniques for PTV_Brain and PTV_Spine in Phase-1 and GTV_Boost in Phase-2. Skin OAR shows the highest Dmax in HIMRT and minimum Dmax in VMAT. Skin_ring at 3mm inner margin from skin showing highest Dmax in H3DCRT. For skin, OAR volumetric doses show better results in HIMRT. Particularly in CSI patients, HIMRT is the choice of treatment because of high conformity, homogenous dose distribution heterogeneity index, and simultaneous sparing of OAR's. There are few studies that compare integral doses for target volumes in CSI patients for HIMRT, 3DCRT, and Rapid arc treatment planning techniques [13,14]. Goswami et al. 2020 studied the dosimetric comparison for CSI patients and compared integral doses delivered to OAR's and target volumes in Rapid arc, direct 3DCRT, and Direct IMRT treatment techniques. The results showed IDs are lower in rapid arc plans, and our study also showed lesser doses in VMAT plans compared to other treatment techniques; hence, the results of our research work have followed the same pattern as previous investigations [15]. Patel et al. studied the comparison of dosimetric parameters and integral doses in VMAT, HT, and 3DCRT for medulloblastoma cases of five children, and their results showed less ID in VMAT plans compared to other techniques [16].The pattern of our results is also similar to prior research works. Our study findings show minimum skin entry exit doses and Integral doses in the VMAT treatment planning technique compared to HIMRT and H3DCRT treatment planning techniques. The study reported by Mohandass P. et al. and Mishra A. et al. is also in favor of VMAT for superior dose distribution with fewer entry-exit doses and fewer skin doses [17,18]. One should consider all the parameters to get better treatment plans for better clinical results.

Conclusion

This study concludes the quantitative analysis of skin entry exit doses, volumetric doses of OARs, and target volumes integral doses. Statistical analysis showed less skin entry-exit and integral doses in VMAT treatment planning techniques (6MV FF) compared to other treatment planning techniques. For all treatment planning techniques, homogenous dose distribution was satisfactory. All dosimetric parameters are deciding factors for the choice of treatment.

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