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Dosimetric comparison of integral dose for different techniques of craniospinal irradiation

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Original Article

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Abstract

Aim: Comparison of the integral dose (ID) delivered to organs at risk (OAR), non-target body and target body by using different techniques of craniospinal irradiation (CSI).
Materials and methods: Ten CSI patients (medulloblastoma) already planned and treated either with linear accelerator three-dimensional conformal radiation therapy (Linac-3DCRT) technique or with linear accelerator RapidArc (Linac-RapidArc) technique by Novalis-Tx Linac machine have been analysed. Retrospectively, these patients are again planned on Radixact-X9 Linac with Helical, Direct-3DCRT and Direct-intensity-modulated radiation therapy (Direct-IMRT) techniques. The dose prescription to planning target volume brain (PTV-Brain) and PTV-Spine is 36 Gy in 20 fractions and is kept the same for all techniques. The target body, non-target body, OARs and total body dose are compared.
Results: ID is lowest in the RapidArc plan for every patient in comparison to Helical and Direct-IMRT. The ID for Body-PTV was found slightly higher in the RapidArc plan in comparison to 3DCRT plans. But there is better normal tissue sparing for most of the OARs in RapidArc plans if it compares with 3DCRT plans.
Findings: RapidArc is a better alternative for the treatment of CSI. It provides better target coverage and better OARs sparing from any other treatment techniques.

Introduction

Medulloblastoma is the most common malignant neoplasm of the central nervous system in children, constituting roughly 20% of all paediatric brain tumours. It is less common and accounts for <1% of adult brain tumours.[1] Craniospinal irradiation (CSI) is used in the management of medulloblastoma.[2] With the recent advancement of new technology, there is an improved outcome for these patients, with the introduction of modern radiotherapy techniques.[3,4] A more mature understanding of the biology of the disease has led to a contemporary clinico-biological risk stratification system for assigning prognosis and deciding treatment.[5] The current standard of care consists of maximal safe resection followed by radiotherapy and chemotherapy, yielding a 5-year survival rate of >80% for average-risk medulloblastoma and >50% for high-risk disease.[6] Radiotherapy for medulloblastoma entails irradiation of the entire neuraxis, that is, CSI with a homogeneous dose. This still remains one of the most technically challenging processes in radiotherapy planning and delivery because of the need to irradiate a very large and complex-shaped target volume uniformly. With continuous improvements in long-term survival, particularly in children with average-risk medulloblastoma, there is a growing concern regarding treatment-related long-term side effects. These include neurocognitive decline, hearing impairment, growth retardation, endocrine dysfunction, cataract formation, cardiomyopathy, impaired fertility and second malignancies.

Field shaping for CSI changed from traditional bony landmarks using two-dimensional (2D) planar radiographs to the advanced computed tomography (CT) simulation techniques.[7,8] Modern CSI techniques have developed with the aim of reduced long-term side-effects in the majority of patients. Conventionally, two lateral fields for the brain and two or three posterior fields for the spine to treat the entire craniospinal axis. Due to field-size restriction, linear accelerator-based three-dimensional conformal radiotherapy (Linac-3DCRT) and, linear accelerator-based volumetric arc therapy (Linac-RapidArc) required field matching of junctions by feathering. Separate isocentre reduced dose homogeneity at junction points and increases overall planning complexity.[9,10] Volumetric-modulated arc therapy (VMAT) is also a multi-isocentric technique for CSI. VMAT can achieve a highly homogenised and conformal dose distribution by using single or multiple arcs at each centre depending on the complexity of target volume.[11] This technique has been discussed by many researchers in their research.[12,13]

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Radixact X9 (Accuray Inc., Madison, WI, USA) radiotherapy is the most widely used form of tomotherapy, delivers dose from any of 360° and uses intensity-modulated radiotherapy (IMRT).[14,15] This machine has the capability to treat the entire patient target volume in a single and continuous arc. It does not require any isocentre shift and no field matching by feathering. This unique feature of Radixact has been explored for CSI with promising dosimetric results.[16] Radixact-Direct is different from Radixact-Helical in that it enables the users to apply any fix beam angle for planning.[17–19] Radixact-Direct further operates in the modes of Direct-3DCRT and Direct-intensity-modulated radiation therapy (Direct-IMRT). In IMRT, the constraint can be applied for both target volume and different organs at risk (OAR) volume, but in 3DCRT, there is no freedom to apply dose constraint to any organs.

This paper aims to compare Linac-RapidArc with Linac-3DCRT, Radixact-Direct-3DCRT, Radixact-Direct-IMRT and Radixact-Helical dosimetrically, in order to identify which planning technique is superior for the treatment of medulloblastoma patients.

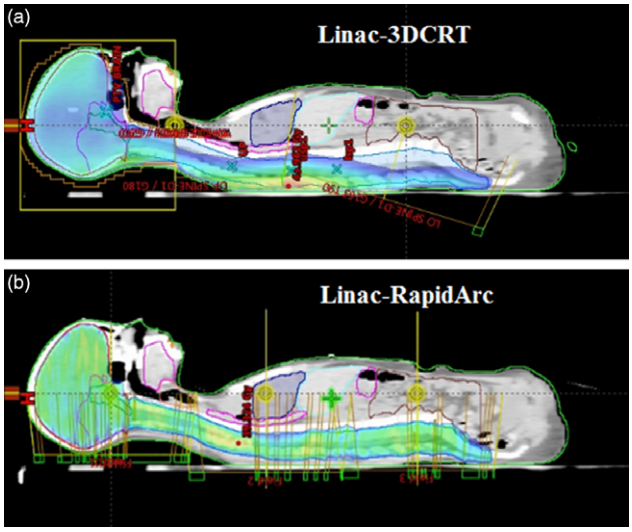

Figure 1. Dose distribution for craniospinal irradiation using techniques (a) Linac-3DCRT, (b) Linac-RapidArc.

Materials and Methods

For comparisons, a prescription of 36 Gy in 20 fractions was applied for all patients.[20] Ten consecutive medulloblastoma patients previously treated with 3DCRT techniques at Novalis-Tx (Varian Linear Accelerator) were replanned with Linac-RapidArc, Radixact-Helical, Radixact-3DCRT and Radixact-IMRT techniques. All ten patients undergo CT simulation (Siemens Biograph) in the supine position. They were immobilised full body to stabilise body positioning for scanning and treatment.

OARs and planning target volumes (PTVs) were contoured by Eclipse vs. 13 (Varian, Palo Alto, CA, USA) treatment planning system (TPS). The target volumes were contoured by the same radiation oncologist to include the cranium and spinal axis. For planning, PTV is split into two parts, one in PTV-Brain (cranial contents) and second in PTV-Spine (inferiorly from C1) to further improve dosimetry. Lists of OARs were contoured by the trained radiation oncologist. These organs include the brainstem, pituitary, optic nerves, optic chiasm, eyes, lenses, right cochlea, left cochlea, both parotids, mandible, larynx, oesophagus, both lung, heart, both breasts, liver, both kidneys, bowels, testes, ovaries and uterus. The body defined as the whole body outside of the contour regions down to a top third of the femur.

All plans were planned again for this study. A standardised planning protocol was applied to all patients for planning. These protocols strongly followed the strategy set out by the radiotherapy department. For medulloblastoma patients, nearly 15–20% of recurrences occur at the cribriform plate due to excessive shielding to protect ocular structures.[21,22] For that reason, in achieving sufficient target coverage in the cribriform plate between the eyes, ocular structures inescapably received unwanted dose from lateral opposing cranial fields. Multileaf collimators (MLCs) were used to shield the lenses and facial structures away from the PTV-Brain for this study.

Linac-3DCRT and Linac-RapidArc

Conventional 3DCRT plans were generated for each patient on an Eclipse TPS using 6 MV X-ray at Novalis-Tx. Fixed beam geometry was used, employing two bilateral half beam blocked cranial fields, collimated to match the divergence of the direct posterior spinal field (Figure 1). Cranial bilateral beams and spinal fields were shaped based on the three-dimensional shape of both PTVs (PTV-Brain and PTV-Spine) using high definition MLCs. MLCs positions were edited to reduce the dose to the OARs without compromising the target coverage.[23] The dose was prescribed and normalised to the reference point at the geometric centre of the PTV-Brain. The spinal field was weighted to achieve optimal coverage of the PTV-Spine. For patients with large spinal lengths, two adjacent direct spinal fields were dosimetrically matched to cover the entire spinal length. For the feathering of dose, junctions shifted 3 cm each on an alternate cycle. For VMAT two isocentre plans made for each patient. The patient planned with RapidArc on Eclipse TPS by using two arcs for each field. There is 3 cm overlapping in each field. The departmental dose constrained template is used for plan optimisation.

Radixact-Helical and Radixact-Direct

Posterior and lateral blocks were added for the Radixact-Direct technique to restrict gantry angles of 90° and 270° for the brain and 180° for the spine. In Radixact-Direct planning, a complete block was added to limit beam entry and exit through both lenses. Field width and pitch for all Radixact plans were set to 2.5 cm and 0.43, respectively. An optimal value of the modulation factor depends on plan complexity. Beam modulation factor starts from value 2.0 and increased up to 3.5 for increase dose conformity at the cost of the increased beam-on time. The Radixact-Direct-3DCRT technique does not allow for applying any dose constraints to OARs, only PTV dose prescription is allowed. The Radixact-Direct-IMRT technique allows for applying dose constraint to OARs and allows for dose modulation to reduced OARs doses. In contrast to Radixact-Direct-IMRT, Radixact-Helical allows continuous rotation of gantry around the patient at the selected modulation factor and selected pitch.

Parameter for dosimetric comparison

All plans were compared for different parameters. Some of these parameters are mean dose to target, mean dose to OARs, mean dose to the patient body and mean dose to Body-PTV. Other than the mean dose, data were also compared for the mean integral dose (ID) to OARs, PTV, patient Body and Body-PTV. ID is defined as

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the total energy absorbed by the organ. The ID calculation is based on mean organ dose, mean organ density and organ volume.[24] It is defined by:

$$\mathrm{ID} = D^{-} \times \rho^{-} \times \mathrm{V(Gy \times kg)}^{24} \quad (1)$$

where D^{-} is the mean organ dose, V is the organ volume and ρ^{-} is the mean organ density.

In this study, we consider all the organs have a uniform density, so ID is calculated by the following equation:

$$\mathrm{ID} = \text{Mean Dose} \times \text{Volume (Gy} \times \text{L)} \quad (2)$$

Statistical tools

One-way analysis of variance (ANOVA) test was applied for testing their significance level. For this statistical analysis, we used IBM Statistical Package for Social Sciences (SPSS) software (release 20.0, SPSS Inc., Chicago, IL, USA). Statistical significance defines as $p < 0.05$.

Results

According to their acceptance criteria to cover target volume, plans for each different modality for Linac-3DCRT, Linac-RapidArc by Novalis-Tx Linac machine and Helical, Direct-3DCRT Direct-IMRT by Radixact-X9 machine were generated. On comparison, there was the same ID deposited within target volume, but at the same time, there was a completely different dose distribution for nearby healthy organs. Dose distributions for all the techniques are shown in Figures 1 and 2. The mean dose variations for all the techniques are shown in Figure 3. Figure 3 displays the mean dose variation for target volume and non-target volume for all the techniques. Figures 4, 5 and 6 show variations in the ID for different normal tissues, patient whole body and body minus target body, respectively, for all the treatment techniques. Statistical analysis (ANOVA t-test) shows that differences are statistically insignificant ($p \geq 0.5$) for PTV volume. But the results are different for healthy tissue, body and non-target body, where results are statistically significant ($p < 0.5$). The ID for PTV volume and OAR volume is calculated by ID formula using Equations (1) and (2). Table 1 shows the mean volume with their standard deviation for all the OARs and PTV also. Table 1 also shows their respective mean dose with standard deviation. Table 2 shows the mean ID to target volume with their statistical significance. For target, $p \geq 0.05$, shows that there is no significant difference in target coverage for all the techniques. Table 3 shows the mean ID to all the OARs, the patient's whole body and body minus planning target volume (Body-PTV) with their statistical significance. In Table 3, the results clearly show that they are statistically significant for all the variables; this shows that techniques play an important role in the treatment of CSI.

The ID to Body and Body-PTV is the lowest for Linac-3DCRT techniques, but there is a significant difference in other OARs doses like heart, oesophagus, lenses, eyes, thyroid and liver. This shows RapidArc can be a better alternative in comparison to conventional techniques. All OARs constraints are met for Linac-RapidArc, Radixact-Helical and Radixact-Direct-IMRT. Between these techniques, Linac-RapidArc provides a lower mean dose for most of the organs with equivalent target coverage and lower ID for Linac-RapidArc.

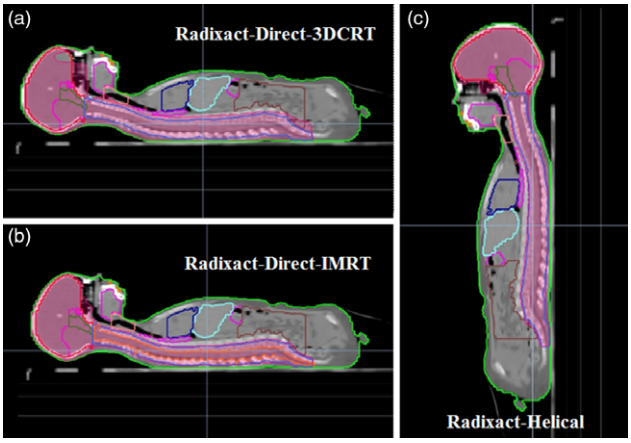

Figure 2. Dose distribution for craniospinal irradiation using techniques (a) Radixact-3DCRT technique, (b) Radixact-Direct-3DCRT, (c) Radixact-Helical.

Discussion

A CSI plan with good homogeneous dose distribution is always the most difficult planning process due to its complex contour of the target volume and long field size. Generally, CSI planned with two appropriately collimated lateral cranial fields shaped with MLCs or conformal blocks matched geometrically onto the beam divergence of direct posterior spinal field(s).[25] In this study, five different techniques of CSI were evaluated, and these techniques were Linac-based RapidArc, Linac-based 3DCRT by Novalis-Tx and Direct-3DCRT, Direct-IMRT and Helical with Radixact-X9 machine.

In this study, the ID delivered to patient body, healthy tissue and target body was calculated for different radiotherapy techniques. Five different delivery techniques were used to compare treatment plans for ten patients. These techniques were Linac-3DCRT, Linac-RapidArc, Radixact-Helical, Radixact-Direct-IMRT and Radixact-Direct-3DCRT. This planning study shows that RapidArc may achieve a significant decrease in body and non-target tissue ID in comparison to Radixact-Helical and Radixact-Direct-IMRT. RapidArc is able to achieve more normal tissue sparing in comparison to the 3DCRT technique for most of the organs. RapidArc additionally improves target dose conformity and homogeneity. Statistical analysis showed that there is no significant difference in ID between all the techniques for the target volume like PTV-Brain and PTV-Spine. But in contrast to this, the ID in the patient body strongly depended on the treatment techniques for Linac-RapidArc, Linac-3DCRT, Radixact-Helical, Radixact-Direct-3DCRT and Radixact-Direct-IMRT.

This retrospective planning study comparing different CSI techniques in ten patients showed clinically relevant dose reduction to the radiosensitive organs is achievable with RapidArc. Particularly, a reduction in mean dose to the heart, oesophagus, lenses, eyes, thyroid and liver is observed with RapidArc technique. The mean dose delivered to non-target tissue is lower for RapidArc in every patient as compared with 3DCRT, IMRT and Helical. This study suggests that RapidArc may be an optimal choice of treatment for CSI on the base of normal tissue sparing and better target coverage. This planning study also shows that Radixact-Helical improves normal tissue sparing in comparison with conventional techniques like Linac-3DCRT and Radixact-Direct-3DCRT for CSI. This study shows RapidArc achieves a high-quality plan with comparable quality of normal tissue sparing

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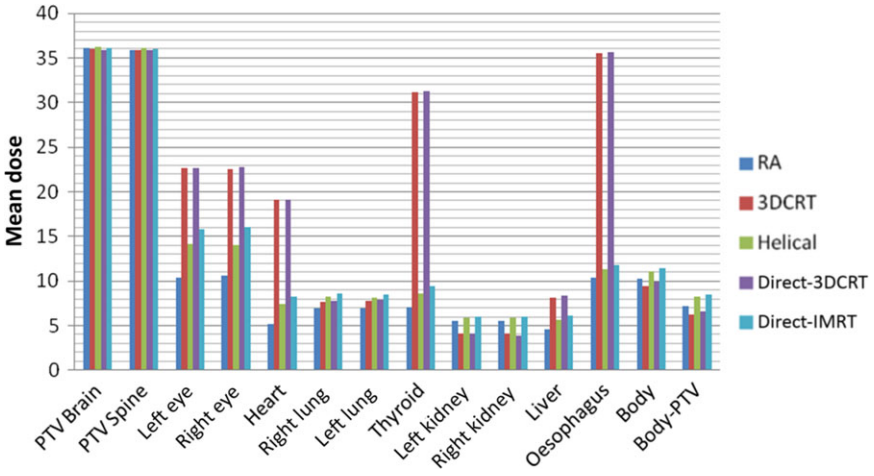

Figure 3. Variations in mean dose of target (planning target volume) and organs at risk for different treatment techniques.

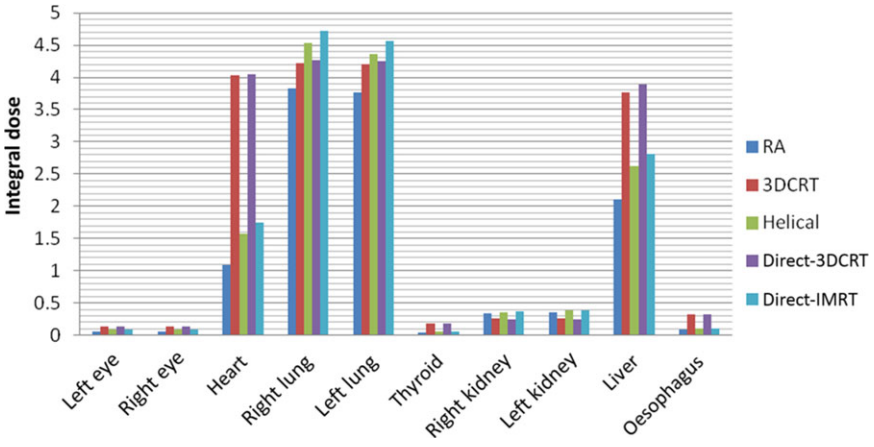

Figure 4. Variations in mean integral dose of organs at risk for different treatment techniques.

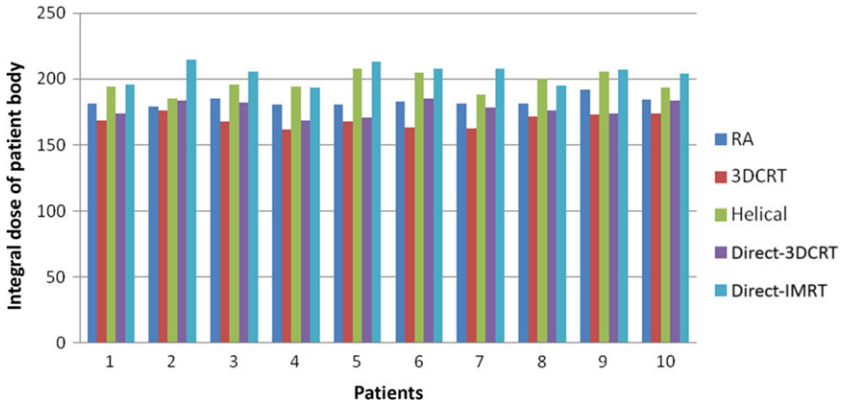

Figure 5. Variations in integral dose of patient body for different treatment techniques.

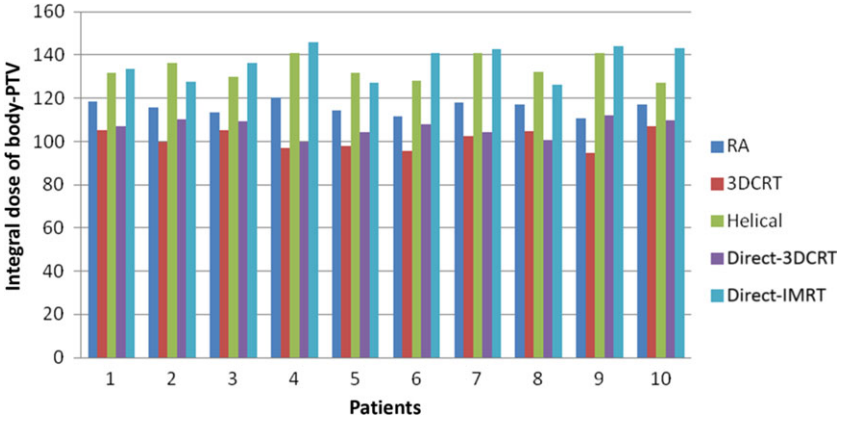

Figure 6. Variations in integral dose of body-planning target volume (Body-PTV) for different treatment techniques.

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Table 1. Dosimetric values (volume and mean dose) of target (planning target volume) and organs at risk resulting from different treatment techniques for craniospinal irradiation

	Mean ± S.D.					
		Mean Dose (Gy)				
Organs	Volume (cc)	Linac-RapidArc	Linac-3DCRT	Radixact-Direct-Helical	Radixact-Direct-3DCRT	Radixact-Direct-IMRT
PTV brain	1490.81 ± 30.03	36.11 ± 0.31	36.06 ± 0.28	36.18 ± 0.44	35.93 ± 0.46	36.09 ± 0.57
PTV spine	145.46 ± 3.88	35.94 ± 0.49	35.92 ± 0.56	36.12 ± 0.45	35.94 ± 0.47	35.95 ± 0.47
Left eye	6.06 ± 0.23	10.41 ± 0.76	22.71 ± 0.63	14.13 ± 0.93	22.65 ± 0.62	15.86 ± 0.83
Right eye	5.93 ± 0.34	10.65 ± 0.76	22.55 ± 0.73	14.01 ± 0.91	22.79 ± 0.67	15.99 ± 0.79
Heart	211.28 ± 2.29	5.19 ± 0.37	19.11 ± 1.17	7.46 ± 0.53	19.12 ± 0.94	8.27 ± 0.62
Right lung	551.29 ± 8.24	6.94 ± 0.66	7.67 ± 0.48	8.24 ± 0.49	7.74 ± 0.47	551.29 ± 8.24
Left lung	538.14 ± 4.71	6.98 ± 0.68	7.79 ± 0.42	8.10 ± 0.43	7.89 ± 0.39	8.49 ± 0.71
Thyroid	5.85 ± 0.38	7.01 ± 0.49	31.18 ± 0.92	8.59 ± 0.51	31.24 ± 0.97	9.44 ± 0.52
Right kidney	61.34 ± 0.81	5.49 ± 0.48	4.13 ± 0.50	5.86 ± 0.76	4.09 ± 0.44	6.03 ± 0.67
Left kidney	64.45 ± 0.47	5.51 ± 0.51	4.14 ± 0.57	5.90 ± 0.67	3.86 ± 0.52	5.95 ± 0.63
Liver	464.12 ± 1.16	4.53 ± 0.44	8.12 ± 0.31	5.66 ± 0.46	8.396 ± 0.51	6.07 ± 0.28
Oesophagus	9.11 ± 0.33	10.33 ± 0.61	35.48 ± 0.72	11.36 ± 0.63	35.69 ± 0.89	11.76 ± 0.61
Body	17827.88 ± 220.71	10.26 ± 0.24	9.45 ± 0.21	11.04 ± 0.38	9.96 ± 0.36	11.47 ± 0.39
Body-PTV	16132.22 ± 111.05	7.17 ± 0.19	6.26 ± 0.28	8.3 ± 0.33	6.6 ± 0.26	8.47 ± 0.43

Abbreviations: S.D., standard deviation; Gy, grey; cc, cubic centimetre; Linac, linear accelerator; 3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; PTV, planning target volume.

Table 2. Mean integral doses with their standard deviation to various planning target volume (PTV) resulting from different planning techniques for craniospinal irradiation

	Mean ± S.D.					
	Integral dose (Gy.L)					
PTV	Linac-RapidArc	Linac-3DCRT	Radixact-Helical	Radixact-Direct-3DCRT	Radixact-Direct-IMRT	*p*-Value (ANOVA test)
PTV brain	53.82 ± 1.02	53.75 ± 1.16	53.93 ± 1.21	53.56 ± 1.18	53.79 ± 1.34	$p \geq 0.05$
PTV bpine	5.23 ± 0.10	5.23 ± 0.16	5.25 ± 0.16	5.23 ± 0.12	5.24 ± 0.14	$p \geq 0.05$

Abbreviations: S.D., standard deviation; Gy, grey; L, litre; 3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; PTV, planning target volume.

Table 3. Mean integral dose with their standard deviation to various organs at risk resulting from different planning techniques for craniospinal irradiation

	Mean ± S.D.					
	Integral dose (Gy.L)					
Organs at risk	Linac-RapidArc	Linac-3DCRT	Radixact-Helical	Radixact-Direct-3DCRT	Radixact-Direct-IMRT	*p*-Value (ANOVA test)
Left eye	0.063 ± 0.0050	0.137 ± 0.0060	0.0856 ± 0.0064	0.137 ± 0.0055	0.096 ± 0.0059	$p < 0.05$
Right eye	0.063 ± 0.0047	0.134 ± 0.0070	0.0830 ± 0.0054	0.135 ± 0.0078	0.095 ± 0.0051	$p < 0.05$
Heart	1.096 ± 0.0853	4.039 ± 0.2732	1.576 ± 0.1171	4.041 ± 0.2135	1.746 ± 0.1343	$p < 0.05$
Right lung	3.827 ± 0.3936	4.227 ± 0.2486	4.539 ± 0.2503	4.269 ± 0.2878	4.715 ± 0.2823	$p < 0.05$
Left lung	3.761 ± 0.3645	4.198 ± 0.2483	4.358 ± 0.2530	4.247 ± 0.2172	4.569 ± 0.3659	$p < 0.05$
Thyroid	0.041 ± 0.0045	0.182 ± 0.0107	0.050 ± 0.0044	0.183 ± 0.0115	0.0551 ± 0.0042	$p < 0.05$
Right kidney	0.337 ± 0.0329	0.253 ± 0.0290	0.359 ± 0.0467	0.251 ± 0.02489	0.370 ± 0.0443	$p < 0.05$
Left kidney	0.355 ± 0.0332	0.267 ± 0.0375	0.380 ± 0.0439	0.249 ± 0.0344	0.384 ± 0.0395	$p < 0.05$
Liver	2.103 ± 0.2007	3.771 ± 0.1460	2.628 ± 0.2178	3.897 ± 0.2404	2.818 ± 0.1338	$p < 0.05$
Oesophagus	0.094 ± 0.0075	0.323 ± 0.0112	0.103 ± 0.0035	0.325 ± 0.0176	0.107 ± 0.0048	$p < 0.05$
Body	182.816 ± 3.5251	168.454 ± 4.9957	196.89 ± 7.4232	177.501 ± 5.9421	204.449 ± 7.4378	$p < 0.05$
Body-PTV	115.698 ± 3.0559	101.019 ± 4.5001	133.896 ± 5.3769	106.469 ± 4.1104	136.722 ± 7.6623	$p < 0.05$

Abbreviations: S.D., standard deviation; Gy, grey; L, litre; Linac, linear accelerator; 3DCRT, three-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy; PTV, planning target volume.

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and ID delivered. It is suggested that each radiotherapy centre carry out its own planning study to find out results based on their departmental protocols, software, hardware and capability. In the future, widespread research is required to estimate the medical implications of these findings in the reduction of treatment toxicities and secondary malignancies.

Limitations and future scope

There are very limited data available for the literature review regarding this study. A most common problem with CSI is that medulloblastoma is a rare ailment, due to this we have a limited sample size suitable for this study ($n = 10$). In the future, we will try to collect more samples for further dosimetric and statistical analysis. Further study is needed to compare dosimetric results and ID for secondary malignancy and induce late effects.

Conclusions

CSI remained one of the most challenging processes in radiotherapy planning, delivery and verification. Newer high-precision techniques have the potential to improve the benefit–risk ratio in CSI. The Linac-based RapidArc plans seem to be ideally suited to plan such long- and complex-shaped target volumes. This study investigated the ID absorbed in the healthy tissue in the whole patient body during radiotherapy of CSI. The dosimetric comparison revealed the lowest ID in normal tissue for RapidArc in comparison to Radixact-Helical and Radixact-Direct-IMRT. The ID to Body and Body-PTV is less for 3DCRT plan in comparison with RapidArc, but RapidArc gives better PTV coverage and less OAR dose in comparison with 3DCRT. This study also helps directly to future treatment options.

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Conflict of Interest. None.

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