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Impact of Multi-criteria Optimization on 6-MV Flattening Filter-Free Volumetric Modulated Arc Therapy for Craniospinal Irradiation

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ABSTRACT

Introduction: Volumetric modulated arc therapy (VMAT) is an advanced technique used for radiotherapy treatment using different optimization modes. The present study aimed to evaluate Multi-criteria Optimization (MCO) influence on VMAT for Craniospinal Irradiation.

Material and Methods: Fifteen CSI patients treated with 23.4 Gy/13 fractions followed by a boost dose of 6-MV flattening filter-free beams were chosen for this study. Conventional VMAT (c-VMAT) plans were generated for Elekta Versa HD™ linear accelerator. Keeping all other parameters constant, c-VMAT plans combined with MCO (MCO-VMAT) were created for comparison. We compared homogeneity index (HI), conformity index (CI), planning target volume (PTV) dose coverage (D98%), organ at risk (OAR) dose, normal tissue integral dose (NTID), volume receiving ≥ 5 Gy and ≥ 10 Gy by normal tissue, delivery time (DT), monitor units (MUs), and calculation time (CT).

Results: Our findings demonstrated that HI and CI improved slightly in MCO-VMAT, in comparison with c-VMAT (P>0.05). No significant dose difference was observed in D98% for PTV and volume receiving the dose of ≥ 5 Gy, ≥ 10 Gy, and NTID (P>0.05). A slight increase was found in maximum dose to PTV in VMAT-MCO, compared to c-VMAT (P>0.05). The mean dose, max dose, and dose received by OAR were significantly lower in VMAT-MCO as compared to c-VMAT (P<0.05). The MU, CT, and DT were noticed to be lower in c-VMAT than MCO-VMAT (P>0.05).

Conclusion: The MCO-VMAT can be used for CSI, without compromising target coverage, reduced OAR dose by accepting a slight increase of MUs, delivery and calculation time as compare to c-VMAT.

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Introduction

Craniospinal irradiation (CSI) is an important method for treating various malignancies of the central nervous system, such as medulloblastoma, brain tumors with the risk of leptomeningeal spread, and other neurologic diseases [1]. The brain, spinal cord, and overlying meninges make up a large volume of CSI targets. Shape and length of the target volume make it a challenging process.

Using the classic three-dimensional conformal radiotherapy (3DCRT) method, CSI may be planned with two parallel opposed fields to treat the brain and a single posterior field for the spinal cord. This technique is complex with a high exit dose to the organ at risk (OAR) and a shifting junction strategy leading to the risk of overdose or underdose along with field matching. Therefore, volumetric modulated arc therapy (VMAT) is used, which can deliver a conformal dose, spare OAR volumes, and reduce treatment time. Moreover, we are able to overcome the field junction difficulties using this technique, compared to the 3DCRT method [2].

Many authors investigated VMAT-based CSI and the results revealed an improvement in dose homogeneity and junction free treatment delivery [3]. In this regard, Fogliata et al. studied the VMAT CSI plan and achieved a highly conformal dose distribution, shorter beam-on time, and satisfying delivery without a change in field junctions over the conventional technique [4].

Furthermore, Lee et al. found enhanced conformity, lower heterogeneity in planned target volume (PTV), and diminished dose to OAR in CSI by

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VMAT, compared to the conventional plan. It is justified to use VMAT CSI for decreasing toxicity to non-target volumes, while appropriate coverage to the target volume is preserved [2].

Nowadays, diverse commercially-available treatment planning systems (TPSs) are applied with different optimization modes during VMAT planning, such as constrained optimization (COM), Pareto mode (PM), and multi-criteria optimization (MCO). Novel MCO mode has the capacity to generate superior treatment plans in terms of dose distribution and planning time, in comparison with the conventional intensity-modulated radiotherapy (IMRT) plans.

Craft et al. tested IMRT with MCO for glioblastoma and pancreatic cancer. Their results showed an improved plan quality with reduced treatment planning time, compared to the standard optimization plan [5]. Moreover, McGarry et al. demonstrated a significant decline in rectal dose using MCO for prostate cancers [6].

Although many authors have evaluated MCO for clinical sites other than CSI, it is necessary to assess CSI because of the large target size, the involvement of various OAR volumes, treatment delivery, and dose-time calculation. To the best of our knowledge, no precise data was available regarding the impact of MCO on CSI using a flattening filter-free (FFF) VMAT technique. Therefore, the purpose of this study was to investigate the effect of MCO on FFF-VMAT plans by comparing the conventional FFF-VMAT plans for CSI using different dosimetric parameters.

Materials and Methods

Patients

For the present study, 15 CSI patients treated with 23.4 Gy/13 fractions followed by a boost dose using the VMAT technique were chosen. Patients were immobilized by thermoplastic molding in the supine position. The simulation was performed utilizing a 16-slice positron emission tomography simulator (Siemens® Biograph Truepoint® HD, Siemens AG, Medical solution, Erlangen, Germany) with a bore size of 70 cm. Slices with a thickness of 3 mm were obtained for VMAT planning.

The target delineations, including gross tumor volume, clinical target volume, PTV, and OAR volume were contoured by a radiation oncologist according to the multidisciplinary protocol of institution with the support of different image fusions [7]. In addition, the volumes of OARs, such as the left lung, right lung, left eye, right eye, left parotid, right parotid, left kidney, right kidney, heart, liver, left lens, right lens, and small bowel were considered. The body volume minus all tumor volumes were taken as normal tissue.

Dosimetric Indices Used in the CSI VMAT Plan

The CSI VMAT plans were generated using a 6-MV FFF photon beam for Elekta Versa HD™ linear accelerator (Elekta Ltd, Crawley, UK) with the leaf width of 0.5 cm at the isocenter. All VMAT plans were produced using Monaco™ version 5.1 (Elekta Ltd, Missouri, USA) TPS.

The FFF beam was used to provide a higher treatment dose rate and dose uniformity within the PTV volume. High dose rates from the FFF beams are now being offset by larger monitor units (MUs) requirement. Increased dose rate led to a decline in treatment time and setup error during treatment delivery.

The segment width of 8 mm, fluence width of 3 mm, medium fluence smoothing, grid size of 0.3 cm, 8 mm segment width, and gantry interval of 20° were applied for the plan. In addition, dual partial arcs were used for cranium (50°– 180° and 180°–310°), upper spine (125°–180° and 180°–235°), and lower spine (110°–180° and 180°–250°). Due to the length of the target, 2-3 isocenters were used during plan generation. The Monte Carlo dose calculation algorithm was used for the final calculation with 2% of statistical uncertainty.

Monaco™ TPS and Optimization Modes

A two-stage process is used for optimizing dose distribution in the Monaco™ TPS. During the first stage, an ideal fluence distribution of beams is optimized to meet the user-defined prescription for a single set of beams. Next, this ideal distribution is transmitted into a set of segments where the shapes and weights are optimized as prescribed in the second stage [8]. Pencil beam algorithm is utilized at the first stage and the Monte Carlo algorithm is used at the final-stage dose calculation.

Different mechanisms for handling the constraints with distinct priorities are offered by the TPS optimization modes and resolve any situations where constraints mutually exclude themselves. The user has the option to choose diverse optimization modes, namely COM, PM, and MCO for VMAT plan generation in Monaco™ TPS [9].

Constrained Optimization (COM): Constrain is defined as anatomical specific functions that have to be fulfilled during optimization. In a planning system, COM allows constrains to occur on priority in normal tissue constrains, which are fulfilled by keeping the target object constrain at risk. For instance, when an underdose volume constrain is used on a target and the constrains on OAR are not being fulfilled, the underdose volume constrain on the target will be relaxed leading the constrains on OAR being met first.

Pareto Mode (PM): On the other hand, in PM, priority is placed on constrains to set the minimum doses on target. The target doses are met, while the risk of not meeting the normal tissue constraints is considered. For example, in this mode, in case an underdose volume constrain is used on a target and a constrain on an OAR is not met, the constrain on the OAR will be relaxed first so that the underdose volume constrain on the target may be achieved as the priority.

Multi-criteria Optimization (MCO): This mode is defined as constrains that are consequently tightened during the whole optimization process provided that they are not the limiting constrains to the objective. It

literally tries to achieve an even reduced dose (tightening the constraint) to the selected OAR although it is still able to meet the target objective.

Conventional and MCO-Guided CSI VMAT Plan

In this study, the reference conventional VMAT (c-VMAT) plans were generated using the COM mode and were clinically approved by a radiation oncologist. By keeping all other parameters constant in the reference plan, re-optimization was performed adding MCO option in the IMRT constrains window for all OAR volumes. The final produced MCO-VMAT plans were used for comparison as shown in figures 1-4.

The results were analyzed for the two different VMAT plans with and without MCO optimization. Fifteen VMAT plans from each category making a total of 30 VMAT plans were generated for dosimetric comparison. Each plan was evaluated using a dose-volume histogram (DVH) created by the planning software. The plan quality was compared using different dosimetry indices as mentioned below. Moreover, dose coverage to PTV, OAR doses, CT, and plan deliverability were analyzed.

Dosimetric Parameters used for Plan Quality Analysis

Conformity Index (CI): It is defined as the ratio of the volume receiving the prescribed dose and volume of PTV**.** The CI id calculated using the following formula and CI=1 is ideal [10]:

$$CI = PTV_V^{100\%}/V_{PTV} \quad (1)$$

Where PTVV100% is the volume receiving the prescribed dose and VPTV is the volume of PTV receiving the prescribed dose.

Homogeneity Index (HI): This index is regarded as the ratio evaluating dose homogeneity in PTV [11].

$$HI = (D_{2\%} - D_{95\%})/D_{50\%} \quad (2)$$

Where $D_{2\%}$, $D_{98\%}$, and $D_{50\%}$ are the doses received by 2%, 98%, and 50% volume of the PTV, respectively.

Normal Tissue Integral Dose (NTID): It is the product of PTV (V_{PTV}) and the mean dose (Dm) of radiation to the body [12].

$$NTID = Dm \times V_{PTV} \text{ [Grayy].[Liter]} \quad (3)$$

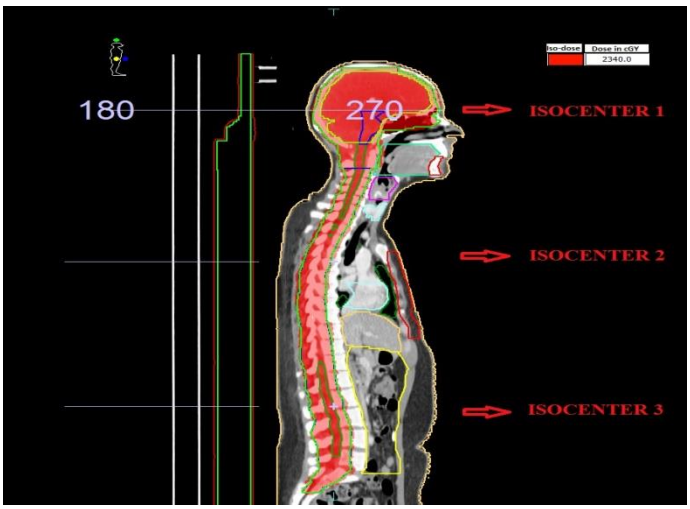

Figure 1. CSI-VMAT with MCO optimization; sagittal view

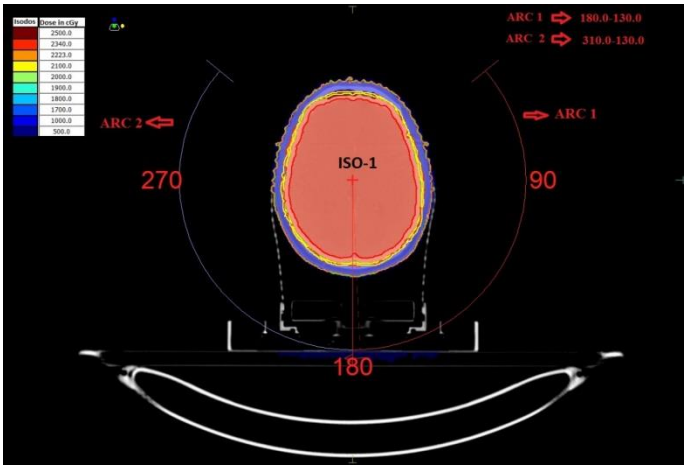

Figure 2. CSI-VMAT with MCO optimization; brain axial view

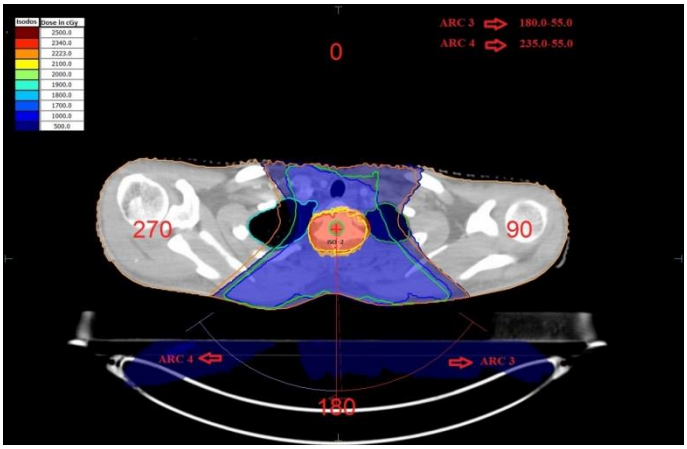

Figure 3. CSI MCO-VMAT upper spine; axial view

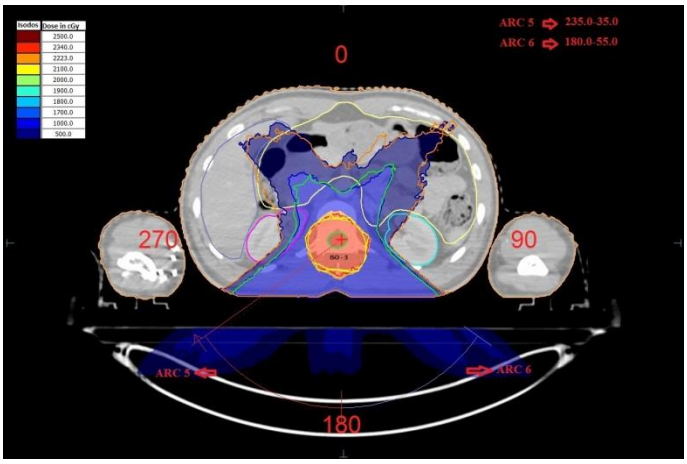

Figure 4. CSI MCO-VMAT plan; lower spine axial view

Moreover, the contribution of the low dose volume of ≥ 5 Gy and ≥ 10 Gy received by the normal tissue are compared.

Calculation Time (CT): The total calculation time estimated from Monaco™ optimization console window for each CSI VMAT plan [11].

CT (min) = start time (min)−end time (min) (4)

The 64-bit operating system was used for this study with the characteristics of HP Z820 workstations, 32 GB RAM, Intel® CPU E5-26700 @ 2.60 GHz (2-Processor).

PTV Dose Coverage and OAR Dose: The dose to PTV was analyzed as D2%, D50%, D95%, and D98% where D was the doses received by 2%, 50%, 95%, and 98% of the PTV. The volume receiving 95% of the prescribed dose was assessed. In addition, the maximum dose (D_{max}), mean dose (D_{mean}), and the dose received by 1 and 2cc of PTV were analyzed. The D_{mean}, D_{max}, and dose received by the left lung, right lung, left eye, right eye, left parotid, right parotid, left kidney, right kidney, heart, liver, left lens, right lens, and small bowel were evaluated.

Delivery time (DT) and Total MUs: The delivery time was calculated for each CSI VMAT plan in the Integrity (Elekta Ltd, Crawley, UK) system used for the treatment delivery.

Statistical Analysis

The plan quality indices were compared for the generated CSI VMAT plans with and without MCO mode and determining their P-value. The data were analyzed by the independent samples t-test using the SPSS software version 16 (IBM, USA).

Results

The plan quality indices were calculated using DVH and the dosimetric and clinical parameters were compared between c-VMAT and MCO-VMAT. According to our findings, some similarities and differences were observed due to the impact of MCO. The comparison results were analyzed using descriptive and inferential statistics and were represented by charts, tables, and figures.

Target

The HI and CI improved in MCO-VMAT plans, compared to c-VMAT plans. However, the dosimetric assessments showed no statistically significant difference in HI (P>0.05), while CI difference was

significant (P<0.05) as shown in Table 1. In addition, the dose coverage to PTV increased in c-VMAT plans for D98%, D50%, D2%, and 95% of the prescribed dose (V95%), in comparison with MCO-VMAT plans. Results of the current study demonstrated that the two plans were not significantly different in this regard (P>0.05).

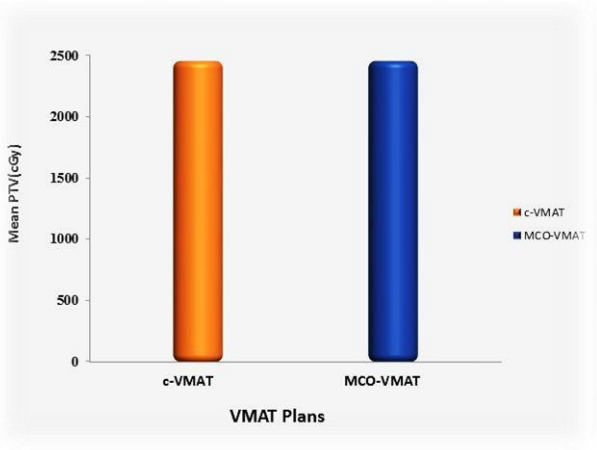

Figure 5.Effect of VMAT-MCO on mean dose to PTV

Figure 5 depicts that the mean dose to PTV was almost similar for both VMAT plans and no statistically significant difference was observed (P>0.05). Furthermore, D_{max}, as well as the volume received by 1 and 2 cc slightly increased in MCO-VMAT plans, compared to c-VMAT plans. However, the latter difference between the two treatments was not statistically significant (P>0.05) as indicated in Table 1.

OAR Volume

According to Table 2, the mean dose, D_{max}, and dose received by the left lung, right lung, left eye, right eye, left parotid, right parotid, left kidney, right kidney, heart, liver, left lens, right lens, and small bowel were markedly lower in MCO-VMAT plans than c-VMAT plans. However, no statistically significant dose difference was observed (P>0.05). As shown in Table 3, the NTID and normal tissue volume receiving a dose of $\geq$ 5 and $\geq$ 10 Gy declined MCO-VMAT plans, compared to c-VMAT plans. The mentioned difference between the plans was not statistically significant (P>0.05).

Calculation Time (CT)

As could be seen in Table 3, calculation time slightly elevated in MCO-VMAT plans, in comparison with c-VMAT plans, which was not significant (P>0.05).

Table 1. Comparison of dose coverage to planning target volume between c-VMAT and MCO-VMAT plans

Plan quality metrics	Plan	Mean±SD	Mean difference	t-value	df	P-value
CI	c-VMAT	1.16±0.12	0.116	2.858	28	0.008
	MCO-VMAT	1.050±0.09				
HI	c-VMAT	0.79±0.02	-0.092	-1.523	28	0.139
	MCO-VMAT	0.17±0.23				
PTV_{mean} (cGy)	c-VMAT	2453.3±34	0.12	0.004	28	0.997
	MCO-VMAT	2453.2±117				
D98% (cGy)	c-VMAT	2440.8±327	166.28	1.845	28	0.076
	MCO-VMAT	2274.5±121				
D2% (cGy)	c-VMAT	2643.5±354	26.22	0.2	28	0.843
	MCO-VMAT	2617.3±365				
D50% (cGy)	c-VMAT	2544.8±336	190.52	1.668	28	0.106
	MCO-VMAT	2354.3±286				
V95%(cGy)	c-VMAT	2471.1±327	-67.533	-0.548	28	0.588
	MCO-VMAT	2403.6±347				
PTV_{max} (cGy)	c-VMAT	2722.6±41	-7.9	-0.463	28	0.647
	MCO-VMAT	2730.5±51				
PTV1cc (cGy)	c-VMAT	2619.7±37	15.426	1.144	28	0.262
	MCO-VMAT	2604.3±35				
PTV2cc (cGy)	c-VMAT	2608.2±38	18.566	1.361	28	0.184
	MCO-VMAT	2589.6±36				

PTV: planning target volume, VMAT: volumetric modulated arc therapy, MCO: multi-criteria optimization, c: conventional, CI: conformity index, HI: homogeneity index, CC: volume, D_{max}: max dose, D_{mean}: mean dose, D98%, D2%, and D50%: dose received by D98%, D2%, and D50% of volume, V95% Gy: volume received by 95% of the prescribed dose, SD: standard deviation, cGy: centigray

Table 2. Comparison of dose to OAR between c-VMAT and MCO-VMAT plans

OAR volume (cGy)	Plan	Mean±SD	Mean difference	t-value	df	P-value
Left eye (D_{mean})	MCO-VMAT	746.1±634	-407.52	-1.832	28	0.078
	c-VMAT	1153.6±582				
Right eye (D_{mean})	MCO-VMAT	798.7±638	-385.28	-1.737	28	0.093
	c-VMAT	1184±574				
Left parotid (D_{mean})	MCO-VMAT	456.6±378	-220.893	-1.774	28	0.087
	c-VMAT	677.5±298				
Right parotid (D_{mean})	MCO-VMAT	445.8±340	-222.18	-1.981	28	0.058
	c-VMAT	668±269				
Left lung (V30)	MCO-VMAT	418.5±248.6	-99.024	-1.169	28	0.252
	c-VMAT	517.5±231.8				
Right lung (V30)	MCO-VMAT	490.1±290.3	-121.276	-1.245	28	0.224
	c-VMAT	611.4±241.1				
Heart (D_{mean})	MCO-VMAT	433.1±238.8	-103.26	-1.43	28	0.164
	c-VMAT	536.4±145				
Left kidney (D_{mean})	MCO-VMAT	293.3±250.4	-94.993	-0.937	28	0.357
	c-VMAT	388.3±302.5				
Right kidney (D_{mean})	MCO-VMAT	341.4±265.3	-100.586	-0.99	28	0.331
	c-VMAT	442±290.7				
Liver (D_{mean})	MCO-VMAT	462.5±160.6	6.546	0.114	28	0.91
	c-VMAT	456±153.1				
Right lens (D_{max})	MCO-VMAT	652.5±510.4	385.52	-1.906	28	0.067
	c-VMAT	1038±594.3				
Left lens (D_{max})	MCO-VMAT	652.5±510.4	-385.52	-1.906	28	0.067
	c-VMAT	1038±594.3				
Bowel (D_{max})	MCO-VMAT	1912.6±563.8	-33.706	-0.171	28	0.865
	c-VMAT	1946.4±512.8				

VMAT: volumetric modulated arc therapy, MCO: multi-criteria optimization, c: conventional, SD: standard deviation, D_{max}: max dose, D_{mean}: mean dose, V30: dose received by 30% volume

Table 3. Comparison of quality metrics between c-VMAT and MCO-VMAT plans

Plan quality metrics	Plan	Mean±SD	Mean difference	t-value	df	P-value
NTID (cGy)	c-VMAT	30.1±13	3.887	0.878	28	0.387
	MCO-VMAT	26.2±10				
5Gy (cc)	c-VMAT	12700.3±2967	974.5	0.878	28	0.388
	MCO-VMAT	11725.7±3111				
10Gy (cc)	c-VMAT	7693.6±2840	770.3	0.873	28	0.39
	MCO-VMAT	6923.2±1898				
MU	c-VMAT	1795.6±256	-251.1	-2.319	28	0.028
	MCO-VMAT	2046.7±331				
CT (min)	c-VMAT	2.59±0.76	-0.36	0.973	28	0.338
	MCO-VMAT	2.95±1.18				
DT (min)	c-VMAT	5.91±0.32	-0.44	0.821	28	0.124
	MCO-VMAT	6.35± 0.42				

NTID: normal tissue integral, VMAT: volumetric modulated arc therapy, MCO: multi-criteria optimization, c: conventional, SD: standard deviation, CC: volume, MU: monitor units, CT: calculation time, DT: delivery time

Delivery Time (DT) and Total Monitor Units (MUs)

Our findings as demonstrated in Table 3, revealed that the two types of VMAT plans were not significantly different in terms of MUs and DT (P>0.05). However, c-VMAT plans were shown to have lower MUs and delivery time than MCO-VMAT plans.

Discussion

The CSI is one of the most challenging processes in radiotherapy planning and delivery. Therefore, the procedure of simulation, planning, and delivery for the CSI technique requires a great deal of care. The majority of patients who receive treatment with CSI are children

and adolescents. Prior to treatment delivery, the evaluation of the OAR dose must be carried out to minimize the complications associated with radiotherapy.

Studenski et al. compared CSI treatment with VMAT and conventional RT. Their results revealed that homogeneous target coverage is achieved in VMAT planning with a reduced dose to multiple critical organs, compared to the conventional 3DCRT [13]. Results of the study conducted by Miralbell et al. showed a significant diminish when the IMRT technique was used instead of the conventional approach in estimating the absolute risk of secondary cancer_in pediatric patients based on dose-volume distributions for the non-target organs [14].

Issues with conventional 3DCRT approach typically occurred between the cranial and spinal fields at the level of cervical vertebrae with a high risk of injuries, such as radiation myelopathy in the cases of overdose or treatment failure due to underdose in field junctions. The CSI-VMAT technique replaces these risks related to geometrical uncertainties with junction free optimization process [15-17]. Consequently, for the present study, every plan was generated using the VMAT technique in order to increase the efficiency of treatment delivery and compare different optimization modes.

The MCO was developed as a tool for improving the efficiency of the treatment planning process. As reported by Nguyen et al., MCO can be used to generate efficient treatment plans for complex plans [18]. Therefore, the present study evaluated MCO-VMAT on CSI and compared this method with c-VMAT.

Results of the current study were supported by Zieminski et al. who compared standard (STD) optimization and MCO using IMRT for whole-brain radiotherapy. These authors reported MCO-VMAT to be the optimal modality in terms of PTV coverage, OAR sparing, and decreased D_{max}, compared to STD-VMAT [19].

A study by Wala et al. evaluated MCO in the IMRT technique for localized prostate cancer. They reported that MCO-based planning for prostate IMRT is more efficient and produces high-quality plans with good target homogeneity and sparing OAR volumes without sacrificing target coverage [20].

The application of MCO on VMAT in the present study was accompanied by favorable target coverage to PTV and a significant reduction in dose to OAR volumes, which can diminish the acute and late toxicity of RT. As a result, MCO is suggested as a suitable option for decreasing dose to OAR volumes in CSI without compromising target dose coverage.

For clinical use, the time taken by each VMAT plan to complete the whole process without compromising plan quality is an important factor. Ghandour et al. evaluated MCO-VMAT using RayStation® TPS for prostate cancer. The results of their evaluations of the plans and dosimetric measurements demonstrated that MCO-VMAT can be efficiently applied clinically with enhanced planning procedure by reducing planning time instead of affecting the dosimetric quality [21].

Craft et al. investigated whether MCO can reduce treatment planning time and improve plan quality in the IMRT technique. Their results revealed with conclusive evidence that MCO-based planning is better regarding planning efficiency, reduced time, and the quality of dose distribution [5]. Kierkels et al. reported in their study that new treatment planners can produce high-quality IMRT plans for the head and neck cancer patients with reduced planning time using MCO [22].

The present study showed that a slight increase in planning time in MCO-VMAT, compared to c-VMAT caused no statistically significant difference. In addition, marginally less delivery time and NTID were observed in c-VMAT than MCO-VMAT without a significant difference. An increased MU in MCO-VMAT will increase patient waiting time on the couch which may lead to setup error during treatment delivery.

Therefore, we used a high-dose FFF-VMAT plan for the current study in order to increase delivery efficiency. According to the qualitative dosimetric comparisons in the present study, MCO-VMAT can generate a better plan in terms of lower dose to critical organs without compromising dose to PTV volume.

Conclusion

In Monaco™ TPS, the user can utilize any of the two optimization modes during VMAT plan generation. The MCO-VMAT can be used for CSI without compromising target coverage or reduced OAR dose. On the other hand, a slight elevation was observed in MUs, delivery time, dose received by normal tissue volume, and CT, compared to c-VMAT.

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