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Comparison of Treatment Planning Parameters of Different Radiotherapy Techniques for Craniospinal Irradiation

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ABSTRACT

Introduction: The current study aimed to compare linear accelerator-based three-dimensional conformal radiotherapy (Linac-3DCRT) technique with different techniques of the Radixact-X9 for the treatment of craniospinal irradiation (CSI).
Material and Methods: Following a retrospective design, 22 CSI patients (Medulloblastoma) treated with Linac-3DCRT using the Novalis-Tx unit were selected for analysis. For each patient plan, additional sets of plans were generated using Helical, Direct-3DCRT, and Direct-intensity-modulated radiotherapy (Direct-IMRT) techniques of the Radixact-X9 unit. The dose prescription for brain planning target volume (brain PTV) and spine PTV were 36 Gy in 20 fractions and kept the same for all techniques. Planning time, patient setup time, homogeneity index (HI), and different dose-volume parameters for both PTV and organs at risk (OARs) were evaluated for comparison.
Results: The Radixact-X9-Helical technique can generate a plan in a more comparable and better manner in respect of maximum and minimum doses for most of the organs. The Radixact-X9-Helical technique resulted in better PTV homogeneity in comparison with Linac-3DCRT, Radixact-X9-Direct-3DCRT, and Radixact-X9-Direct-IMRT. The values of HI were 3.57±0.77, 17.37±1.44, 8.15±1.02, and 8.62±0.98, respectively.
Conclusion: Not only administration of the Radixact-X9-Helical treatment technique is easier, but also can generate a better homogeneous plan than other treatment techniques like 3DCRT and IMRT regarding different parameters for comparisons like dose-volume received by OARs, patient setup time, move isocenter, and many more. So it can be an integral part of the radiotherapy department, according to their clinical needs like shorter treatment time with good sparing of critical OARs.

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Introduction

Medulloblastoma is the most common malignant neoplasia of the central nervous system (CNS) in children, which constitutes about 20% of pediatric brain tumors. It is less common among adults (a prevalence of<1%) [1]. Recently developed radiotherapy technologies resulted in better outcomes for such patients [2, 3]. A good understanding of anatomy and radiobiology can help clinicians for making better decisions regarding the diagnosis and treatment of this disorder [4]. Currently used standards of care contain safe and maximum resection, followed by chemotherapy and radiotherapy, resulting in a 5-year rate of >80% for average-risk patients and >50% for high-risk patients [5]. In craniospinal irradiation (CSI), the planning target volume (PTV) has a complex shape and large volume, because it is highly challenging to plan and deliver. For children, there has been a continuous improvement in the long-term survival of medulloblastoma cases. Despite providing good survival, it has some important long-term side effects, including growth issues, hearing problems, endocrine dysfunction, cataract, neurocognitive decline, cardiomyopathy, second malignancies, and infertility.

In contrast to the traditional landmark technique on X-ray film, computed tomography (CT) simulation is a modern technique of field-shaping [6, 7]. Modern radiotherapy techniques developed for CSI are intended to minimize long-term side effects with a more conformal and homogeneous dose to target. The conventional bilateral field for the brain with two or three posterior fields for the spine is sufficient to cover the whole target. Due to field size limitation in Linac, junction matching is always necessary for underdose and overdose areas. Multiple isocentric techniques are associated with reduced homogeneity; however, they increase the complexity of planning [8, 9]. Radixact-X9 (Accuray, WI, USA), the generally advanced form of previous tomotherapy unit, can give the dose in any direction of 360º by using intensity-

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modulated radiotherapy (IMRT) technique [10, 11]. In Radixact-X9, it does not require field matching; hence, we can treat a long target without compromising homogeneity. As a result of its distinctive property, it's widely using for treating CSI-related. There is a different treatment option in the Radixact-X9 unit, such as helical mode and direct mode. The latter comprises of using multiple pre-defined fixed beam angles for planning [12-14], which is further divided into Direct-intensity-modulated radiotherapy (Direct-IMRT) and Direct-three-dimensional conformal radiotherapy (Direct-3DCRT). In Radixact-X9-Helical and Radixact-X9-IMRT techniques, users can use multi-leaf collimators (MLCs) to generate fluency. For these types of techniques, different constraints can be applied to various organs at risk (OARs) at the same time. However, for Linac-3DCRT and Radixact-X9-3DCRT, users can deliver the required dose to target without any constraint to different OARs. The current study aimed to compare the different treatment planning parameters in treating CSI, using the Linac-based 3DCRT technique and by different types of planning modalities of the Radixact-X9 unit.

Materials and Methods

Following a retrospective design, 22 CSI patients (Medulloblastoma) treated with Linac-based 3DCRT techniques at the Novalis-Tx unit were investigated in the present study. For each patient plan, additional sets of plans were generated using Helical, Direct-3DCRT, and Direct-IMRT techniques of the Radixact-X9 unit. For each patient, a total of four plans were generated, which yielded 88 treatment plans. All 22 patients underwent CT simulation (Siemens Biograph) in the supine position with proper and stable immobilization. A prescription dose of 36 Gy in 20 fractions was applied for all patients. The same dose prescription was used for plans developed for all techniques [15]. We used the same PTV and OARs, contoured on Eclipse version 13 (Varian, Palo Alto, CA, USA) treatment planning system (TPS) for Novalis-Tx and Radixact-X9 unit. For the planning purpose of all modalities at Radixact-X9, we used Precision version 2.0.0.1 TPS. All contouring procedures for both PTV and OARs were performed by a well-trained single radiation oncologist. The contours included brain PTV, spine PTV, brainstem, chiasm, optic nerves, eyes, parotids, larynx, lungs, breasts, heart, kidneys, liver, esophagus, bowel, and mandible. For planning purposes, PTV was divided into two separate parts, the brain (Intracranial contents) and spine cord (Inferiorly to C1 vertebrae). All 10 patients were contoured once and planned again as per the standard protocol of Radiation Therapy Oncology Group (RTOG), Task Group (TG), and Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) guidelines. For medulloblastoma patients, approximately 15-20% of recurrences occurred at the cribriform plate due to excessive shielding to protect ocular structures [16, 17]. Based on what was mentioned above, for achieving ample target coverage in the cribriform plate between eyes, the ocular structure received an unnecessary dose from the bilateral cranial field. Here, MLCs were used for providing structural shielding in order to overcome this problem.

Linac-3DCRT technique plan

To generate a 3DCRT plan at the Novalis-Tx unit, we used the bilateral half beam block technique to match the divergence of the direct posterior spine field, as shown in Figure 1(A). We used MLCs to shape brain PTV and spine PTV for decreasing the excessive dose to the OARs [18]. Due to the larger length of spine PTV, multiple posterior beams with a collimator and couch rotation were used, such that there was no overlap between junctions. Afterward, all junctions were shifted by 3 cm on each alternate cycle for the feathering of the dose. The dose was normalized at different reference points for whole PTV, like the upper, middle, and lower reference points, according to their field arrangement (Figure 1(A)).

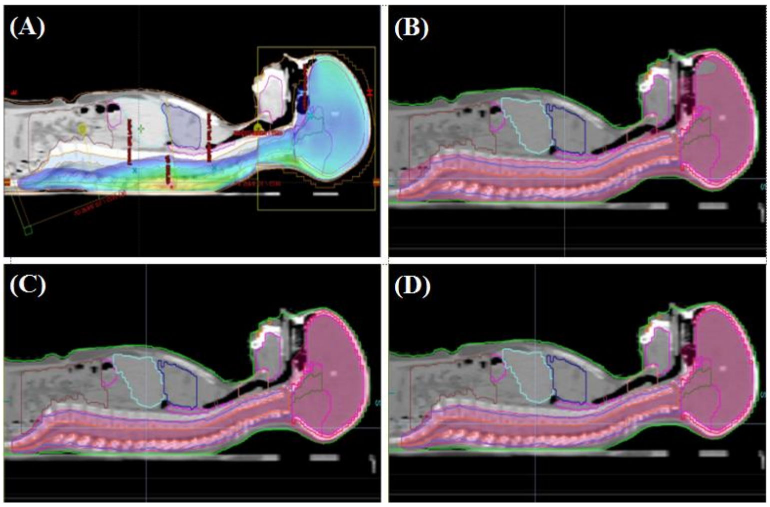

Figure 1. Illustration of craniospinal irradiation of a reference patient in sagittal view using (A) Linear accelerator-based three-dimensional conformal radiotherapy technique (B) Radixact-X9 based three-dimensional conformal radiotherapy technique (C) Radixact-X9 based direct intensity-modulated radiotherapy technique (D) Radixact-X9 based helical technique

The upper reference point was used for bilateral half beam block arrangement, the middle reference point was used for middle half beam block arrangement, and the lower reference point was used for lower field arrangement.

Helical, Direct-3DCRT, and Direct-IMRT techniques plans of Radixact-X9 unit

For all Radixact-X9 plans, field width and pitch were set at 2.5 cm and 0.430, respectively. A dose calculation was performed only at high resolution. Initially, a modulation factor was set at 2.0 and it was increased systematically up to 3.5, as per a requirement of the plan. In order to reduce excessive doses to OARs, different blocks were added. For Helical and Direct-IMRT techniques, after every 50 iteration, planning parameters were changing manually, as per as need of the plan based on the target and OARs doses. A similar direct-3DCRT planning approach was used for the Linac-3DCRT technique, but the only difference was in the Direct-3DCRT. It worth noting that there should be no concern about isocenter placement and beam matching, which is a key factor in Radixact-X9 techniques.

Treatment planning parameter for comparison

For all techniques, different dose-volume parameters were evaluated from cumulative dose-volume histograms (cDVH) for both PTV and OARs. Here, in order to evaluate the plans, we considered several treatment parameters for comparison. The parameters included planning time, patient setup time, move isocenter time, beam on time, OARs maximum dose (D_{max}), OARs mean dose (D_{mean}), homogeneity index (HI), and different dose-volume parameters (Obtained from cumulative dose-volume histograms) like the volume of OARs receiving 5 Gy, 15 Gy and 25 Gy (V_{5Gy}, V_{15Gy}, V_{25Gy}).

Beam-on time for Linac-3DCRT was calculated at the dose rate of 600 MU/min.

HI was calculated using the following formula:

$$HI = (D_{2\%} - D_{98\%}) / D_{RX} \times 100\%$$

Where

$D_{2\%}$ and $D_{98\%}$ are doses of PTV volume and D_{RX} is prescription dose to PTV volume. The lower value of HI presented better results in form of homogeneity.

Statistical tools

One-Way ANOVA test was applied for testing the significance level. Analyses were performed using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Statistical significance was considered when p-value<0.05.

Results

The craniospinal irradiation of a reference patient in a sagittal view using Linac-based 3DCRT, Radixact-X9-Direct-3DCRT, Radixact-X9-Direct-IMRT, and Radixact-X9-Helical techniques, are shown in Figures 1 (A), (B), (C), and (D), respectively. For Radixact-X9 unit-based plans the dose distribution was more homogeneous compared to the Linac-based plan. Linac-based plans produced overdose or underdose at junction despite feathering. Radiaxact-X9 plans had lesser D_{mean} for most of the OARs. The OARs constraints met their tolerance criteria in all Radixact-X9 based treatment plans and Linac-based treatment plans also. The statistical results regarding the dose-volume details are provided in Tables 1, 2, and 3; in addition, their graphical representation is provided in Figures 2, 3, and 4.

Table 1.Comparison of volumes receiving over 5 Gy (V_{5Gy}) for various organs at risk using different treatment techniques

OARs	V_{5Gy} (Mean ± S.D)				*P* value (Anova test)
	Linac-3DCRT	Radixact-X9-Helical	Radixact-X9-Direct-3DCRT	Radixact-X9-Direct-IMRT	
Brainstem	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0	P ≥ 0.05
Chiasm	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0	P ≥ 0.05
Optic Nerves	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0	P ≥ 0.05
Eyes	90.46 ± 2.19	70.55 ± 1.99	79.82 ± 1.84	70.36 ± 2.15	P < 0.05
Parotids	95.0 ± 1.72	96.77 ± 1.38	92.05 ± 2.49	84.91 ± 1.69	P < 0.05
Larynx	96.18 ± 1.37	84.95 ± 2.10	90.55 ± 2.11	90.68 ± 1.84	P < 0.05
Lungs	40.27 ± 1.93	75.27 ± 1.42	8.95 ± 2.24	8.14 ± 1.86	P < 0.05
Breasts	8.50 ± 1.50	47.91 ± 7.57	0.0 ± 0.0	0.0 ± 0.0	P < 0.05
Heart	90.36 ± 1.81	27.50 ± 1.68	56.95 ± 1.43	52.23 ± 2.25	P < 0.05
Kidneys	40.86 ± 2.08	25.82 ± 1.68	5.73 ± 1.35	4.95 ± 1.17	P < 0.05
Liver	47.36 ± 7.46	70.45 ± 1.92	29.77 ± 2.09	26.18 ± 1.50	P < 0.05
Oesophagus	100 ± 00	94.95 ± 1.59	96.14 ± 1.36	92.23 ± 2.41	P < 0.05
Bowel	55.41 ± 1.85	80.41 ± 1.84	40.27 ± 2.39	39.68 ± 1.91	P < 0.05
Mandible	80.14 ± 1.73	84.86 ± 1.64	40.91 ± 2.20	25.68 ± 1.94	P < 0.05

Note: OARs: Organs at risk; V_{5Gy}: Volumes of OARs receiving over 5 Gy; S.D: Standard deviation; Linac: Linear accelerator; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy; Radixact-X9: Radixact-X9 unit

Table 2. Comparison of volumes receiving over 15 Gy (V_{15Gy}) for various organs at risk using different treatment techniques

OARs	V_{15Gy} (Mean ± S.D)				*P* value (Anova test)
	Linac-3DCRT	Radixact-X9-Helical	Radixact-X9-Direct 3DCRT	Radixact-X9-Direct IMRT	
Brainstem	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0	P ≥ 0.05
Chiasm	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0	P ≥ 0.05
Optic Nerves	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0	P ≥ 0.05
Eyes	70.63 ± 2.24	5.36 ± 1.43	50.73 ± 2.0	30.36 ± 2.11	P < 0.05
Parotids	84.82 ± 1.53	9.68 ± 1.73	89.82 ± 2.34	65.23 ± 1.38	P < 0.05
Larynx	89.0 ± 1.90	45.10 ± 2.45	75.10 ± 1.99	66.36 ± 2.21	P < 0.05
Lungs	33.05 ± 1.94	15.82 ± 1.82	6.5 ± 1.89	4.77 ± 1.54	P < 0.05
Breasts	3.68 ± 1.075	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	P < 0.05
Heart	85.45 ± 1.79	5.14 ± 1.58	46.68 ± 8.94	45.23 ± 1.87	P < 0.05
Kidneys	35.68 ± 1.96	15.59 ± 1.68	4.77 ± 1.99	3.09 ± 0.97	P < 0.05
Liver	46.27 ± 2.86	10.95 ± 2.0	20.77 ± 1.71	18.41 ± 3.13	P < 0.05
Oesophagus	100 ± 0.0	47.77 ± 7.47	94.95 ± 1.68	90.86 ± 1.81	P < 0.05
Bowel	52.14 ± 1.25	35.23 ± 2.31	30.95 ± 1.49	30.23 ± 1.85	P < 0.05
Mandible	47.86 ± 7.52	25.64 ± 1.84	15.55 ± 1.57	8.41± 1.40	P < 0.05

Note: OARs: Organs at risk; V_{15Gy}: Volumes of OARs receiving over 15 Gy; S.D: Standard deviation; Linac: Linear accelerator; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy; Radixact-X9: Radixact-X9 unit

Table 3. Comparison of volumes receiving over 25 Gy (V_{25Gy}) for various organs at risk using different treatment techniques

OARs	V_{25Gy} (Mean ± S.D)				*P* value (Anova test)
	Linac-3DCRT	Radixact-X9-Helical	Radixact-X9-Direct-3DCRT	Radixact-X9-Direct-IMRT	
Brainstem	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0	P ≥ 0.05
Chiasm	100 ± 0.0	100 ± 0.0	100 ± 0.0	100 ± 0.0	P ≥ 0.05
Optic Nerves	100 ± 0.0	75.27 ± 1.67	96.59 ± 1.26	80.36 ± 2.19	P < 0.05
Eyes	54.45 ± 2.09	0.0 ± 0.0	30.32 ± 1.98	15.27 ± 1.42	P < 0.05
Parotids	75.18 ± 1.56	0.0 ±0.0	72.32 ± 3.17	45.14 ± 1.91	P < 0.05
Larynx	30.45 ± 2.28	3.68 ± 1.62	25.41 ± 2.13	11.09 ± 1.93	P < 0.05
Lungs	25.68 ± 2.21	3.23 ± 1.23	3.05 ± 0.72	3.09 ± 1.23	P < 0.05
Breasts	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	P < 0.05
Heart	25.77 ±2.18	0.0 ± 0.0	4.95 ± 1.39	3.59 ± 1.18	P < 0.05
Kidneys	26.95 ± 1.29	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	P < 0.05
Liver	15.73 ± 1.61	3.68 ± 1.36	3.09 ± 1.23	1.5 ± 0.74	P < 0.05
Oesophagus	90.86 ± 1.81	10.95 ± 2.01	75.09 ±1.99	65.18 ± 1.37	P < 0.05
Bowel	46.27 ± 2.86	3.09 ± 1.23	4.91 ± 1.15	3.09 ± 1.23	P < 0.05
Mandible	10.91 ± 1.90	3.55 ± 1.14	4.91 ± 1.15	3.09 ± 1.23	P < 0.05

Note: OARs: Organs at risk; V_{25Gy}: Volumes of OARs receiving over 25 Gy; S.D: Standard deviation; Linac: Linear accelerator; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy; Radixact-X9: Radixact-X9 unit

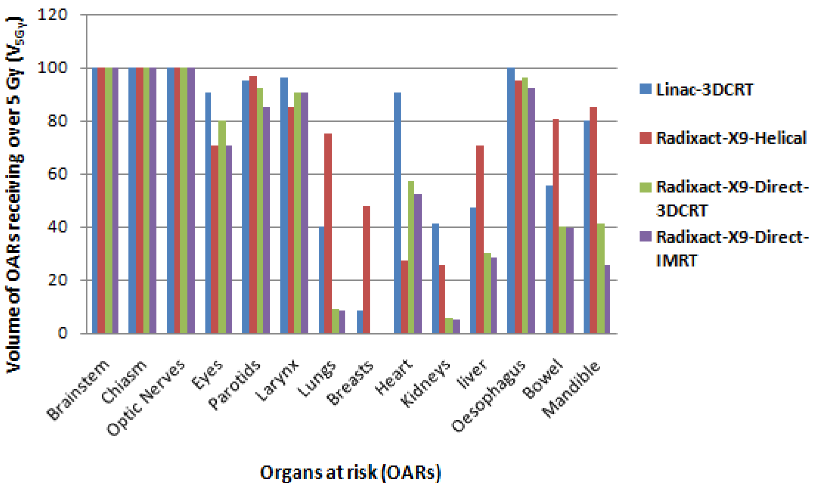

Figure 2. Graphical representation for comparison of percentage volumes receiving over 5 Gy (V_{5Gy}) for various organs at risk using different treatment techniques

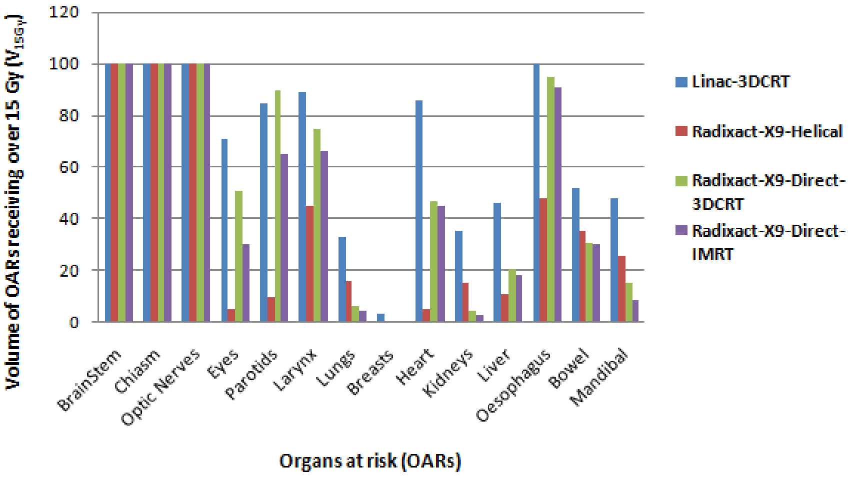

Figure 3. Graphical representation for comparison of percentage volumes receiving over 15 Gy (V_{15Gy}) for various organs at risk using different treatment techniques

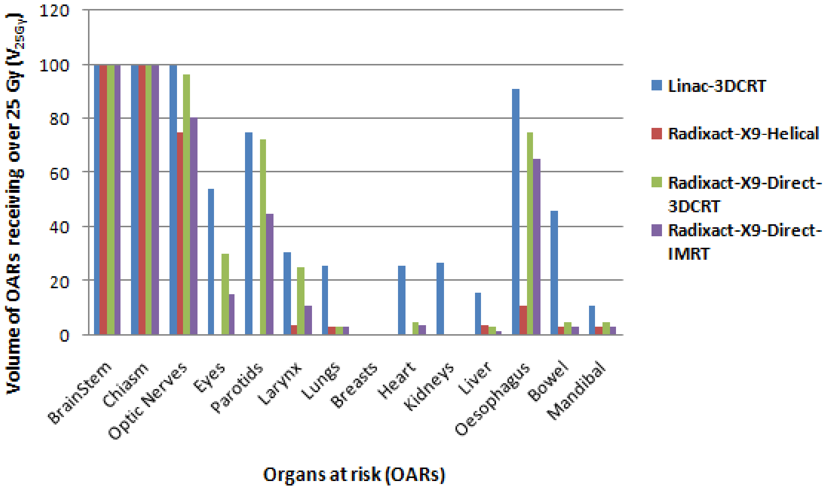

Figure 4. Graphical representation for comparison of percentage volumes receiving over 25 Gy (V_{25Gy}) for various organs at risk using different treatment techniques

Table 4. Comparison of homogeneity index for craniospinal irradiation using different treatment techniques

Treatment Techniques	Number of patients	Homogeneity Index (HI)		*P* value (Anova test)
		Mean	S.D	
Linac-3DCRT	22	17.37	1.44	P < 0.05
Radixact-X9-Helical	22	3.57	0.77	P < 0.05
Radixact-X9-Direct-3DCRT	22	8.15	1.02	P < 0.05
Radixact-X9-Direct-IMRT	22	8.62	0.98	P < 0.05

Note: HI: Homogeneity index; S.D: Standard deviation; Linac: Linear accelerator; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy; Radixact-X9: Radixact-X9 unit

Table 5. Comparison of different parameters for craniospinal irradiation using different techniques

Parameters	(Mean ± S.D)				*P* value (Anova test)
	Linac-3DCRT	Radixact-X9-Helical	Radixact-X9-Direct-3DCRT	Radixact-X9-Direct-IMRT	
Planning Time (minutes)	117.73 ± 15.09	356.45 ± 40.21	113.59 ± 18.77	157.27 ± 32.54	P < 0.05
Patient Setup Time (seconds)	499.86 ± 16.54	255.0 ± 22.29	259.09 ± 22.27	257.0 ± 22.17	P < 0.05
Move Isocenter Time (seconds)	149.0 ±15.68	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	P < 0.05
Beam on Time (seconds)	125.0 ± 17.75	1394.0 ± 154.26	815.0 ± 123.08	951.0 ± 157.23	P < 0.05

Note: S.D: Standard deviation; Linac: Linear accelerator; 3DCRT: Three-dimensional conformal radiotherapy; IMRT: Intensity-modulated radiotherapy; Radixact-X9: Radixact-X9 unit

As shown in Table 4, it is clear that the Radixact-X9-Helical plan provided better dose homogeneity than other techniques. The above parameter has a crucial role in deciding about the treatment (i.e. dose and volume of irradiation). In addition, there some other parameters that have an important role in patient's comfort during the treatment period, including planning time, patient in/out time, patient setup time, move isocenter time, and beam-on time. All of these parameters are further discussed in Table 5.

Discussion

Due to outsize target volume and large field size, CSI planning is not an easy task with uniform dose coverage. Currently, 3D volumetric image is widely using for radiotherapy planning. Two properly well collimated lateral cranial fields with geometrically matched with the divergence of direct posterior spinal fields, usually used in conventional CSI planning [19]. The current study aimed to, firstly, fill up the space for CSI treatment and, secondly, helping directly to future treatment options. In this study, four different techniques of CSI were evaluated (i.e. Direct-3DCRT, Direct-IMRT, and Helical with Radixact-X9 machine as well as the Linac based-3DCRT by Novalis-Tx Linac) [20]. Dose homogeneity was better in the Radixact-X9-Helical technique plan compared to other plans [Table 4]. Direct-3DCRT technique and Direct-IMRT technique can deliver dose at fixed pre-defining angles only. Direct-IMRT produced better constraints to different OARs at the same time and optimizes plans, according to their PTV dose. However, in Direct-3DCRT, we can prescribe the dose to PTV only without applying any constraint to OARs. This is the main restriction of the Direct-3DCRT plan. In contrast to the Direct-3DCRT plan, a dose constraint can be applied to OARs for Direct-IMRT techniques. Similar to inverse planning, it can be performed by rotating gantry in 360º, instead of pre-defined fixed gantry angle, as in the Direct-IMRT technique. This type of planning comes in the helical mode in Radixact-X9. Due to its ability to rotate by 360º, we can get more degrees of freedom for dose delivery, and also it is possible the prescribed dose, especially to a cribriform plate with less dose to the eye and optic nerves. In helical planning, the main benefit is for structure, which lies anterior to the spine like the heart, esophagus, and larynx. Overall, the helical technique proposed better OARs sparing with better homogeneity, but it should be used with care, as if be administered in the long-term, it may increase patients' movement due to enhanced distress [Table 5]. As a result, there is a dose difference in the prescribed and delivered dose. The Radixact-X9-Direct-3DCRT technique may be the choice of treatment for claustrophobic patients and for those patients who require anesthesia. The Radixact-X9-Direct-IMRT technique maybe the choice of treatment in cases that are in the need of spare certain lateral structures such as breasts in order to minimize the probability of developing secondary malignancy, especially for the young age patients. The Radixact-Helical technique is the choice of treatment in cases that there is a need for achieving better homogeneity and sparing OARs. Complete coverage of the cribriform plate is not possible if PTV is cover by the eye in the view of the cranial field. In that case, the Radixact-X9-Helical technique should be used to overcome this problem. Although it seems that Linac-3DCRT is better in terms of resource distribution, mainly because its treatment duration and planning are shorter. it worth noting that these benefits do not outweigh the problem in dose homogeneity and OARs sparing.

Conclusion

A CSI is always a tough planning procedure in terms of plan delivery and plans verification due to outsize target volume and large field size. The benefit-risk ratio can be easily improved with the use of modern techniques of radiotherapy. For CSI type-outsize target volume, the helical planning procedure meets the criteria of a most preferable plan. A helical plan can be easily implemented without junction matching and complex verification procedures. An inbuilt image guidance dose delivery gives an extra edge in such a large complex target volume [19]. This study cleared much doubt regarding complex CSI planning by traditional Linac-3DCRT technique and different techniques of Radixact-X9, like Helical, Direct-IMRT, and Direct-3DCRT. In addition, it was found that Radixact-Helical and Radixact-Direct techniques plans provide better sparing of OARs with good homogeneity in comparison to the Linac-based 3DCRT technique. It is very difficult to point out any single winner in this race. The Radixact-X9-Helical plan resulted in lesser D_{mean} and D_{max} doses for most of the OARs. Radixact-X9-Helical achieved good homogeneity compared to other techniques like Linac-3DCRT, Radixact-X9-Direct IMRT, and Radixact-X9-Direct-3DCRT. Overall, Radixact-X9-Helical maybe an appropriate option for cases that require shorter treatment time with better OARs sparing and good dose homogeneity. Thus, it is suggested that each radiotherapy center should do its own planning investigation in order to obtain the results based on their in-house protocols, software, hardware, and expertise. Every technique has its own advantage and disadvantages. This study can help us to better understand all of these variable parameters in a more comparable and tabulated format. Evidence provided by the current study can play a crucial role to choose a treatment option for various patients.

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