Evaluation of Monaco dose calculation errors for out-of-field regions in intensity modulated radiotherapy of nasopharyngeal cancer

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► ***Original article***

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ABSTRACT

Background: The aim of this study is to assess the accuracy of dose calculations by Monaco Treatment Planning System (TPS) for critical organs positioned in out-of-field (OOF) regions during two intensity-modulated radiation therapy (IMRT) techniques in patients diagnosed with nasopharyngeal cancer (NPC). ***Materials and Methods:*** Computed tomography (CT) images from 10 NPC patients (aged 54-77 years) were used for treatment planning using 7 and 11 fields IMRT techniques with the Monaco TPS. Doses for organs at risk (OARs) in OOF regions, including the eyes, lenses, and optic nerves, were calculated using the TPS and compared with measurements obtained from the OCTAVIUS 4D phantom. Additionally, dose distributions derived from TPS calculations were compared with measurements using the gamma analysis method, with a threshold dose set at 10% of the maximum dose. ***Results:*** Although gamma pass rates exceeded 95% for all patients when OOF regions were excluded, measurements indicated that the Monaco TPS generally underestimated doses to OOF organs by approximately 25%. This underestimation tended to increase with lower dose values, and TPS errors varied across different tissues, including the eyes, lenses, and optic nerves. ***Conclusion:*** In conclusion, the Monaco TPS demonstrates significant underestimation errors in dose calculations, especially for organs located in OOF regions during IMRT for NPC patients. Considering the potential risk of secondary cancers, it is imperative to prioritize meticulous attention to ensure precise dose estimation in OOF regions by the TPS.

INTRODUCTION

Radiotherapy is one of the main modalities commonly used for cancer treatment (1-3). Computerized treatment planning systems (TPSs) are used to design the radiotherapy treatment plans and calculate the delivered dose within patients' body volume. Ensuring the accuracy of TPS calculations is a critical procedure that must be undertaken across various scenarios with minimal uncertainty (4-6). Model-based dose calculation algorithms such as analytical anisotropic algorithm (AAA) and collapse cone convolution (CCC) aim to improve the dose calculation accuracy and mitigate uncertainties, particularly in the out-of-field (OOF) regions (7, 8). Additionally, newer algorithms utilizing Monte Carlo calculations, such as X-ray voxelized Monte Carlo (XVMC), can offer more precise calculations of OOF doses (9, 10).

One of the primary concerns in low-dose regions is the risk of radiation-induced secondary cancers (11-14). Organs situated outside the radiation field may also receive low doses of radiation, raising serious concerns regarding potential secondary cancer risks (15, 16). The probability of secondary cancers mainly depends on the volume of low dose region and the amount of the low doses. Additionally, several factors - including the number of radiotherapy fractions, the distribution of delivered doses, biological characteristics of exposed organs, irradiation field size, and the primary irradiated volume-can influence the likelihood of secondary cancer induction (17-20). Various components can contribute to OOF doses, such as leakage radiation, collimator scatter, and patient/phantom scatter. Patient scatter predominantly affects the dose near the field edge, while leakage radiation emerges as the primary contributor at considerable distances from the field edge (21).

Several investigations assessed the OOF doses calculated by TPS and compared them with dosimetry measurements (8, 20, 22-24). For instance, Mahmoudi *et al.* (23) investigated the OOF doses calculated by Monaco TPS (Elekta company, Sweden) in intensity modulated radiation therapy (IMRT) on CIRS thorax phantom (CIRS Dynamic Thorax phantom, Norfolk, USA). The doses were compared with the 3-dimensional (3D)

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measurements of OCTAVIUS-4D phantom (PTW, Freiburg, Germany), and point dose measurements by Farmer (0.6 cm^3, type 30013, PTW, Freiburg, Germany) and Semiflex (0.07 cm^3, type 31021, PTW, Freiburg, Germany) dosimeters. They reported that the TPS dose calculations for nearly all of the distances by an average of 40%, and this underestimation worsened from 10 cm to 13 cm distances situated in OOF regions. Furthermore, the TPS dose calculations had a higher than 10% overestimation in 1 cm distance from the OOF edge in water equivalent medium. In another study, Moghaddam *et al.* [8] evaluated the OOF doses calculated with AAA algorithm of Eclipse TPS (version 13.0.20, Varian Medical Systems, Palo Alto, CA) using sliding window IMRT for 9 coplanar fields technique in prostate cancer patients. The TPS dose calculations were compared with 3D measurements of Delta4 phantom (ScandiDose, Sweden). They concluded that AAA algorithm had poor dose calculation accuracy in OOF regions with a significant dose underestimation. Majer *et al.* [20] measured IMRT and 3D conformal radiotherapy (3D-CRT) OOF doses for brain tumors radiotherapy using anthropomorphic pediatric phantoms (Inc., Norfolk, VA, USA), and compared them with Eclipse TPS (AAA dose calculation algorithm, v.8.6, Varian medical systems, USA) calculations. Based on their findings, for both IMRT and 3D-CRT techniques, TPSs underestimated OOF doses. The above-mentioned studies stated that commercial TPSs using various dose calculation algorithms mainly underestimated the OOF doses.

Advanced techniques in radiation therapy incorporate multi-leaf collimators (MLCs) to improve dose conformity. In modulated radiotherapy techniques like IMRT, a higher number of monitor units (beam on time) are utilized. This can lead to an increase in contributions from leakage radiation to the OOF dose, subsequently raising the risk of secondary cancers [25, 26]. Furthermore, radiation therapy planning systems cannot be adequately commissioned for OOF dose calculations [19]. Therefore, evaluating TPS dose calculation uncertainties in OOF regions can be helpful for clinical practices and estimating the related risks. In the current study, we assessed the Monaco TPS dose calculation errors in OOF regions for IMRT treatment of nasopharyngeal cancers (NPCs). To the best of our knowledge, there has been no investigation evaluating the accuracy of OOF Monaco dose calculations in IMRT for NPCs.

MATERIALS AND METHODS

Patients

Computed tomography (CT) scans of 10 patients diagnosed with NPC (5 males and 5 females) with ages ranging from 54 to 77 years (average age: 61.6±12.2 years) were used for treatment planning and dose calculations without considering the identifying information. Since the study was retrospective, consent forms were not obtained from patients. Given that definitive chemo-radiotherapy is the standard treatment for NPC across all stages except T1N0, where radiotherapy alone is recommended [27], patients in stages T1 to T4 were included in this study, provided they had not undergone prior radiotherapy, chemotherapy, or surgery treatments.

Treatment planning

Two simultaneously integrated boost IMRT (SIB-IMRT) coplanar fields techniques including 7 fields (gantry angles of 0, 51, 102, 153, 204, 255, and 306 degrees) and 11 fields (gantry angles of 0, 30, 65, 95, 130, 160, 190, 225, 255, 290, and 320 degrees) were designed in Monaco TPS (version 5.11, Elekta. AB, Stockholm, Sweden) for each patient on the CT images with contoured organs. All treatment plans were designed with 6 MV photon beams produced by an Elekta Synergy linear accelerator (Elekta Corporation, Sweden) to deliver the prescribed dose uniformly to planning target volumes (PTV) and spare the organs at risk (OARs), including chiasma, optic nerves, parotids, eyes, lens, and brain stem.

The delineation of the gross tumor volume (GTV) was based on the visible tumor tissue observed in the CT images. The clinical target volume (CTV) encompassed a 1-1.5 cm expansion from GTV and included a low-risk CTV consisting of the skull base, parapharyngeal space, pterygoids, ethmoid sinuses, posterior one-third of the maxillary sinus, sphenoid sinus, and the nasal cavity. A 5 mm margin was applied to the PTV of the CTV, except for areas adjacent to critical organs. The prescribed dose for the target and high-risk lymph nodes was considered 70 and 54 Gy, respectively. The target volumes needed to receive their prescribed doses homogeneously, ensuring 95% coverage of the entire target tissue volume. Additionally, the volume of target tissue receiving doses higher than 105% of the prescribed dose was restricted to 2% of the total volume. The dose distribution for all treatment plans was computed using the Monte Carlo-based (XVMC) dose calculation algorithm.

The optimization dosimetric constraints for OARs and target tissue were defined before the IMRT optimization procedure. The constraints were as follows: the maximum dose received by the spinal cord must be lower than 45 Gy, the maximum dose of optical nerves, chiasm, and brain stem must be lower than 50 Gy, the eye lenses maximum dose must be lower than 4 Gy, the mean doses of eye, parotids, and cochlea must be lower than 30, 26, and 45 Gy, respectively. V_{30Gy} (the volume received at least 30 Gy), and V_{40Gy} of parotid glands must be lower than

50% and 33%, respectively. V_{50Gy}, and V_{40Gy} of eyes must be lower than 0.1 cc and 50%, respectively. The target volumes must receive their prescribed doses homogeneously. In this regard, the whole volume of target tissues must be covered with 95% of the prescribed dose. Furthermore, the volume of the target tissue received higher doses, higher than 105% of the prescribed dose, must be limited to 2% of volume. Figure 1 displays the dose distribution samples in coronal and axial images for a patient who underwent treatment using the 7-field coplanar SIB-IMRT technique.

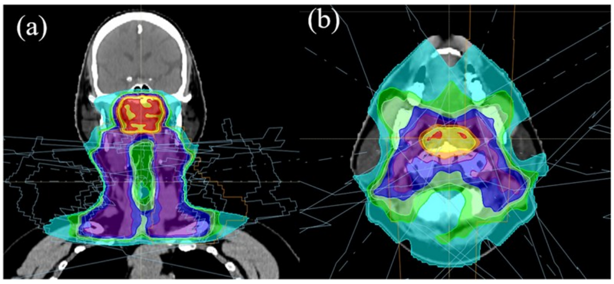


Figure 1. Dose distributions of a patient treated with the 7-field coplanar SIB-IMRT technique in coronal **(a)** and axial **(b)** views.

Dosimetric comparison and gamma analysis

The measurement procedures were performed using the OCTAVIUS 4D phantom (PTW, Freiburg, Germany), with the PTW 2-D array detectors 1500 and the standard head top. The OCTAVIUS 4D cylindrical phantom is constructed from polystyrene with a density of 1.05 g/cm^3 (32 cm in diameter and 34.3 cm in length). This phantom can measure dose levels at various gantry angles by utilizing an inclinometer fixed to the exterior of the gantry. Moreover, it assesses the 3-D distribution of dose subsequent to measuring radiation within its volume. However, it cannot assess radiation fields with couch angles due to the adverse impact of ionizing radiation on its electronic parts; consequently, the couch angles are set to zero for all patient plans.

To acquire the dose distribution calculated by the TPS, CT images of the phantom, were imported into the TPS as a new patient and dose calculations were performed on this phantom using the Monaco TPS dose calculation algorithm. The OCTAVIUS 4D phantom was then irradiated by the same treatment planning. Then the resulting 3-D dose distribution within the phantom volume was obtained using the OCTAVIUS 4D-specific software package (Version 7.0, PTW Company, Germany) [(28)]. To derive volumetric dose distribution from 2-D measurements, a convolution-based algorithm developed by PTW company was employed [(28)].

The organ doses calculated from the dose distributions measured by the phantom in OOF dose regions were compared with the TPS-calculated organ doses for each patient. Following the TECDOC 1540 and TRS 430 protocols, the disparity between the calculated and measured doses was determined using the equation 1 [(29)].

$$\text{TPS error}(\%)=(D_{calculation}-D_{measurement})/D_{measurement}\times 100 \quad (1)$$

Where; $D_{calculation}$ and $D_{measurement}$ represent the TPS calculation and OCTAVIUS4D measured doses, respectively.

To compare the TPS calculated and OCTAVIUS measured dose distributions, gamma analysis was performed for each plan using VeriSoft software (PTW, Germany) with 3% (dose difference)/3mm (distance to agreement) criteria based on TG-119 protocol [(30)]. The global maximum dose point (maximum dose in 3D dose distribution) was used as the normalization point for both the measured and planning dose distributions and a 10% maximum dose threshold was considered that determined the regions under the threshold value, gamma values will not be calculated.

Statistical analysis

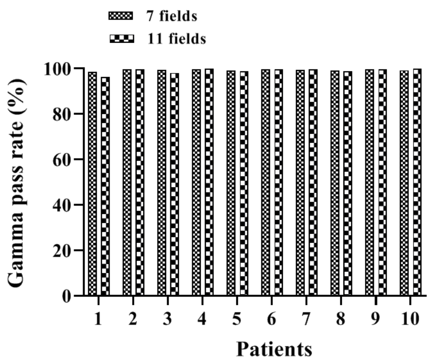
The organ means doses obtained from TPS calculations were compared with those of measurements using pair t-test statistical analysis for each treatment planning technique. A significance level of $P<0.05$ was utilized in the analysis. It must be mentioned that the normality of data distributions for each organ was previously evaluated by Kolmogorov-Smirnov statistical analysis. The statistical analyses were performed by Statistical Package for the Social Sciences (SPSS) software (Version 12, IBM, USA).

RESULTS

Gamma analysis

The results of the gamma passing rates for comparing the dose distributions obtained by the TPS calculations and phantom measurements for both 7 and 11 fields for each patient are depicted in Figure 2. Our findings revealed that the gamma passing rates in IMRT plans were higher than 95% for all patients, considering the DD of 3%, DTA of 3mm, and threshold dose of 10%. This indicates that the TPS dose calculation demonstrates sufficient accuracy without considering the OOF regions.

Figure 2. The percentage of gamma passing rate (obtained by the TPS and phantom) for both 7 and 11 fields.



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***Dosimetric* comparison**

Eyes: Table 1 presents the mean dose values calculated by the Monaco TPS and measured by OCTAVIUS 4D phantom for the right and left eyes as the organs in OOF regions. The TPS consistently underestimated the dose values for the eyes by approximately 32% and 22% in the 7 and 11 fields IMRT techniques, respectively. Additionally, in two patients (patients' numbers 1 and 6), overestimation with lower calculation errors was observed. Table 2 illustrates the maximum dose values of the right and left eyes calculated by the Monaco TPS and measured by the OCTAVIUS 4D phantom. It is evident that the TPS exhibited considerable dose calculation errors, predominantly underestimating the maximum dose for the eyes by about 21% and 12% for the 7 and 11 fields IMRT techniques, respectively. Overestimation of eye maximum dose was also observed in five patients (patients' numbers 1, 2, 4, 5, and 6). Statistical analysis between the eye doses (mean and maximum) obtained from TPS calculations and phantom measurements revealed significant differences for both the 7 and 11 fields techniques ($P<0.001$).

Table 1. Comparison of the calculated and measured dose values (mean dose) for the right and left eyes in the 7 and 11 fields' nasopharyngeal IMRT techniques.

Patient No.	TPS (Gy)-7 fields (Gy)	OCTAVIUS (Gy)- 7 fields (Gy)	TPS error (%)	Absolute TPS error (%)	TPS (Gy)-11 fields (Gy)	OCTAVIUS (Gy)-11 fields (Gy)	TPS error (%)	Absolute TPS error (%)
Right eye (mean dose)								
1	0.90	1.20	-25.00	25.00	3.80	2.70	**40.74**	40.74
2	3.50	4.60	-23.91	23.91	3.80	5.00	-24.00	24.00
3	0.90	1.70	-47.06	47.06	0.80	1.50	-46.67	46.67
4	24.40	24.60	-0.81	0.81	23.40	24.20	-3.31	3.31
5	13.08	13.50	-3.11	3.11	12.26	12.40	-1.13	1.13
6	14.40	12.80	**12.50**	12.50	15.30	13.80	**10.87**	10.87
7	0.40	1.00	-60.00	60.00	0.40	1.00	-60.00	60.00
8	0.70	1.50	-53.33	53.33	0.70	1.50	-53.33	53.33
9	0.40	0.90	-55.56	55.56	0.40	0.90	-55.56	55.56
10	0.60	1.30	-53.85	53.85	0.96	1.30	-26.15	26.15
Mean	5.93	6.31	-31.01	33.51	6.18	6.43	-21.85	32.18
SD	8.42	8.06	26.65	23.04	8.03	7.86	33.31	22.13
Left eye (mean dose)								
1	0.60	1.20	-50.00	50.00	3.70	2.30	**60.87**	60.87
2	5.10	5.30	-3.77	3.77	3.70	5.10	-27.45	27.45
3	0.80	1.60	-50.00	50.00	0.70	1.40	-50.00	50.00
4	25.90	26.40	-1.89	1.89	24.40	25.00	-2.40	2.40
5	12.50	13.00	-3.85	3.85	13.08	14.00	-6.57	6.57
6	10.30	9.80	**5.10**	5.10	10.80	10.30	**4.85**	4.85
7	0.40	1.00	-60.00	60.00	0.40	1.00	-60.00	60.00
8	0.80	1.60	-50.00	50.00	0.70	1.50	-53.33	53.33
9	0.50	1.10	-54.55	54.55	0.50	1.10	-54.55	54.55
10	0.60	1.30	-53.85	53.85	0.70	1.40	-50.00	50.00
Mean	5.75	6.23	-32.28	33.30	5.87	6.31	-23.86	37.00
SD	8.37	8.25	27.11	25.70	7.94	7.95	38.38	24.17

TPS: treatment planning system; Dcal: dose calculated by TPS; Dmeas: dose measured by OCTAVIUS phantom

Table 2. Comparison of the calculated and measured dose values (maximum dose) for the right and left eyes in the 7 and 11 fields' nasopharyngeal IMRT techniques.

Patient No.	TPS (Gy)-7 fields (Gy)	OCTAVIUS (Gy)- 7 fields (Gy)	TPS error (%)	Absolute TPS error (%)	TPS (Gy)-11 fields (Gy)	OCTAVIUS (Gy)-11 fields (Gy)	TPS error (%)	Absolute TPS error (%)
Right eye (max dose)								
1	0.90	1.60	-43.75	43.75	21.10	15.50	**36.13**	36.13
2	21.80	19.60	**11.22**	11.22	21.10	20.70	**1.93**	1.93
3	1.40	2.30	-39.13	39.13	1.20	2.00	-40.00	40.00
4	45.80	41.00	**11.71**	11.71	43.20	40.10	**7.73**	7.73
5	38.80	35.10	**10.54**	10.54	37.00	32.00	**15.63**	15.63
6	45.10	37.10	**21.56**	21.56	36.70	32.40	**13.27**	13.27
7	0.60	1.30	-53.85	53.85	0.60	1.30	-53.85	53.85
8	1.20	2.00	-40.00	40.00	1.30	2.10	-38.10	38.10
9	0.70	1.20	-41.67	41.67	0.70	1.20	-41.67	41.67
10	0.90	1.60	-43.75	43.75	0.90	1.60	-43.75	43.75
Mean	15.72	14.28	-20.71	31.72	16.38	14.89	-14.27	29.20
SD	20.13	17.17	30.08	16.24	17.62	15.45	32.24	17.83
Left eye (max dose)								
1	1.10	1.70	-35.29	35.29	25.80	17.20	**50.00**	50.00
2	25.50	24.00	**6.25**	6.25	25.80	25.00	**3.20**	3.20
3	1.20	2.10	-42.86	42.86	1.10	1.80	-38.89	38.89
4	49.60	48.00	**3.33**	3.33	46.50	45.20	**2.88**	2.88
5	48.80	39.30	**24.17**	24.17	51.20	40.10	**27.68**	27.68
6	36.40	31.90	**14.11**	14.11	40.50	36.60	**10.66**	10.66
7	0.60	1.30	-53.85	53.85	0.60	1.30	-53.85	53.85
8	1.30	2.10	-38.10	38.10	1.60	2.10	-23.81	23.81
9	0.90	1.60	-43.75	43.75	0.90	1.60	-43.75	43.75
10	0.90	1.70	-47.06	47.06	1.10	1.90	-42.11	42.11
Mean	16.63	15.37	-21.30	30.88	19.51	17.28	-10.80	29.68
SD	21.23	18.55	29.55	17.83	20.96	18.08	34.80	19.01

TPS: treatment planning system; Dcal: dose calculated by TPS; Dmeas: dose measured by OCTAVIUS phantom

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Lenses: The maximum dose values calculated by the Monaco TPS and measured by OCTAVIUS 4D phantom for the right and left eye lens are depicted in table 3. The TPS underestimated the OOF doses (about 31%). The overestimation with lower calculation errors were also found in two patients (patient number 5 and 6) for 7 fields IMRT technique and in two patients for 11 fields technique (patient number 1 and 6). Statistical analysis revealed significant differences between the maximum lens doses obtained from TPS calculations and phantom measurements for the evaluated IMRT techniques (P<0.001).

Optic nerves: Our results indicate that the TPS overestimated the maximum dose of optic nerves for three patients (numbers 1, 5, and 6) for both the right and left optic nerves in both the 7 and 11 fields techniques (table 4). However, for the remaining patients, the TPS significantly underestimated the maximum dose of optic nerves in both the 7 and 11 IMRT techniques (P<0.001).

Table 3. Comparison of the calculated and measured dose values (maximum dose) for the right and left lens in the 7 and 11 fields' nasopharyngeal IMRT techniques.

Patient No.	TPS (Gy)-7 fields (Gy)	OCTAVIUS (Gy)- 7 fields (Gy)	TPS error (%)	Absolute TPS error (%)	TPS (Gy)-11 fields (Gy)	OCTAVIUS (Gy)-11 fields (Gy)	TPS error (%)	Absolute TPS error (%)
Right lens (max dose)								
1	0.70	1.20	-41.67	41.67	2.90	1.90	**52.63**	52.63
2	2.60	3.70	-29.73	29.73	2.90	4.10	-29.27	29.27
3	1.00	1.70	-41.18	41.18	0.70	1.50	-53.33	53.33
4	11.30	13.50	-16.30	16.30	9.60	14.30	-32.87	32.87
5	9.00	10.80	-16.67	16.67	9.20	9.60	-4.17	4.17
6	12.90	12.80	**0.78**	0.78	14.80	15.10	-1.99	1.99
7	0.40	1.00	-60.00	60.00	0.40	0.90	-55.56	55.56
8	0.80	1.80	-55.56	55.56	0.90	1.60	-43.75	43.75
9	0.50	1.00	-50.00	50.00	0.50	1.00	-50.00	50.00
10	0.70	1.30	-46.15	46.15	0.60	1.30	-53.85	53.85
Mean	3.99	4.88	-35.65	35.80	4.25	5.13	-27.21	37.74
SD	5.01	5.27	19.63	19.32	5.10	5.68	34.26	20.36
Left lens (max dose)								
1	0.70	1.20	-41.67	41.67	2.20	1.70	**29.41**	29.41
2	2.30	3.60	-36.11	36.11	2.20	3.50	-37.14	37.14
3	0.90	1.50	-40.00	40.00	0.70	1.30	-46.15	46.15
4	9.30	15.00	-38.00	38.00	8.20	12.40	-33.87	33.87
5	9.70	9.60	**1.04**	1.04	9.40	9.60	-2.08	2.08
6	8.80	7.20	**22.22**	22.22	8.80	7.80	**12.82**	12.82
7	0.50	1.00	-50.00	50.00	0.40	1.00	-60.00	60.00
8	1.00	1.60	-37.50	37.50	0.80	1.50	-46.67	46.67
9	0.60	1.10	-45.45	45.45	0.60	1.10	-45.45	45.45
10	0.60	1.40	-57.14	57.14	0.70	1.50	-53.33	53.33
Mean	3.44	4.32	-32.26	36.91	3.40	4.14	-28.25	36.69
SD	4.06	4.78	24.52	15.60	3.79	4.20	30.55	18.00

TPS: treatment planning system; Dcal: dose calculated by TPS; Dmeas: dose measured by OCTAVIUS phantom

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Table 4. Comparison of the calculated and measured dose values (maximum dose) for the right and left optic nerves in the 7 and 11 fields' nasopharyngeal IMRT techniques.

Patient No.	TPS (Gy)-7 fields (Gy)	OCTAVIUS (Gy)- 7 fields (Gy)	TPS error (%)	Absolute TPS error (%)	TPS (Gy)-11 fields (Gy)	OCTAVIUS (Gy)-11 fields (Gy)	TPS error (%)	Absolute TPS error (%)
Right optic nerve (max dose)								
1	1.90	1.70	**11.76**	11.76	11.90	7.60	**56.58**	56.58
2	13.40	16.70	-19.76	19.76	11.90	16.80	-29.17	29.17
3	1.50	2.10	-28.57	28.57	1.60	1.90	-15.79	15.79
4	52.90	56.20	-5.87	5.87	54.70	58.70	-6.81	6.81
5	43.30	32.50	**33.23**	33.23	44.70	34.80	**28.45**	28.45
6	54.80	50.70	**8.09**	8.09	54.40	48.90	**11.25**	11.25
7	0.70	1.50	-53.33	53.33	0.60	1.50	-60.00	60.00
8	1.10	2.10	-47.62	47.62	1.10	2.10	-47.62	47.62
9	0.60	1.20	-50.00	50.00	0.70	1.30	-46.15	46.15
10	0.80	1.70	-52.94	52.94	0.80	1.80	-55.56	55.56
Mean	17.10	16.64	-20.50	31.12	18.24	17.54	-16.48	35.74
SD	23.43	21.89	31.20	19.09	23.36	21.93	38.95	19.99
Left optic nerve (max dose)								
1	1.00	1.70	-41.18	41.18	8.20	5.60	**46.43**	46.43
2	9.80	13.50	-27.41	27.41	8.20	12.40	-33.87	33.87
3	1.20	2.00	-40.00	40.00	1.10	1.80	-38.89	38.89
4	53.90	59.40	-9.26	9.26	54.70	57.00	-4.04	4.04
5	44.70	34.60	**29.19**	29.19	44.20	35.20	**25.57**	25.57
6	53.40	48.70	**9.65**	9.65	52.00	46.30	**12.31**	12.31
7	0.60	1.50	-60.00	60.00	0.60	1.50	-60.00	60.00
8	1.20	2.10	-42.86	42.86	1.10	2.10	-47.62	47.62
9	0.70	1.40	-50.00	50.00	0.70	1.40	-50.00	50.00
10	0.80	1.80	-55.56	55.56	0.90	1.80	-50.00	50.00
Mean	16.73	16.67	-28.74	36.51	17.17	16.51	-20.01	36.87
SD	23.70	22.41	29.51	17.55	23.19	21.36	37.27	17.98

TPS: treatment planning system; Dcal: dose calculated by TPS; Dmeas: dose measured by OCTAVIUS phantom

DISCUSSION

In the present study, we assessed the accuracy of OOF dose calculation by the Monaco TPS in IMRT of NPC using OCTAVIUS-4D phantom measurements. It has been reported that IMRT may generate larger OOF dose regions compared to the 3D-CRT technique in head and neck radiotherapy [17]. Hence, we exclusively focused on evaluating IMRT techniques in this study. Furthermore, 3D-CRT is unable to spare OARs such as the optic nerve or chiasm in nasopharyngeal radiotherapy; hence, it is common practice to utilize IMRT or VMAT radiotherapy techniques for nasopharyngeal patients [19].

In AAPM-TG158 guideline, it is recommended that the use of TPSs for dose calculations in OOF regions should be performed with caution [31]. Accurate dose calculations in OOF regions is important for secondary cancer estimation, fetus delivered dose for pregnant patients or implanted electronic devices [32]. It has been reported that a 50% change in low dose leads to a considerable difference in second cancer risk [21]. There are several studies investigated the OOF doses calculated by various TPSs in several radiotherapy techniques, emphases the important of this subject [8, 20, 22-24]. For example, Auerbach *et al.* [33] assessed the OOF doses in hippocampus for radiotherapy of common cancers, using an anthropomorphic Alderson phantom and thermoluminescent detectors (TLDs). They found that for carcinomas in the head and neck, the hippocampal region received doses ranging from 37.4 to 154.8 mGy per single fraction. The hippocampal dose varied notably among naso-, oro-, and hypopharynx carcinomas, with the highest values observed for nasopharynx carcinoma. In another study, Elmtalab and Abedi [18] examined OOF region doses, including parotid glands, left and right eye lenses, and thyroid gland, as well as, the risk of secondary thyroid cancer, resulting from 3D-CRT (15 - and 18-MV) and IMRT (6-MV) techniques using TLD in a head and neck homogeneous phantom. The study revealed that TPS underestimated OOF doses in both of the 3D-CRT and IMRT techniques. Error rates in TPS increased as the distance from the field edge incremented, ranging from 0.3 to 11.9 cm, and varied across different treatment techniques.

Our results demonstrate that the majority of OOF doses calculated by the Monaco TPS were underestimated, with an average error of 25%. Nevertheless, there were instances where the TPS overestimated patient organ doses, albeit with lower error values. Interestingly, our findings reveal that higher dose calculation errors tended to occur for lower doses, a trend consistent with previous studies [22–24]. Bahreyni Toossi *et al.* [24] assessed the accuracy of TiGRT TPS dose calculations for OOF regions in the left breast using a RANDO phantom delivered on a Siemens Primus machine with 6 MV energy. Their study, which measured dose values using TLDs-100, reported a 39% underestimation of OOF doses by the TiGRT TPS, particularly for regions

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close to the treatment field edge. Similar to our findings, they also noted instances of overestimation errors by the TPS for higher dose values. In another study by Huang *et al.* [22], the accuracy of OOF doses calculated by the Pinnacle TPS for IMRT of breast, lung, and pediatric brain cancers was investigated. They demonstrated a 50% underestimation of OOF doses by the TPS, with this underestimation increasing with distance from the field edges. Similarly, Mahmoudi *et al.* [23] evaluated the OOF dose calculation error of the Monaco TPS for IMRT of a C-shaped target in a CIRS thorax phantom. They found a mean error value of approximately 40% for OOF dose underestimation by the Monaco TPS, with the underestimation being more significant at distant locations for all evaluated materials and irradiated dose rates. The results were consistent with findings from TiGRT, Eclipse, and Pinnacle TPSs [22, 24, 34]. Considering our findings and those from previous investigations, it's evident that TPS dose calculations are not entirely reliable in OOF regions, especially low-dose regions. The research conducted by Diallo *et al.* [35] highlighted a significant finding regarding secondary cancers. According to their research, approximately 66% of secondary cancers were observed to occur beyond the treatment volume. Specifically, these secondary cancers manifested at a distance of 5 cm or more from the field border. Given these significant dose calculation errors, it is not advisable to rely solely on TPS results to assess the secondary cancer risks associated with OOF regions.

It is crucial for a Monte Carlo-based dose calculation TPS like Monaco to accurately calculate doses in all tissues, including OOF regions. The low accuracy observed in TPS dose calculations for OOF regions primarily stems from inappropriate or erroneous TPS commissioning or data entry. Insufficient dosimetric data regarding field edges, penumbra, and scatter radiation may contribute to OOF dose calculation errors. Obtaining dosimetric data for field edges and penumbra necessitates the use of small volume dosimeters, measurements in small increments, and small field dosimetry for the small segments commonly employed in IMRT planning. While international or national protocols/guidelines such as AAPM TG-119 [30] and IAEA-TECDOC-1583 [36] exist for auditing the commissioning procedure, they do not specifically address or evaluate dose calculation errors in OOF regions. Hence, there is a clear need to enhance audit protocols to assess commissioning deficiencies in OOF regions.

The current study had several limitations, including the use of only 6 MV photon beams, which are the most commonly utilized X-ray energy for IMRT, and the restriction to only NPC cases. Future studies could explore the applicability of other TPS dose calculation algorithms across different anatomical sites. Furthermore, additional research could investigate other radiotherapy techniques and irradiation energies to provide a more comprehensive understanding of dose calculation accuracy.

CONCLUSION

Comparison of the calculated TPS dose with measurements performed by the OCTAVIUS 4D phantom revealed significant high dose calculation errors (approximately 25% underestimation) by the Monaco TPS in estimating the dosimetric parameters of organs located in OOF dose regions, including the eyes, lens, and optic nerve, in IMRT for NPC. It appears that more accurate data entry or commissioning, as well as the development of new protocols for evaluating the accuracy of TPS dose calculation in OOF regions, are essential. This is particularly crucial given the high dependency of secondary cancer probabilities on the dose and volume of OOF regions.

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Author contribution: L.K and S.R.M were responsible for the study conception, design, acquisition of data, and finalizing of the manuscript. All the authors contributed to data analyzing and writing the manuscript draft. Furthermore, all authors read and approved the final manuscript.

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