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ORIGINAL ARTICLE

Dosimetric effect of different isocenter for nasopharyngeal carcinoma with volumetric modulated arc therapy

Yong Sang[1,2] | Guoping Shan[1,2] | Kainan Shao[1,2] | Fujun Hu[2,3] | Tongxing Liu[2,3]

[1]Department of Radiation Physics, Zhejiang Cancer Hospital, Hangzhou, Zhejiang, China

[2]Key Laboratory of Radiation Oncology in Zhejiang Province, Hangzhou, Zhejiang, China

[3]Department of Radiation Oncology, Zhejiang Cancer Hospital, Hangzhou, Zhejiang, China

Correspondence
Yong Sang, Department of Radiation Physics, Zhejiang Cancer Hospital, No.1, BanShan East Rd. Hangzhou, Zhejiang 310022, China.
Email: zjcancerh@163.com

Abstract

Objective: The purpose of this study was to analyze the dosimetric effect of different isocenters with volumetric modulated arc therapy for nasopharyngeal carcinoma (NPC).

Methods: A total of 20 NPC patients who had received radiotherapy were re-planned by the volumetric modulated arc therapy plan. Three volumetric modulated arc therapy plans with different isocenters were generated for each patient: the first plan using the center of $PGTV_{nx}$ as the isocenter (AP-V), the second plan using the center of $PGTV_{nd}$ as the isocenter (BP-V), and the third plan using the center of PTV_2 as the isocenter (CP-V). The conformity and homogeneity indexes of the target, dose-volume histogram of organs at risk, normal tissue, volume of dose, and monitor units were compared for the three plans.

Results: AP-V provided a significantly lower maximum dose for the optic nerves and optic chiasm; lower mean dose for the eyeballs; lower absolute volume >10 Gy, absolute volume >20 Gy, and absolute volume >30 Gy; and fewer monitor units than BP-V and CP-V. BP-V and CP-V provided a significantly lower absolute volume >50 Gy than AP-V. In the conformity indexes of $PGTV_{nd}$ and PTV_2, BP-V and CP-V were significantly better than in AP-V. In the homogeneity index of PTV_2, BP-V and CP-V were significantly better than in AP-V. In general, there is no significant difference between BP-V and CP-V.

Conclusions: All three plans achieved the clinical demands. AP-V decreased the volumes of absolute volume >10 Gy, absolute volume >20 Gy, and absolute volume >30 Gy, whereas BP-V and CP-V decreased the volume of absolute volume >50 Gy. In terms of organs at risk, AP-V offered better protection of the optic nerves, optic chiasm, and eyeballs for NPC than BP-V and CP-V. Most importantly, AP-V enhanced the utilization of the monitor units. For this reason, we propose that the radiotherapy technician put the location position in the $PGTV_{nx}$ center during simulation of the NPC patients. We further propose that the isocenter be moved to the geometric center of $PGTV_{nx}$ if the NPC patient plan has higher dosimeter requirements for the optic nerves, optic chiasm, or eyeballs.

KEYWORDS

dosimetric comparison, isocenter, nasopharyngeal carcinoma, volumetric modulated arc therapy

1 | INTRODUCTION

Nasopharyngeal carcinoma (NPC) represents approximately 0.7% of all tumors, and is distinctly endemic in Southeast Asia.[1,2] Because of its anatomical characteristics, biological properties, and radiosensitivity, radiation therapy has been the mainstay treatment modality for non-metastatic NPC patients. Volumetric modulated arc therapy (VMAT) is currently widely used in the treatment of patients with NPC because of

TABLE 1 T, N, and M stages of 20 patients

Stage	N0	N1	N2	N3	M0	M1	Sum
T1	0	0	1	1	2	0	2
T2	0	0	3	1	4	0	4
T3	1	1	5	2	9	0	9
T4	0	3	1	1	5	0	5
Sum	1	4	10	5	20	0	20

the dosimetric advantage over intensity-modulated radiation therapy (IMRT), as well as its lower radiotherapy time (RT).[3–8] Because the current RT technology is mainly the isocentric irradiation technique, the position of the isocenter is very important. There are numerous literature reports regarding the dosimetric effects of errors of the isocenter on a variety of cancers with VMAT or IMRT.[9–15] To our knowledge, no data are available on the dosimetric impact of different isocenters for NPC patients regardless of VMAT or IMRT status. Therefore, the present study aimed to elucidate the dosimetric effects of different isocenters for NPC with VMAT.

2 | METHODS

2.1 | Patients

A total of 20 non-metastatic NPC patients who had received VMAT treatment between April 2018 and July 2018 in Zhejiang Cancer Hospital were re-planned for our study. The study population included 15 men and five women, and the median age was 53 years (range 38–79 years). T1, T2, T3, and T4 had two, four, nine, and five patients, respectively, according to International Union Against Cancer 2010. The data of the tumor stages are shown in Table 1. This study was approved by the institutional review board of Zhejiang Cancer Hospital, and all the patients provided voluntary informed consent to participate in the study.

2.2 | Volume definition and dose prescription

As described previously, the gross tumor volume of the nasopharynx (GTV_{nx}) includes the primary tumor and metastatic retropharyngeal lymph nodes.[16] Metastatic cervical lymph nodes are defined as the gross tumor volume of the involved cervical lymph nodes (GTV_{nd}). The high-risk clinical target volume CTV_1 includes the GTV_{nx} and GTV_{nd} with a margin of 5–10 mm, entire nasopharynx, inferior two-thirds of the sphenoid sinus, anterior third of the clivus, pterygoid fossae, posterior third of the nasal cavity and maxillary sinuses, parapharyngeal space, retropharyngeal nodes, and drainage of the upper neck. The low-risk clinical target volume CTV_2 encompasses the CTV_1 with a margin of 3–5 mm, lower neck, and supraclavicular lymphatic drainage region. The planning target volume (PTV) is defined as the area 3–5 mm outside of CTV or GTV. The dose prescribed was as follows: 70 Gy to $PGTV_{nx}$ and $PGTV_{nd}$, 60 Gy to PTV_1, and 54 Gy to PTV_2 (The PGTV is defined as the area 3 mm outside of GTV. The PTV is defined as the area 3–5 mm outside of CTV. So $PGTV_{nx}$ is defined as the area 3 mm outside of GTV_{nx}, $PGTV_{nd}$ is defined as the area 3 mm outside of GTV_{nd}, PTV_1 is defined as the area 3–5 mm outside of CTV_1, PTV_2 is defined as the area 3–5 mm outside of CTV_2). The total doses of $PGTV_{nx}$, $PGTV_{nd}$, PTV_1, and PTV_2 were given in 33 fractions. All patients were irradiated with one fraction daily, 5 days per week. In the study, organs at risk (OARs) mainly included the brainstem, spinal cord, lenses, eyeballs, optic nerves, optic chiasm, temporal lobes, and parotid glands.

2.3 | Choosing the isocenter position

We usually moved the isocenter to the geometric center of the target volume if the location position was not suitable for the plan. There were four target volumes for NPC patients. Of these, the highest dose targets were $PGTV_{nx}$ and $PGTV_{nd}$, and the lowest dose target was PTV_2. Thus, three isocenters were generated for each patient: the first using the geometric center of $PGTV_{nx}$ as the isocenter (AP), the second using the geometric center of $PGTV_{nd}$ as the isocenter (BP), and the third using the geometric center of PTV_2 as the isocenter (CP). Therefore, each patient had three different VMAT plans with different isocenters: the first plan using the geometric center of $PGTV_{nx}$ as the isocenter (AP-V), the second plan using the geometric center of $PGTV_{nd}$ as the isocenter (BP-V), and the third plan using the geometric center of PTV_2 as the isocenter (CP-V). The positions of the isocenters are shown in Figure 1.

2.4 | Planning design

A trilogy machine model was used in the study. We adopted RayArc of Raystation Planning System 4.5.1 (Raysearch Laboratories AB, Stockholm, Sweden) to design all VMAT plans. The multi-leaf collimator (MLC) of the Varian Trilogy machine has 40 pairs of blades. The MLC thickness of the middle 20 pairs of blades is 0.5 cm. There are 10 pairs of MLC blades on each side and the MLC thickness is 1 cm. All patients finished the 33 fractions RT simultaneously with an integrated boost technique. Photon beams of 6 MV were applied to all three plans. Each plan had two full arcs of a clockwise rotation from 182° to 178°, and counterclockwise rotation from 178° to 182°. The gantry interval was set as 4° between each control point in our planning to optimize the calculation time and accuracy of treatment planning. There were 180 control points for each plan. The collimator angle was 10° considering the tongue-and-groove effect.[3] The dose grid resolution was set to $0.25 \times 0.25 \times 0.25$ cm for all plans, considering the accuracy of calculation and a computed tomography image slice thickness of 0.25 cm.

The dose constraints for each target and OARs of all plans were as follows: the prescribed dose of each target should cover 95% of the target volume. In addition, it was necessary to evaluate the three-dimensional dose distribution. The brainstem maximum point dose (D_{max}) <54 Gy, spinal cord D_{max} <40 Gy, lenses D_{max} <6 Gy, eyeballs mean point dose (D_{mean}) <30 Gy, optic nerves and optic chiasm D_{max} <54 Gy, temporal lobes V_{65Gy} <1cc, and parotid glands V_{30Gy} <50% results are shown in Table 2. In the plan design, the OARs functions and weights were identical in the three plans of each patient;

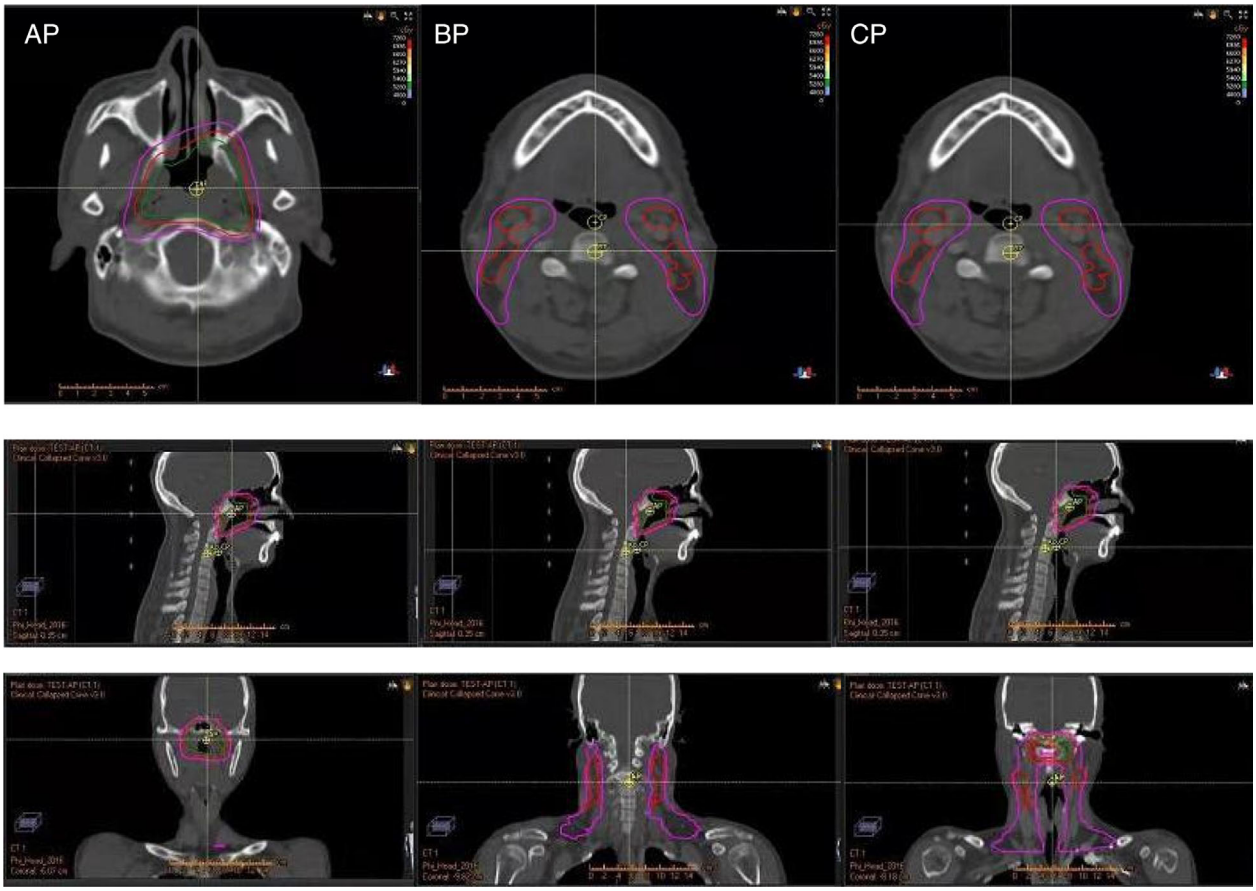

FIGURE 1 Isocenter positions of AP, BP, and CP with transverse, sagittal, and coronal planes. AP, the geometric center of target $PGTV_{nx}$; BP, the geometric center of target $PGTV_{nd}$; CP, the geometric center of target PTV_2

TABLE 2 Planning objectives for target volumes and organs at risk

Targets	Maximum dose $PGTV_{nx}$, $PGTV_{nd}$ Coverage $PGTV_{nx}$, $PGTV_{nd}$, PTV_1, PTV_2	<110% prescribed dose $D_{95\%}$ ≥prescribed dose
OAR	Brainstem	D_{max} <54 Gy
	Spinal cord	D_{max} <40 Gy
	Lenses	D_{max} <6 Gy
	Eyeballs	D_{mean} <30 Gy
	Optic nerves	D_{max} <54 Gy
	Optic chiasm	D_{max} <54 Gy
	Temporal lobes	V_{65Gy} <1cc
	Parotid glands	V_{30Gy} <50%

Dmax, maximum dose; D_{mean}, mean dose; OAR, organ at risk.

the functions and weights for the targets were slightly different to meet the clinical requirements of the target volumes.

2.5 | Plan comparisons

The dosimetric comparison criteria of the plans are as follows:

1. Conformity index (CI): measurement of how conformal the dose distribution is along the target volume. Formula: $CI = TV_{PV} \times TV_{PV} / (V_{PTV} \times V_{TV})$. Possible values for CI range from 0 to 1. A CI value closer to 1 indicates better dose conformity in the PTV (V_{TV} is the treatment volume of the prescribed isodose line, V_{PTV} is the volume of PTV, and TV_{PV} is the volume of PTV covered by the prescription dose).[17,18]
2. Homogeneity index (HI): measurement of how uniform the dose distribution is in all four targets $PGTV_{nx}$, $PGTV_{nd}$, PTV_1, and PTV_2. Formula: $HI = D_{5\%} / D_{95\%}$. A higher HI indicates poorer homogeneity.[3,19]
3. OAR: determination of D_{max} to serial organs, such as the brainstem, spinal cord, lenses, optic nerves, and optic chiasm; the mean dose of eyeballs, the absolute volume V_{60Gy} of temporal lobes, and the volume percentage V_{30Gy} of the parotid glands.
4. Normal tissue (NT) volume of dose: evaluation of absolute dose volume to the NT of V_{10Gy}, V_{20Gy}, V_{30Gy}, V_{40Gy}, and V_{50Gy} (which represent the absolute volume more than 10 Gy, 20 Gy, 30 Gy, 40 Gy, and 50 Gy, respectively).
5. Monitor units (MUs): comparison of the MUs for the three group plans of AP-V, BP-V, and CP-V. The delivery time was not included in the study, because two full arcs were used for all plans and the delivery time was almost identical for the three plans of each patient.

TABLE 3 Plan comparison for the CI and HI of $PGTV_{nx}$, $PGTV_{nd}$, PTV_1, and PTV_2

				P-value		
	AP-V	BP-V	CP-V	AP-V *vs* BP-V	AP-V *vs* CP-V	BP-V *vs* CP-V
CI-$PGTV_{nx}$	0.370 ± 0.0115	0.371 ± 0.118	0.374 ± 0.113	0.765	0.140	0.167
HI-$PGTV_{nx}$	1.057 ± 0.006	1.057 ± 0.006	1.056 ± 0.006	0.943	0.221	0.367
CI-$PGTV_{nd}$	0.321 ± 0.098	0.328 ± 0.102	0.330 ± 0.105	0.003	0.002	0.198
HI-$PGTV_{nd}$	1.051 ± 0.005	1.050 ± 0.006	1.050 ± 0.006	0.125	0.195	0.752
CI-PTV_1	0.648 ± 0.155	0.648 ± 0.149	0.649 ± 0.143	0.204	0.079	0.538
HI-PTV_1	1.178 ± 0.016	1.177 ± 0.018	1.178 ± 0.017	0.680	0.694	0.652
CI-PTV_2	0.722 ± 0.031	0.738 ± 0.027	0.739 ± 0.032	0.000	0.000	0.538
HI-PTV_2	1.336 ± 0.006	1.333 ± 0.007	1.332 ± 0.006	0.001	0.001	0.492

AP-V, the first plan using the center of $PGTV_{nx}$ as the isocenter; BP-V, the second plan using the center of $PGTV_{nd}$ as the isocenter; CI-, conformity index of; CP-V, the third plan using the center of PTV_2 as the isocenter; HI-, homogeneity index of; The target $PGTV_{nx}$, $PGTV_{nd}$, PTV_1, PTV_2 are defined in "2.2 Volume definition and dose prescription".

2.6 | Statistical analysis

Results are described as the mean ± standard deviation. The two-tailed Wilcoxon matched-pairs signed-rank sum test was carried out to analyze the difference between the three different isocenter plans in the CI and HI of the targets, D_{max}, D_{mean}, V_{60Gy}, and V_{30Gy} of the OARs; the NT absolute dose volumes of V_{10Gy}, V_{20Gy}, V_{30Gy}, V_{40Gy}, and V_{50Gy}; and the MUs. A two-tailed *P*-value <0.05 is considered statistically significant. All analyses were carried out using the statistical software SPSS 19.0 (IBM Corporation, Armonk, NY, USA).

3 | RESULTS

3.1 | Target CI and HI

For a paired comparison, the CIs of $PGTV_{nd}$ and PTV_2 with BP-V and CP-V were found to be statistically significantly greater than that of AP-V. The HIs of PTV_2 with BP-V and CP-V were found to be statistically significantly smaller than that of AP-V. $PGTV_{nx}$ and PTV_1 were found to have no statistically significant differences with the three groups in the CI and HI (Table 3).

3.2 | OARs

All the doses for the OARs met the clinical demands. In comparison with BP-V and CP-V, AP-V performed statistically significantly better in sparing the optic nerves, optic chiasm, and eyeballs. The D_{max} of the AP-V L-optic nerve was reduced by 12.3% compared with BP-V, and 10.6% compared with CP-V. The D_{max} of the AP-V R-optic nerve was reduced by 7.8% compared with BP-V, and 7.0% compared with CP-V. The D_{max} of the AP-V optic chiasm was reduced by 15.2% compared with BP-V, and 13.9% compared with CP-V. The mean dose of the AP-V left eyeball was reduced by 6.8% compared with BP-V, and 4.9% compared with CP-V. The mean dose of the AP-V right eyeball was reduced by 8.3% compared with BP-V, and 7.8% compared with CP-V. There were no statistically significant differences between BP-V and CP-V in terms of the D_{max} of the optic nerves, optic chiasm, and mean dose of the eyeballs. There were no statistically significant differences between the three groups in terms of the D_{max} of the brainstem, spinal cord, lenses, V_{60Gy} of the temporal lobes, and V_{30Gy} of the parotid glands (Table 4).

3.3 | NT dose volume and MUs

In the present study, we counted the absolute volume of NT with V_{10Gy}, V_{20Gy}, V_{30Gy}, V_{40Gy}, and V_{50Gy}. V_{10Gy} of AP-V was statistically significantly reduced by 3.7% with BP-V, and 3.0% with CP-V. V_{20Gy} of AP-V was statistically significantly reduced by 1.6% with BP-V, and 1.6% with CP-V. V_{30Gy} of AP-V was statistically significantly reduced by 1.4% with BP-V, and 1.9% with CP-V. However, V_{50Gy} of AP-V was statistically significantly increased by 1.4% with BP-V, and 1.9% with CP-V. V_{10Gy}, V_{20Gy}, V_{30Gy}, and V_{50Gy} were not statistically significantly different between BP-V and CP-V. V_{40Gy} was not statistically significant in the three groups. The MUs of AP-V were found to be statistically significantly reduced by 11.5% with BP-V, and 10.2% with CP-V (Table 5).

4 | DISCUSSION

The treatment of NPC has included CRT, 3D-CRT, IMRT, and VMAT. IMRT and VMAT are the main RT techniques for NPC patient treatment. For VMAT and IMRT, different settings in the plan design might cause dosimetry differences in the plans for a variety of cancers; these differences include the number of arcs,[6,20,21] the spacing units of the gantry for VMAT,[22] the angle of the collimator,[23] the calculation grid size,[24] and the photon energy.[25]

The isocenter is very important, because RT usually uses an isocentric irradiation technique. The movement of the isocenter for the gamma knife is convenient, and more multi-isocenter irradiation technology is used. There are several studies regarding the dosimetric differences of different isocenters for the gamma knife.[26,27] In addition,

TABLE 4 Dosimetric comparison for organs at risk between the first plan using the center of $PGTV_{nx}$ as the isocenter, the second plan using the center of $PGTV_{nd}$ as the isocenter, and the third plan using the center of PTV_2 as the isocenter

					P-value		
		AP-V	BP-V	CP-V	AP-V *vs* BP-V	AP-V *vs* CP-V	BP-V *vs* CP-V
Brainstem	D_{max}(Gy)	53.79 ± 2.80	54.11 ± 2.38	53.41 ± 2.75	0.737	0.140	0.332
Spinal cord	D_{max}(Gy)	39.57 ± 0.76	39.48 ± 1.81	39.57 ± 1.89	0.681	0.305	0.444
L-eyes	D_{max}(Gy)	5.44 ± 0.66	5.39 ± 0.44	5.42 ± 0.54	0.255	0.322	0.940
R-eyes	D_{max}(Gy)	5.37 ± 0.72	5.43 ± 0.30	5.37 ± 0.49	0.559	0.287	0.268
L-eyeball	D_m (Gy)	5.07 ± 0.84	5.44 ± 0.60	5.33 ± 0.74	0.003	0.016	0.140
R-eyeball	D_m (Gy)	4.85 ± 0.54	5.29 ± 0.42	5.26 ± 0.45	0.000	0.002	0.380
L-optic nerve	D_{max}(Gy)	37.73 ± 15.47	43.03 ± 10.55	42.23 ± 12.90	0.004	0.003	0.808
R-optic nerve	D_{max}(Gy)	40.51 ± 12.54	43.96 ± 9.33	43.56 ± 10.86	0.010	0.044	0.911
Optic chiasm	D_{max}(Gy)	38.23 ± 16.23	45.11 ± 11.30	44.39 ± 12.38	0.000	0.006	0.550
L-temporal lobe	V_{60Gy}(cc)	0.66 ± 1.18	0.69 ± 1.33	0.64 ± 1.20	0.850	0.329	0.315
R-temporal lobe	V_{60Gy}(cc)	0.75 ± 0.94	0.78 ± 1.07	0.72 ± 1.00	0.693	0.340	0.368
L-parotid gland	V_{30Gy}(%)	45.81 ± 2.75	45.40 ± 2.88	45.04 ± 2.87	0.332	0.117	0.433
R-parotid gland	V_{30Gy}(%)	45.56 ± 2.43	45.77 ± 2.72	45.07 ± 2.36	0.490	0.156	0.135

AP-V, the first plan using the center of $PGTV_{nx}$ as the isocenter; BP-V, the second plan using the center of $PGTV_{nd}$ as the isocenter; CP-V, the third plan using the center of PTV_2 as the isocenter; D_{max}, maximum dose; D_m, mean dose; L, left; R, right; V_{60Gy} (cc), absolute volume >60 Gy; V_{30Gy} (%), volume percentage >30 Gy. The target $PGTV_{nx}$, $PGTV_{nd}$, PTV_2 are defined in "2.2 Volume definition and dose prescription".

TABLE 5 Plan comparison for normal tissue, dose-volume histogram and monitor units

				P-value		
	AP-V	BP-V	CP-V	AP-V *vs* BP-V	AP-V *vs* CP-V	BP-V *vs* CP-V
V_{10Gy}(cc)	4622 ± 917	4800 ± 1031	4763 ± 991	0.001	0.000	0.108
V_{20Gy}(cc)	3403 ± 619	3460 ± 625	3458 ± 609	0.019	0.004	0.926
V_{30Gy}(cc)	2272 ± 414	2322 ± 414	2313 ± 423	0.011	0.025	0.601
V_{40Gy}(cc)	1416 ± 271	1418 ± 281	1409 ± 266	0.765	0.313	0.212
V_{50Gy}(cc)	876 ± 174	864 ± 177	860 ± 169	0.011	0.000	0.295
MUs	500 ± 36	565 ± 40	557 ± 46	0.000	0.000	0.467

AP-V, the first plan using the center of $PGTV_{nx}$ as the isocenter; BP-V, the second plan using the center of $PGTV_{nd}$ as the isocenter; CP-V, the third plan using the center of PTV_2 as the isocenter; MUs, monitor units; V_{10Gy} (cc), absolute volume >10 Gy; V_{20Gy} (cc), absolute volume >20 Gy; V_{30Gy} (cc), absolute volume >30 Gy; V_{40Gy} (cc), absolute volume >40 Gy; V_{50Gy} (cc), absolute volume >50 Gy.

there are reports of multi-isocenter technology of RT with a linear accelerator.[28,29]

Linear accelerator RT currently uses the isocentric irradiation technique, which generally just has an isocenter for the treatment. In most hospitals globally, if multi-isocenter technology is used, the RT technician needs to enter the machine room to move the treatment bed. This is very inconvenient and increases the patient's irradiation time, which is not conducive to the stability of the patient's RT position.

Our comparative planning study first compared the dosimetric difference produced by different single isocenters for NPC with VMAT. However, no literature has reported the dosimetric difference of any cancer produced by different single isocenters, regardless of whether it is IMRT or VMAT. For the cancer of the chest and abdomen, there were generally only one or two target volumes, and the technician usually put the positioning point in the center of PTV_2 when located; the difference between the isocenter positions of the two target areas was small. The dosimetric differences were also small. However, NPC generally had four target volumes, and the position of the nasopharynx and the neck was different. If the center of each target volume was used as the isocenter, the positions of the four isocenters were different. This might result in a dosimetric difference for the VMAT plans using the four different isocenters. Therefore, it would be meaningful to discuss the dosimetric difference resulting from the different isocenters of the VMAT plans for NPC.

In the present study, the AP-V showed its superiority in protecting the optic nerves, optic chiasm, and eyeballs compared with BP-V and CP-V. In the NT, AP-V also showed its superiority in V_{10Gy}, V_{20Gy}, and V_{30Gy}. The AP-V could also use fewer MUs to meet the clinical requirements. The first reason might be that the MLC of each control point would first open near the isocenter point when the treatment planning system received the VMAT plan.

This makes it more likely that the plans would preferentially meet the critical organ and target requirements near the isocenter. Because most OARs of NPC were around the $PGTV_{nx}$, it could increase the utilization of MUs and protect the OARs around the $PGTV_{nx}$ better when the isocenter was in the center of $PGTV_{nx}$.

In this study, BP-V and CP-V showed no significant differences in CI, HI, dose of OARs, NT dose volume, and MUs, because the isocenter positions of BP-V and CP-V did not differ much. BP-V and CP-V were better in the CI and HI of PTV_2, and the CI of $PGTV_{nd}$ compared with AP-V. In NT, BP-V and CP-V showed their superiority in V_{50Gy}. The possible reason was that the isocenter of CP-V was in the center of PTV_2 and the target dose of PTV_2 was 54 Gy. Because the MLC of each control point would first open near the isocenter point, CP-V had more advantages in the isodose of 50 Gy, and CI and HI of PTV_2. For the same reason, BP-V had an advantage over CI of $PGTV_{nd}$. The isocenter position of BP-V and CP-V was so close that BP-V and CP-V had the same advantage compared with AP-V.

5 | CONCLUSIONS

The three plans all meet the clinical requirements. The MUs of the AP-V plans were significantly reduced by 11.5% with BP-V, and 10.2% with CP-V. In addition, the change in head contour is smaller than that of the neck during radiotherapy. Thus, the set-up error is smaller when the location position is in the geometric center of $PGTV_{nx}$ than in in the geometric center of $PGTV_{nd}$ or PTV_2. We propose that the RT technician put the location position in the geometric center of $PGTV_{nx}$ during location of the NPC patients. We further suggest that the isocenter be moved to the geometric center of $PGTV_{nx}$ if the NPC patient plan has higher dosimeter requirements for the optic nerves, optic chiasm, or eyeballs.

ORCID

Yong Sang https://orcid.org/0000-0003-4999-1223

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