Evaluation of Target Autocrop Function in Nasopharyngeal Carcinoma SIB IMRT Plan

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Abstract

Purpose

A new target autocrop function was introduced in the Varian Eclipse™ treatment planning software (version 15.5 above). The study aimed to evaluate this new target autocrop impact on nasopharyngeal carcinoma (NPC) plan quality and delivery efficiency.

Methods

Randomly 66 approved NPC simultaneous integrated boost (SIB) intensity modulated radiation therapy (IMRT) treatment plans were retrospectively studied. The manual cropping-based plans served as reference and were designed using sliding-window IMRT. Reference plans were re-optimized with identical planning parameters following the institutional clinical protocol except for the optimization objective of the manual cropping targets deleted. Additionally, each target within 5mm of another had one lower objective at 100% volume and one upper objective at 0% volume for the autocrop plans. Plan quality was assessed based on selected parameters, including TCP (tumor control probability), NTCP (normal tissue complication probability), conformity index (CI), homogeneity index (HI), and dose-volume characteristics. Additionally, the delivery efficiency, the total plan treatment time defined as a sum of monitor units (MUs) for each treated field, and delivery accuracy, γ passing rate of treatment plan quality assurance (QA) also were compared.

Results

Both the manual cropping plans and the autocrop plans could be approved by an experienced oncologist. Overall, the autocrop plans could provide approximately a 13% reduction in linac MU while maintaining comparable plan quality, radiobiological ranking, and accuracy to that of the manual cropping plans.

Conclusions

The new target autocrop tip facilitated the SIB IMRT plans for nasopharyngeal cancer patients. The autocrop could guarantee the quality and delivery accuracy of the radiotherapy plan, improved the planning efficiency, treatment efficiency, and reduced machine wear and tear. It was a promising tool for optimal plan selection for NPC SIB IMRT.

Introduction

NPC is particularly prevalent in the east and southeast Asia. Treatment options include radiotherapy or chemotherapy, or a combination of both. NPC is highly sensitive to ionizing radiation, and radiotherapy is the mainstay treatment modality for non-metastatic disease. The widespread application of

individualized IMRT strategy and advanced imaging-guided technique has contributed to improved survival with reduced toxicities.^[1-3]

Radiotherapy techniques have been progressed from conventional two-dimensional radiotherapy (2DRT) to three-dimensional conformal radiotherapy (3DCRT) and then to IMRT in the last two decades. Considered the complexity of the shape and configuration of tumor and lymph nodes in the target volume and the proximity of OARs, surgery is usually not feasible for the primary treatment of NPC. IMRT is the current preferred method^[4,5] and has better clinical outcomes in treatment plans for NPC patients, such as achieving more accurate target dose distribution and better protection of normal tissues.^[6-8]

At present, IMRT is mainly simultaneous integrated boost (SIB) IMRT, which allows for concurrent dose escalation to the primary tumor with multiple prescription doses during optimization, could conform to the tumor shape better, and protect the normal tissue physically.^[9,10] The planning target volume (PTV)s include layering structures PGTVnx, PGTVnd, PCTVnd, PCTV1, PCTV2 in the SIB-IMRT for NPC. Monaco® treatment planning systems (TPS) identifies the ownership of organ overlap region by ordering organs from top to bottom, using the parameter “optimize over all voxels in volume” and the optional physical parameters “shrink margin”. Conventionally, Pinnacle® and Eclipse TPS before version 15.5 handle the overlap organ region by the manual cropping and add the optimization objectives during the optimization phase by professionally trained medical dosimetrists and physicists by time and effort consuming steps.

Several variables affect the quality of the radiotherapy plan: patient anatomy, dosimetrist’s experience, physician’s plan objectives, TPS optimization algorithm, patient load, etc.^[11] The new target autocrop function had been introduced in the Varian Eclipse TPS (version 15.6.06). The purpose of the study was to understand the impact to plan quality and delivery efficiency using the function target autocrop in Eclipse TPS.

Materials And Methods

Patients and Treatment Planning

Approved 66 NPC patients with SIB IMRT plans were analyzed retrospectively, 16 of whom had high-risk lymph nodes. This study was approved by the medical ethics committee of second affiliated hospital of army medical university, PLA. (2021-Research No. 038-01)

Computer tomography (CT) images were acquired on a Philips Brilliance Big Bore CT scanner (Philips, Cleveland, OH, USA), the slice thickness was 3 mm. Nasopharynx gross tumor volume (GTVnx), lymph node gross tumor volume (GTVnd), clinical target volume (CTV1, CTV2) were delineated. CTVnd was obtained by GTVnd expansion when the lymph nodes were the high-risk region. CTV1 referred to the outward expansion of GTVnx by 0.5 ~ 1.0cm in the front, the upper, the lower, and the sides, and 0.3 ~ 0.5cm in the back (the appropriate distance of outward expansion was determined by the tumor involvement and the distance between the tumor and the spinal cord, brainstem, and other tissue

structures). CTV2 consisted of two parts. One was CTV1 enlarged by 0.5 ~ 1.0cm in the front, the upper, the lower, and the sides, and then enlarged by 0.3 ~ 0.5cm (the appropriate distance is determined according to the tumor involvement and the distance between the tumor and the spinal cord, brain stem, and other tissue structures). The other was GTVnd, its lymphatic drainage area, and the negative lymphatic drainage area requiring prophylactic irradiation. The planning target volume (PTV) was created based on each target volume with an additional 3mm margin, considering setup variability.

The prescription dose to PGTVnx, PGTVnd, PCTV1, PCTV2 were 69-72Gy, 60-70Gy, 60-64Gy, 50-56Gy in 30-33 fractions, respectively. When the lymph nodes were the high-risk region, the prescription dose to PGTVnx, PGTVnd, PCTVnd, PCTV1, PCTV2 were 70Gy, 66-70Gy, 60Gy, 60Gy, 54Gy in 33 fractions, respectively. Critical organs at risk, including the brain stem, spinal cord, lens, optic nerve, optic chiasma, parotid gland, were also contoured by the certified oncologist.

All IMRT plans were generated using the Eclipse planning system (Varian Medical System, Palo Alto, CA) with 120 MLC. The Anisotropic Analytical Algorithm (AAA, version 15.6.06) dose calculation algorithm was chosen for dose calculation using the dose calculation grid resolution of $0.25 \times 0.25 \times 0.25 \text{ cm}^3$. The treatment couch was not considered in the dose calculation. All cases used nine equally spaced beams for IMRT sliding window plans. The collimator rotation and jaw positions were optimized and fixed by the dosimetrists.

A new target autocrop function was introduced in the Varian Eclipse TPS to handle the overlapping targets volume. The principle diagram was shown in Fig.1. After activating the target autocrop function, TPS automatically identified the target areas with contradictory doses objective and overlapping areas, such as PGTV and PCTV in Fig.1(a), which required different prescription doses. Then, a 5mm buffer ring between the PGTV and PCTV would be formed, and the optimization and calculation for the PCTV would be carried out automatically according to the shaded area in Fig.1(b).

The manual cropping plans, which oncologists had been accepted and approved, served as reference. Reference plans were re-optimized with identical planning optimization parameters and OAR constraints following the institutional clinical protocol except for the optimization objective of the manual cropping targets deleted. Additionally, each target had one lower objective at 100% volume and one upper objective at 0% volume for the autocrop plans.

All plans were performed on a Varian Trilogy linear accelerator, which adopted 6 MV photon and a sliding-window technique. The accelerator is equipped with a multi-leaf collimator containing 120 leaves, 80 5.0 mm central leaves, and 40 10.0 mm peripheral leaves.

Plan Quality Evaluation

The treatment plan was evaluated by multiple parameters, which included target coverage criteria, normal tissue sparing criteria, biological parameters TCP and NTCP, treatment efficiency, as well as accuracy. The paired t-tests were performed to assess statistically significant differences ($p < 0.05$).

In terms of target coverage criteria, PTV dose-volume histogram (DVH) parameters, including $D_{2\%}$, $D_{98\%}$, D_{mean} , HI (homogeneity index), CI (conformal index), were computed and recorded with the ICRU83 report^[12], defined as follows:

$$HI = \frac{D_2 - D_{98}}{D_{mean}}$$

$$CI = \frac{TV_{RI}}{TV} \times \frac{TV_{RI}}{V_{RI}}$$

Where RI represents the prescribed dose, TV_{RI} is the volume of target covered by prescribed dose, TV is the target volume, and V_{RI} is the volume of the body covered by prescribed dose. Variables were assessed for organs at risk (OARs), including mean dose (D_{mean}), maximum dose (or point in a significant volume, D_{max} or D_1), volume receiving a fixed-dose level, and dose levels delivered to a certain volume.

Radiation biological parameters tumor control probability (TCP) and normal tissue complication probability (NTCP) were calculated from the extracted differential dose volume histogram (DVH) data based on the Niemierko model.^[13,14]

The equivalent uniform dose (EUD) was calculated by:^[15]

$$EUD = \left(\sum_1^N v_i D_i^a \right)^{\frac{1}{a}}$$

where V_i is fractional volume, D_i is dose bin, and a value is the tumor normal tissue-specific parameter that describes the dose-volume effect. For NPC cases, " a " value is -13.^[16,17] The TCP could be calculated based on the equivalent uniform dose:^[18]

$$TCP = \frac{1}{1 + \left[\frac{TCD_{50}}{EUD} \right]^{4r_{50}}}$$

where TCD_{50} is the tumor dose required for producing 50% TCP and r_{50} is the slope of dose response at 50% TCP. Okunieff et al^[19] reported that tumor-specific parameters for head and neck squamous cell (macroscopic) were $TCD_{50}=51.77\text{Gy}$, $r_{50}=2.28$. Also, the NTCP was determined below:

$$NTCP = \frac{1}{1 + \left[\frac{TD_{50}}{EUD} \right]^{4r_{50}}}$$

where TD_{50} is the dose at which probability of complication becomes 50% in 5 years and r_{50} is the slope of sigmoidal dose response curve of normal tissue at 50% complication probability. These specific parameters given for normal tissue were based on the reports of Emami et al^[20] and Burman et al^[21] (Table 1).

Table 1 Specific parameters given for normal tissue based on the reports of Emami et al.^[19] and Burman et al.^[20]

Structure	Endpoint	a	r_{50}	TD_{50} (Gy)
Brainstem	Necrosis	7	3	65
Spinal cord	Myelitis/necrosis	7.4	4	66.5
Optic chiasm	Blindness	25	3	65
Optic nerve	Blindness	25	3	65
Lens	Cataract	3	1	18
Parotid	Xerostomia	5	6	46

The dose delivery efficiency of each plan was evaluated based on the total number of MU, which were compared between the autocrop plan and the manual cropping plan. Additionally, the agreement of the planning and delivered doses was assessed by studying the patient-specific QA results. The QA of the auto-crop plan and the manual cropping plan was performed with PTW seven29, and the gamma passing rates were compared. The criteria for gamma analysis was 3%/3mm, with a 10% dose threshold.

Results

A total of 132 clinically acceptable IMRT plans were achieved in all 66 cases. For each patient case, two IMRT plans were generated with different target crop methods: the manual cropping and autocrop, respectively. The manual cropping and autocrop methods were sufficient to produce highly conformal treatment plans for NPC cases to meet the treatment goals. On average, the two types of plans provided comparable plan quality in terms of target dose coverage, dose homogeneity, and critical structure sparing. Additionally, the radiation biological parameters TCP and NTCP only had subtle differences ($p < 0.05$).

The average planning target volume of all these patients whose lymph nodes were the low-risk region were $65.61 \pm 36.77 \text{ cm}^3$, $16.30 \pm 17.73 \text{ cm}^3$, $17.20 \pm 19.32 \text{ cm}^3$, $163.16 \pm 112.28 \text{ cm}^3$, $625.98 \pm 153.03 \text{ cm}^3$ for PGTV_{nx}, PGTV_{nd(L)}, PGTV_{nd(R)}, PCTV1, PCTV2, respectively. While the average planning target volume of all these patients whose the lymph nodes are the high-risk region were $118.63 \pm 76.69 \text{ cm}^3$, $27.80 \pm 15.00 \text{ cm}^3$, $27.33 \pm 16.50 \text{ cm}^3$, $70.91 \pm 22.91 \text{ cm}^3$, $60.26 \pm 28.67 \text{ cm}^3$, $252.18 \pm$

140.57 cm³, 792.15 ± 154.95 cm³ for PGTVnx, PGTVnd(L), PGTVnd(R), PCTVnd(L), PCTVnd(R), PCTV1, PCTV2, respectively.

The detailed DVH statistical results on the plan quality index are summarized in Tables 2, 3, and 4. Figure 1 shows the dose in color wash from the manual cropping and autocrop plans of a randomly selected case. There was no significant difference in the minimum dose, maximum dose, and mean dose for planning targets volume between the manual cropping and autocrop plans ($p < 0.05$). The mean HI and CI were statistically equivalent concerning the two target crop methods. The mean HI values were within 0.15 and 0.20 for the manual cropping and autocrop plans, respectively. The mean CI are 0.91 and 0.89, which also could be seen from Fig. 1.

In this particular case (Fig. 1), the quality of the autocrop plans was almost equivalent to the manual cropping plan. The maximum dose, minimum dose, and mean dose of PGTVnx in the autocrop plan decreased by 0.38%, 0.71%, 0.39%, respectively. Additionally, for the lymph nodes PGTVnd(L) and PGTVnd(R) in the autocrop plan, the maximum dose, minimum dose, and mean dose increased by 1.80%, 0.22%, 1.13% and 1.69%, 0.05%, 0.94%, separately. For the planning clinical target volume PCTV1 and PCTV2, the difference of the maximum dose, minimum dose, and mean dose between the two type plans were 0.31%, -0.55%, -0.24%, and 0.28%, -0.47%, -0.68% respectively. The doses to the OARs were slightly increased but are well below the normal tissue limit. The CI of PCTV2 decreased from 0.92 (the manual cropping plan) to 0.88 (the autocrop plan). Both types plans were prescribed to similar doses in the color wash, except the 40Gy dose color wash of the manual cropping plan was slightly more compact than that of the autocrop plan, but that were both considered to be good results in clinical practice.

The maximum, D_1 , mean, and V_x values of DVH parameters showing OAR sparing of the manual cropping and autocrop plans for 66 cases are shown in tables 3. The average maximum doses of the brain stem, lens, and right optic nerve were slightly increased in the autocrop plans, and the spinal cord maximum dose, parotid mean dose, and V_{30} were more increasing, while the increase was all within 3%. The average maximum doses of the optic chiasm and left optic nerve were insignificant decreased in the autocrop plans ($p = 0.03$).

Table 4 summarizes the results in terms of the number of MUs for fraction and γ passing rate (3%, 3mm) averaged for the 66 cases. Compared to the manual cropping plans, the autocrop plans achieved a 12.9% relative decrease in the mean number of MUs (1412 MU vs 1230 MU). All 132 plans passed our institutional IMRT QA standard (γ passing rate $\geq 90\%$). The comparable agreement between the planned and delivered doses (insignificant difference γ passing rate) were found for the two methods. The average γ passing rate of the manual cropping plans was $97.7 \pm 2.2\%$ (range: 91.6% ~ 99.8%) compared to the autocrop plans $98.2 \pm 1.9\%$ (range: 92.2% ~ 99.3%).

The biological parameters NTCP estimates for the critical organs at risk, and the expected TCP values for the PGTVnx are quantified, as depicted in Table 5. The average EUD and TCP of the PGTVnx were $64.28 \pm 2.22\text{Gy}$, $87.36 \pm 3.36\%$ for the manual cropping plans, while $64.00 \pm 2.09\text{Gy}$, $86.97 \pm 3.21\%$ for the

autocrop plans. The average EUD for OARs in the autocrop plans was a slight increase compared to the manual cropping plans. The average NTCP for the Optic chiasm slight decreased: the manual cropping plan was $1.14 \pm 2.17\%$, and the autocrop plan was $1.08 \pm 2.14\%$. The average NTCP for left and right lens remained the same: $0.02 \pm 0.05\%$, $0.02 \pm 0.08\%$ in the manual cropping plans, while $0.02 \pm 0.06\%$, $0.02 \pm 0.08\%$ in the autocrop plan, separately. The average NTCP for brain stem ($1.85 \pm 2.28\%$ to $2.00 \pm 2.37\%$), spinal cord ($(1.42 \pm 2.85) \times 10^{-3}\%$ to $(2.07 \pm 4.13) \times 10^{-3}\%$), left parotid ($0.65 \pm 1.70\%$ to $0.94 \pm 2.21\%$) and right parotid ($0.57 \pm 1.23\%$ to $0.92 \pm 1.84\%$) were slightly increase compared to the manual cropping plans ($p < 0.05$).

Table 2 Planning target volume quality index comparison between the manual-crop and autocrop plans for these NPC patients whose the lymph nodes are the low-risk region.

Table 3 Planning target volume quality index comparison between the manual-crop and autocrop plans for these NPC patients whose the lymph nodes are the high-risk region.

Note: $D_{98\%}$ is the minimum dose, D_{mean} is the mean dose, $D_{2\%}$ is the maximum dose, HI is heterogeneity index, CI is conformal index, "Avg." is the abbreviation of average. "M" and "A" represent the manual-crop and the autocrop plans, respectively.

Table 4 OAR sparing comparison between the autocrop and manual-crop plans for all patients.

Structures	Volume [cm ³]	Dose volume index	Avg. $\pm$ SD		Range	
			D _M	D _A	D _M	D _A
PGTVnx	65.61 $\pm$ 36.77	D _{98%} [Gy]	71.00 $\pm$ 1.55	71.07 $\pm$ 1.24	63.49 ~ 73.47	66.05 ~ 74.58
		D _{2%} [Gy]	75.32 $\pm$ 0.98	74.83 $\pm$ 0.97	72.22 ~ 78.02	72.59 ~ 77.15
		D _{mean} [Gy]	73.63 $\pm$ 0.82	73.26 $\pm$ 0.74	70.77 ~ 75.75	70.80 ~ 74.83
		HI	0.06 $\pm$ 0.02	0.05 $\pm$ 0.02	0.03 ~ 0.18	0.02 ~ 0.15
PGTVnd(L)	16.30 $\pm$ 17.73	D _{98%} [Gy]	65.36 $\pm$ 3.06	66.74 $\pm$ 3.40	59.23 ~ 70.90	59.16 ~ 71.17
		D _{2%} [Gy]	68.23 $\pm$ 3.31	69.92 $\pm$ 3.82	62.25 ~ 73.13	62.97 ~ 75.45
		D _{mean} [Gy]	66.95 $\pm$ 3.10	68.42 $\pm$ 3.50	61.50 ~ 72.24	62.09 ~ 72.78
		HI	0.04 $\pm$ 0.02	0.05 $\pm$ 0.03	0.02 ~ 0.16	0.01 ~ 0.19
PGTVnd(R)	17.20 $\pm$ 19.32	D _{98%} [Gy]	65.56 $\pm$ 2.78	65.68 $\pm$ 2.64	60.24 ~ 71.04	61.42 ~ 71.32
		D _{2%} [Gy]	68.23 $\pm$ 2.92	68.27 $\pm$ 2.94	61.99 ~ 73.19	63.25 ~ 74.39
		D _{mean} [Gy]	67.02 $\pm$ 2.80	67.31 $\pm$ 2.77	61.31 ~ 72.27	62.60 ~ 72.94
		HI	0.04 $\pm$ 0.02	0.04 $\pm$ 0.01	0.02 ~ 0.14	0.02 ~ 0.21
PCTV1	163.16 $\pm$ 112.28	D _{98%} [Gy]	62.09 $\pm$ 1.34	62.42 $\pm$ 1.60	59.56 ~ 65.15	58.38 ~ 65.56
		D _{2%} [Gy]	75.08 $\pm$ 0.97	74.60 $\pm$ 0.95	71.85 ~ 77.82	72.25 ~ 77.02
		D _{mean} [Gy]	70.00 $\pm$ 1.54	70.29 $\pm$ 1.38	65.02 ~ 72.31	65.15 ~ 72.95
		HI	0.19 $\pm$ 0.02	0.17 $\pm$ 0.03	0.13 ~ 0.26	0.12 ~ 0.27
PCTV2	625.98 $\pm$ 153.03	D _{98%} [Gy]	54.50 $\pm$ 1.58	54.58 $\pm$ 2.03	49.85 ~ 58.91	50.06 ~ 62.25
		D _{2%} [Gy]	74.44 $\pm$ 0.97	74.07 $\pm$ 0.93	71.28 ~ 77.04	71.66 ~ 76.28

D_{mean} [Gy]	62.07 ± 1.68	63.61 ± 2.21	58.31 ~ 66.29	59.69 ~ 70.38
HI	0.32 ± 0.02	0.31 ± 0.03	0.26 ~ 0.38	0.18 ~ 0.36
CI	0.91 ± 0.04	0.90 ± 0.04	0.80 ~ 0.98	0.83 ~ 0.98

Structures	Volume [cm ³]	Dose volume index	Avg. $\pm$ SD		Range	
			D _M	D _A	D _M	D _A
PGTVnx	118.63 $\pm$ 76.69	D _{98%} [Gy]	69.78 $\pm$ 1.49	69.63 $\pm$ 1.62	64.84 ~ 71.06	63.88 ~ 70.78
		D _{2%} [Gy]	74.74 $\pm$ 0.39	74.65 $\pm$ 0.41	73.88 ~ 75.31	73.86 ~ 75.25
		D _{mean} [Gy]	72.82 $\pm$ 0.41	72.64 $\pm$ 0.32	71.63 ~ 73.21	71.95 ~ 73.01
		HI	0.07 $\pm$ 0.02	0.07 $\pm$ 0.02	0.05 ~ 0.14	0.05 ~ 0.15
PGTVnd(L)	27.8 $\pm$ 15.00	D _{98%} [Gy]	69.13 $\pm$ 4.32	70.47 $\pm$ 1.26	53.63 ~ 71.44	66.80 ~ 72.12
		D _{2%} [Gy]	73.52 $\pm$ 1.42	73.87 $\pm$ 1.43	69.51 ~ 75.50	69.97 ~ 75.60
		D _{mean} [Gy]	71.94 $\pm$ 1.17	72.33 $\pm$ 1.24	68.31 ~ 73.44	68.45 ~ 73.59
		HI	0.06 $\pm$ 0.066	0.05 $\pm$ 0.02	0.03 ~ 0.30	0.03 ~ 0.09
PGTVnd(R)	27.33 $\pm$ 16.50	D _{98%} [Gy]	70.22 $\pm$ 1.31	69.83 $\pm$ 2.94	65.89 ~ 71.42	59.73 ~ 72.35
		D _{2%} [Gy]	73.70 $\pm$ 1.65	73.75 $\pm$ 1.63	68.30 ~ 75.17	68.63 ~ 75.71
		D _{mean} [Gy]	72.09 $\pm$ 1.45	72.16 $\pm$ 1.44	67.33 ~ 73.29	67.85 ~ 74.07
		HI	0.05 $\pm$ 0.01	0.05 $\pm$ 0.04	0.04 ~ 0.08	0.03 ~ 0.21
PCTVnd(L)	70.91 $\pm$ 22.91	D _{98%} [Gy]	63.34 $\pm$ 3.38	63.10 $\pm$ 1.63	60.53 ~ 70.59	61.10 ~ 65.79
		D _{2%} [Gy]	73.71 $\pm$ 0.91	74.03 $\pm$ 1.04	72.46 ~ 75.33	72.41 ~ 75.33
		D _{mean} [Gy]	69.71 $\pm$ 1.02	70.47 $\pm$ 0.80	68.20 ~ 71.67	69.30 ~ 72.29
		HI	0.15 $\pm$ 0.05	0.16 $\pm$ 0.03	0.03 ~ 0.21	0.10 ~ 0.19
PCTVnd(R)	60.26 $\pm$ 28.67	D _{98%} [Gy]	64.27 $\pm$ 3.90	63.10 $\pm$ 1.63	60.60 ~ 70.85	61.10 ~ 65.79
		D _{2%} [Gy]	73.92 $\pm$ 0.78	74.03 $\pm$ 1.04	72.74 ~ 75.02	72.41 ~ 75.33

PCTV1	252.18 ± 140.57	D _{mean} [Gy]	69.94 ± 1.31	70.47 ± 0.80	67.31 ~ 72.06	69.30 ~ 72.29
		HI	0.14 ± 0.06	0.16 ± 0.03	0.05 ~ 0.21	0.10 ~ 0.19
		D _{98%} [Gy]	61.14 ± 0.61	61.24 ± 1.28	60.09 ~ 62.10	59.31 ~ 63.68
		D _{2%} [Gy]	74.55 ± 0.42	74.45 ± 0.40	73.69 ~ 75.13	73.65 ~ 74.99
		D _{mean} [Gy]	69.82 ± 0.71	70.08 ± 0.42	68.08 ~ 70.76	69.47 ~ 70.98
PCTV2	792.15 ± 154.95	HI	0.19 ± 0.01	0.19 ± 0.02	0.18 ~ 0.21	0.14 ~ 0.22
		D _{98%} [Gy]	54.06 ± 1.11	54.38 ± 0.71	51.06 ~ 55.06	52.92 ~ 55.40
		D _{2%} [Gy]	74.10 ± 0.57	72.83 ± 74.86	73.10 ~ 74.89	72.83 ~ 74.86
		D _{mean} [Gy]	63.38 ± 1.25	64.83 ± 1.18	61.47 ~ 65.91	62.82 ~ 67.15
		CI	0.89 ± 0.03	0.85 ± 0.03	0.82 ~ 0.93	0.80 ~ 0.92

OARs	Parameters	Avg. $\pm$ SD		Range		rel. Avg. [%]
		D _M	D _A	D _M	D _A	
Brain stem	D _{max} [Gy]	56.14 $\pm$ 7.60	56.29 $\pm$ 7.04	37.16 ~ 68.06	39.18 ~ 68.75	-0.27
	D ₁ [Gy]	50.99 $\pm$ 7.04	51.66 $\pm$ 6.42	36.03 ~ 62.38	36.60 ~ 62.51	-1.31
Spinal cord	D _{max} [Gy]	34.58 $\pm$ 2.88	35.60 $\pm$ 2.81	31.25 ~ 44.90	31.87 ~ 45.09	-2.95
	D ₁ [Gy]	32.40 $\pm$ 2.33	33.13 $\pm$ 2.52	29.78 ~ 42.59	28.24 ~ 42.39	-2.25
Optic chiasm	D _{max} [Gy]	43.81 $\pm$ 17.05	43.13 $\pm$ 17.19	6.28 ~ 70.18	6.24 ~ 70.94	1.55
	D ₁ [Gy]	41.88 $\pm$ 17.47	41.63 $\pm$ 17.26	5.79 ~ 67.39	5.84 ~ 68.28	0.60
Optic nerve L	D _{max} [Gy]	42.00 $\pm$ 18.01	41.74 $\pm$ 17.65	7.85 ~ 75.36	7.49 ~ 74.78	0.62
	D ₁ [Gy]	40.01 $\pm$ 18.15	40.14 $\pm$ 17.68	7.15 ~ 74.91	6.78 ~ 74.57	-0.32
Optic nerve R	D _{max} [Gy]	43.63 $\pm$ 17.36	43.17 $\pm$ 17.35	6.78 ~ 72.14	6.75 ~ 70.18	1.05
	D ₁ [Gy]	41.60 $\pm$ 17.43	41.49 $\pm$ 17.34	6.20 ~ 70.44	6.18 ~ 68.69	0.26
Len L	D _{max} [Gy]	6.89 $\pm$ 2.59	7.01 $\pm$ 2.53	2.00 ~ 14.88	2.00 ~ 14.88	-1.74
	D ₁ [Gy]	6.69 $\pm$ 2.58	6.74 $\pm$ 2.45	1.97 ~ 14.78	1.98 ~ 14.41	-0.75
Len R	D _{max} [Gy]	7.22 $\pm$ 2.78	7.30 $\pm$ 2.93	2.02 ~ 19.06	2.04 ~ 21.19	-1.11
	D ₁ [Gy]	7.00 $\pm$ 2.78	7.07 $\pm$ 2.84	2.01 ~ 18.93	2.02 ~ 20.51	-1.00
Parotid L	D _{mean} [Gy]	25.16 $\pm$ 2.71	26.32 $\pm$ 2.67	18.73 ~ 31.24	19.76 ~ 31.85	-2.34
	V ₃₀ [%]	19.46 $\pm$ 12.28	20.15 $\pm$ 12.66	2.71 ~ 31.24	2.67 ~ 31.85	-2.60
Parotid R	D _{mean} [Gy]	25.34 $\pm$ 2.56	26.58 $\pm$ 2.72	17.59 ~ 30.18	18.10 ~ 31.87	-2.48
	V ₃₀ [%]	18.92 $\pm$ 12.07	19.82 $\pm$ 12.73	2.56 ~ 30.18	2.72 ~ 31.87	-2.72

Note: $D_{\max}$ is the maximum dose, D_1 is minimal dose to 1% of structure, V_{30} is the volume that received 30Gy dose. “rel.” represents relative value. “M” and “A” represent the manual-crop and the autocrop plans, respectively.

Table 5 The MU per fraction and γ passing rate (3%, 3mm) with regard to two different crop methods.

	Avg. $\pm$ SD		Range	
	D_M	D_A	D_M	D_A
MU	1412 ± 214	1230 ± 164	1048 ~ 2050	955 ~ 1860
γ passing rate [%]	97.7 ± 2.2	98.2 ± 1.9	91.6 ~ 99.8	92.2 ~ 99.3

Table 6 The EUD values, NTCP estimates for OAR, and the expected TCP values for target volume with regard to two different crop methods.

	EUD [%]		TCP [%] or NTCP [%]	
	Manual-crop plans	Autocrop plans	Manual-crop plans	Autocrop plans
Target				
PGTVnx	64.28 ± 2.22	64.00 ± 2.09	87.36 ± 3.36	86.97 ± 3.21
OAR				
Brainstem	43.38 ± 6.01	44.23 ± 5.71	1.85 ± 2.28	2.00 ± 2.37
Spinal cord	31.75 ± 2.18	33.43 ± 2.42	$(1.42 \pm 2.85) \times 10^{-3}$	$(2.07 \pm 4.13) \times 10^{-3}$
Optic chiasm	33.38 ± 14.44	33.43 ± 14.23	1.14 ± 2.17	1.08 ± 2.14
Optic nerve L	29.99 ± 14.41	30.99 ± 13.93	0.64 ± 1.59	0.74 ± 1.95
Optic nerve R	31.54 ± 13.78	31.85 ± 13.71	0.65 ± 1.52	0.79 ± 2.11
Len L	1.53 ± 0.76	1.55 ± 0.74	0.02 ± 0.05	0.02 ± 0.06
Len R	1.59 ± 0.77	1.59 ± 0.75	0.02 ± 0.08	0.02 ± 0.08
Parotid L	33.47 ± 4.58	34.08 ± 5.05	0.65 ± 1.70	0.94 ± 2.21
Parotid R	33.95 ± 4.11	34.71 ± 4.21	0.57 ± 1.23	0.92 ± 1.84

Discussion

The SIB IMRT allows for concurrent dose escalation to the primary tumor with complex multiple level prescription doses during optimization. However, it makes treatment planning more difficult and complex. The traditional manual cropping target is a tedious job in the Eclipse TPS. A simple autocrop target method was suggested in this study to take some of the clinical load off.

Planning target quality indices indicated there was a slight difference in the EUD, TCP, NTCP, $D_{\min}$, $D_{\max}$, D_{mean} , HI, CI for SIB IMRT plans with different target crop methods. Planning studies are often subjected to uncertainties from the different treatment planning conditions (optimization parameters and objectives), so an effort is made to minimize these effects by a selection of the same parameters. The minuscule decreased plan quality for the autocrop method was expected because the new autocrop plan was just a re-optimization based on the approved manual cropping plan clinically and without more optimization and calculation to keep the optimization conditions consistent, but the manual cropping plans were optimized at least once. However, the autocrop plans also were considered clinically acceptable and excellent by an experienced oncologist.

What is surprising is the magnitude of the improvement in delivery efficiency between the autocrop plans and the manual cropping plans. A previous article^[22] on SIB NPC focused on Eclipse TPS (version 8.6) slide-window IMRT techniques, which mean MU of the ten cases enrolled was 1537MU. The other two articles^[23,24] referred to the mean MU of SIB IMRT for NPC were 1288 and 1379, respectively. These results were similar to the comparative study of these in the current article. In our study, the mean MUs for the two target crop methods were 1412 MU and 1230 MU, severally. Reducing the MU to the autocrop plans by an average of 182MU (12.9%) could potentially lead to less radiation dose transmitted through the MLC and a meaningful decrease in linac burden. Besides, the shorter delivery time increases machine throughput and is also favorable for patients for yielding reduced intrafraction motion, increased patient comfort, especially for patients who cannot remain stable on the treatment couch for a long time.

The in-depth reason why the autocrop plans give lower MU may be explained as follows: The structures of the radiotherapy target volume in nasopharyngeal carcinoma are complex, and there are at least two to three overlapping areas. When physicists manually identify the ownership scope of the targets volume overlap region and give optimization objectives, personal expertise and experience have great influence. If the ownership scope of the target volume overlap region is judged to be improper or/and the given optimization objectives are not good, it will increase the optimization difficulty of the radiotherapy plan. The treatment planning system solves this "problem" by increasing the number of small area segments so as to increase the number of MU as a whole. If the new target autocrop function is adopted, the above problem may not be encountered.

To the best of our knowledge, this is the first article on the dosimetric and radiation biological comparison between the target autocrop and manual cropping methods for radiotherapy treatment of SIB NPC in the Eclipse TPS. The comparison and evaluation of the radiotherapy plan are commonly based on the three-dimensional dose distribution and DVH indexes.^[25-28] Besides, the radiobiological ranking by calculating indices EUD, TCP, and NTCP is also applied widely.^[29-32] A previous paper^[33] proposed a composite plan

quality index integrated dosimetric and radiobiological quality indices. In our study, both dosimetric and radiobiological quality indices were considered, respectively. The differences in all the indices between the two crop methods were small. Kim et al.^[34] investigated out that the mean TCP of the tumor GTV for head and neck IMRT was about 89.5%, which was a similar result in our study.

In brief, each plan was evaluated rigorously using the dosimetric parameters, radiobiological parameters, and gamma passing rate. All parameters results were deemed acceptable for the manual cropping and autocrop plans suggesting that the autocrop plans can be dosimetrically and radiobiologically equivalent to the manual cropping plans and a faster and equally effective treatment delivery which can be offered to patients. Our study had a potential limitation that all the autocrop plans were once re-optimization plans and had not been optimized and adjusted many times which would make the dose distribution become not better. In the future, the target autocrop function will be used for the radiotherapy plan directly and investigated the plan quality compared to the manual cropping one.

Conclusion

A new target autocrop function was evaluated in this study to facilitate the SIB IMRT plans for nasopharyngeal cancer patients. The introduction of the tip can not only guarantee the quality and delivery accuracy of the radiotherapy plan but also make the operation simpler, improve the treatment efficiency, reduce the dosimetrist's intervention, and machine wear and tear. It will be a promising tool for optimal plan selection for NPC SIB IMRT.

Declarations

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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Figures

Figure 1

The principle diagram of the autocrop target method. (a) A target area with conflicting gross tumor volume (PGTV) and planning target volume (PCTV). (b) The TPS automatically forms a 5mm buffer ring between the PGTV and PCTV, the optimization and calculation for the PCTV are automatically carried out according to the shaded area.

Figure 2

A comparison of dose in color wash for a case in axial (left), coronal (middle), and sagittal (right) planes. (a) manual-crop plan, and (b) autocrop plan.