Evaluation of Auto-Planning in VMAT for Locally Advaced Nasopharyngeal Carcinoma

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Abstract

The aim of this study is to demonstrate the feasibility of Auto-Planning module for locally advanced nasopharyngeal carcinoma (NPC). A total of 22 patients with locally advanced NPC were enrolled in this study. For each patient, volumetric modulated arc therapy (VMAT) plans were generated manually by an experienced physicist and automatically by the Auto-Planning module. The dose distribution, dosimetric parameters, monitor units and planning time were compared between automatic plans (APs) and manual plans (MPs). Meanwhile, the overall stage of disease was factored into the evaluation. The targets dose coverage of APs was similar to that of MPs. For most of the organs at risk (OARs) except spial cord, the dose parameters of APs were superior to that of MPs. The D_{max} and V_{50} of brain-stem were statistically decreased by 1.0 Gy and 1.32% respectively, while the D_{max} of optic nerves and optic chiasm were also lower in the APs (both $P < 0.05$). APs provide a similar or superior plan quality to MPs in most cases, except for several patients with stage IV. The dose differences for most OARs were similar between the two types of plans and independent of the overall stage. Nevertheless, the APs provided better brain-stem sparing in patients with stage III, while better the parotid glands sparing in patients with stage IV. Moreover, the monitor units and planning time were significantly decreased in the APs. In general, Auto-Planning was a potential technology on the implementation of VMAT treatment planning for locally advanced NPC.

1. Introduction

Nasopharyngeal carcinoma (NPC) is one of the most common malignancies in Southeast Asia and China.[1] Radiotherapy has become the preferred treatment of NPC, due to its high sensitivity to radiation. With the development of radiotherapy technology, volumetric modulated arc therapy (VMAT) has been gradually used in the treatment of NPC.[2] It has been comfirmed that VMAT could generally improve the target coverage and organs at risk (OARs) dose sparing for head and neck tumors, compared with intensity-modulated radiation therapy (IMRT).[3–5] However, due to the irregular turmor targets, numerous surrounded OARs and strict dosimetric criterias, the radiotherapy plan designing for NPC is quite challenging and demanding. In order to obtain a high-quality treatment plan, radiotherapy physicists need to spend a lot of time and effort on modifying the optimization functions and continuously optimizing. Futhermore, the quality of treatment plan depends largely on the individual experience and skill of the physicist, and it may be varying considerably between physicists and treatment centers.[6,7]

As one promising solution for these problems, automatic planning has been proposed to reduce planning time, improve plan quality and consistency without manual intervetion.[8] Commercial softwares have been developed and used clinically, including RapidPlan (Varian Medical Systems, Palo Alto, CA)[9,10], Multi-Criteria Optimization (RaySearch Laboratories, Stockholm, Sweden)[11,12] and Auto-Planing (Philips Medical Systems, Best, The Netherlands)[13–15]. The Auto-Planning module integrated in Pinnacle[3] treatment planning system (TPS) could automatically set center point, beam angles, help strustures, optimization goals, constraints, and weights.[14] It has been demonstrated that automatic planning was feasible in many sites of cancer, such as head and neck[13,15,16], lung[17], breast[18], eso[7,19], pelvic[20] and so on. In most of these studies, automatic planning could achieve similar or better results compared with manual plans. However, there have been few reports of automatic planning for NPC, espically for locally advanced NPC.[21]

Due to the irregular shape of the target volumes and numerous closely OARs, the design of treatment plan for locally advanced NPC were really time-consuming and challenging. In particular, the parotid glands and brain stem are often close to or even partial overlapping with the targets. Dry mouth[22] and fatigue[23] caused by the overdose delivered to these organs could seriously affect the quality of patients's life after radiotherapy treatment. It is difficult to balance the target coverage and OARs constrain, even for experienced physicists. Therefore, automatic planing for locally advanced NPC could be much help to the clinical work. In this paper, Auto-Planning module in Pinnacle[3] was used to generate 22 VMAT automatic plans for locally advanced NPC. The feasibility and efficacy of Auto-Planning were evaluated by comparing dosimetry against the corresponding manual VMAT plans from a skilled planner. Futhermore, the difference of plan quality were analyzed separately between the overall stages for a more comprehensive evaluation.

2. Material And Methods

2.A patient characterstics

Between October 2020 and February 2021, 22 locally advanced NPC patients who received treatment in Fujian tumor hospital were retrospectively selected. These patients were immobilized using a thermoplastic mask in the supine position. Planning CT with a slice thickness of 3-mm (Brilliance CT Big Bore, Philips Medical Systems Inc., Cleveland, OH, USA) and preteatment enhanced magnetic resonance imaging (Philips Achieva 3.0T) were performed for each patient. There were 17 males and 5 females aged 30 years to 76 years (median age: 48 years). The overall stage distribution was stage III: 50% (11 cases) and IVA/B: 50% (10 cases with IVA and 1 case with IVB), accorading to the Chinese 2008 staging system for NPC. The study has been approved by the ethics committee of Fujian Cancer Hospital (ethics number: SQ2016-048-01) and all patients provided written informed consent prior to enrollment in the study. All methods were performed in accordance with the Declaration of Helsinki as well as relevant guidelines and regulations.

2.B Target volume delineation and dose prescription

The target volumes were contoured by experienced physicians in accordance with an institutional treatment protocol. The primary nasopharyngeal tumor (GTV-T) and definitive bilateral lymph nodes (GTV-NL and GTV-NR) were determined by imaging, endoscopic examinations and clinical. A high risk region (CTV1) was defined as GTV-T with a magin of 5-10 mm, including the nasopharyngeal mucosa, while a low risk region (CTV2) was defined as potentially involved regions. The bilateral low-risk nodal regions (CTV-NL and CTV-NR) included disease at levels II-V. The seven planning target volumes (PTVs), including GTV-T-P, CTV1-P, CTV2-P, GTV-NL-P, GTV-NR-P, CTV-NL-P and CTV-NR-P, were expanded from corresponding target volume by 3mm. The OARs included lens, eyes, optic nerves, optic chiasm, brain stem, spinal cord, parotid glands, temporal lobe, mandible, temporomandibular joint, oral cavity and thyriod.

2.CTreatment Planning and Dose Prescription

The prescribed dose was 69.96 Gy to GTV-T-P / GTV-NL-P / GTV-NR-P, 60.06 Gy to CTV1-P, 56.1 Gy to CTV2-P and 52.8 Gy to CTV-NL-P / CTV-NR-P. Manual VMAT plans (MPs) were generated in the Pinnacle^3(version 16.2, Philips Radiation Oncology Systems, Madison, WI). The Auto-Planning module was used to create automatic VMAT plans (APs). Both plans were designed by the same physicist for an Elekta Synergy accelerator with 6 MV X-ray beams and double coplanar full arcs. One clockwise (CW) arc was set from 182 to 178 with a 10° collimator angle and one counterclockwise (CCW) arc was set from 178 to 182 with a 350° collimator angle. Gantry spacing was 4°. The same template listed in Table 1 was used for all APs and the template parameters could be adjusted based on the patients' annatomy. APs could be slight manual intervened no more than three times.

Table 1. OARs optimization goals in treatment planning

OARs	Type	Dose (Gy)	Volume(%)	Priority	Compromise
Left lens	Max Dose	5	-	High	No
Right lens	Max Dose	5	-	High	No
Left optic nerves	Max Dose	48	-	High	No
Right optic nerves	Max Dose	48	-	High	No
Optic chiasm	Max DVH	48	0	High	No
Brain stem	Max DVH	50	5	High	Yes
Brain stem	Max DVH	40	15	High	Yes
Spinal cord	Max Dose	38	-	High	No
Parotids left	Max DVH	40	20	Medium	Yes
Parotids left	Max DVH	26	45	Medium	No
Parotids right	Max DVH	40	20	Medium	Yes
Parotids right	Max DVH	26	45	Medium	Yes
Oral cavity	Max DVH	30	70	Low	Yes
Thyroid	Max DVH	40	60	Low	Yes
Mid	Max Dose	38	-	Medium	Yes
Ring1	Max DVH	50	10	Medium	Yes
Ring1	Max Dose	52	-	Medium	Yes
Ring2	Max DVH	45	8	Medium	Yes
Ring2	Max Dose	47	-	Medium	Yes
Ring3	Max DVH	40	6	Medium	Yes
Ring3	Max Dose	42	-	Medium	Yes
Ring4	Max DVH	35	4	High	Yes
Ring4	Max Dose	37	-	High	Yes
Ring5	Max DVH	30	2	High	Yes
Ring5	Max Dose	32	-	High	Yes

2.D Plan evaluation and statistical analysis

For quantitative comparisons, several dosimetric parameters were collected. Planning target volumes (PTVs) dose corresponding to 2% of volume (D_2), 95% of volume (D_{95}) and 98% of volume (D_{98}),conformity index (CI = ($V_{prescription\ in\ PTV}$ /V_{PTV})*($V_{prescription\ in\ PTV}$/$V_{prescription}$)) and homogeneity index ((HI = (D_2-D_{98})/$D_{prescription}$)) were all evaluated. For parallel OARs such as parotid grands, mean dose (D_{mean}) or V_x (the percentage volume receiving x Gy dose) were analyzed. For serial OARs such as spial cord, D_{max} or D_{2cc} (max dose or dose corresponding to 2cc volume) were calcultaed. Meanwhile, the monitor unit (MU) per fraction and planning duration were also recorded for comparison.

The Wilcoxon’s signed rank test was carried out between APs and MPs for dosimetric parameters previously described. Statistical Package for the Social Sciences (SPSS 21.0; SPSS Inc., Chicago, IL, USA) was used to perform these tests and $P<0.05$ was considered statistically significant.

3. Result

3.A Targets Dose comparison

Most of the plans including APs and MPs met the prescribed requiement of targets, as shown in Table 2. In general, the pass rate of dose criteria and dose distribution in the targets were similar in the two groups of plans. In terms of GTV-NL-P/GTV-NR-P/CTV1-P/CTV2-P, there is no statistical difference in the listed parameters between APs and MPs. However, compared to the MPs, the D_2 and HI of GTV-T-P was slightly higher in the APs by 0.7% and 2.8% ($P<0.05$), indicating more hot regions in the APs. Meanwhile, the D_{95} of CTV-NL-P and CTV-NR-P was higher in the APs too.

Table 2. Dosimetric comparison of PTVs in manual and automatic VMAT (mean ± SD)

Targets	Index	Criteria	Pass rate (%)		Mean dese ± SD		P
			AP	MP	AP	MP	
GTV-T-P	D2(Gy)				75.11±0.47	74.59±0.61	0.016
	D95(Gy)	>69.96	95.45	95.45	70.23±0.37	70.29±0.28	0.664
	HI				0.071±0.010	0.069±0.012	0.025
CTV-1-P	D95(Gy)	>60.06	100.00	100.00	63.73±1.12	63.89±1.23	0.218
	CI				0.342±0.121	0.345±0.116	0.372
CTV-2-P	D95(Gy)	>56.1	100.00	95.45	58.13±0.81	57.59±1.06	0.071
	CI				0.368±0.094	0.435±0.212	0.291
GTV-NL-P	D2(Gy)				73.99±0.88	73.84±1.03	0.084
	D95(Gy)	>69.96	95.45	95.45	70.42±0.46	70.23±0.36	0.092
	HI				0.061±0.017	0.060±0.019	0.075
GTV-NR-P	D2(Gy)				74. 08±0.64	73.91±0.66	0.138
	D95(Gy)	>69.96	95.45	90.91	70.31±0.36	70.13±0.34	0.073
	HI				0.067±0.012	0.065±0.013	0.067
CTV-NL-P	D95(Gy)	>52.8	100.00	95.45	53.98±1.26	53.65±1.47	0.000
CTV-NR-P	D95(Gy)	>52.8	95.45	95.45	54.35±0.68	53.61±0.49	0.000
PTV-6996	CI				0.941±0.021	0.943±0.016	0.638
PTV-5280	CI				0.440±0.062	0.444±0.067	0.848

3.B OARs Dose comparison

The exposure dose of OARs was summarized in the Table 3. The pass rate of dose criteria for all OARs was similiar or increased in the APs compared with MPs, except for V_{30} of right parotid grand. Meanwhile, most objective parameters for APs were lower than MPs. The D_{max} of left optic nerves, right optic nerves, optic chiasm and brain stem were decreased by 1.9Gy, 2.4Gy, 1,2Gy and 1.0Gy in the APs, respectively (both $P < 0.05$). The V_{50} of brain stem, D_{2cc} of mandible and D_{mean} of oral cavity were also statistically lower in the APs, by 1.32%, 1.0Gy and 1.5Gy. However, the max dose of spial cord was incresed by 1.0Gy in the APs ($P<0.05$). By the way, the volume of low-dose (lower than 30Gy) region was significantly decreased in the APs, from 2497.8cc to 2395.6cc ($P<0.05$).

Table 3. Dosimetric comparison of OARs in manual and automatic VMAT (mean ± SD)

OARs	Index	Criteria	Pass rate (%)		Mean dese ± SD		P-value
			AP	MP	AP	MP	
Left lens	D_{max} (Gy)	< 8 Gy	100.00	100.00	4.76±1.24	4.80±1.04	0.768
Right lens	D_{max} (Gy)	< 8 Gy	100.00	100.00	5.33±2.19	5.01±1.17	0.911
Left optic nerves	D_{max} (Gy)	< 54 Gy	86.36	81.82	38.28±16.76	40.18±15.95	0.016
Right optic nerves	D_{max} (Gy)	< 54 Gy	81.82	77.27	41.45±16.74	43.88±17.37	0.003
Optic chiasm	D_{max} (Gy)	< 54 Gy	81.82	72.73	46.92±15.08	48.15±13.28	0.040
Brain stem	D_{max} (Gy)	< 54 Gy	54.55	45.45	52.98±7.76	53.96±6.55	0.046
Brain stem	V_{50} (%)	< 5 %	72.73	63.64	7.94±7.67	9.26±8.05	0.009
Spinal cord	D_{max} (Gy)	< 45 Gy	100.00	100.00	40.68±1.52	39.65±0.97	0.003
Parotid left	D_{mean} (Gy)	< 30 Gy	22.73	0.00	34.01±6.13	34.56±5.33	0.181
	V_{30} (%)	< 50 %	81.82	81.82	46.13±15.51	47.74±13.17	0.149
Parotid right	D_{mean} (Gy)	< 30 Gy	18.18	4.55	35.18±5.49	35.36±4.10	0.205
	V_{30} (%)	< 50 %	50.00	54.55	49.76±14.28	49.60±9.35	0.394
TM joint	D_{2cc} (Gy)	< 70 Gy	50.00	50.00	60.12±10.57	61.13±9.51	0.108
Mandible	D_{2cc} (Gy)	< 70 Gy	95.45	95.45	58.11±7.54	59.15±6.72	0.006
Temporal lobes	D_{2cc} (Gy)	< 60 Gy	77.27	77.27	60.11±6.51	60.27±6.69	0.455
Oral cavity	D_{mean} (Gy)	< 45 Gy	100.00	95.45	32.96±4.88	34.49±6.39	0.013
Thyroid	V_{40} (Gy)	< 80%	72.73	68.18	64.11±26.34	65.69±23.34	0.274

3.C MU and planning time comparison

The average MU was 643.59±45.42 in APs and 672.12±51.82 in MPs respectively. The APs reduced the average MU by 4.2% ($P<0.05$).

The overeall planning time of APs, including the manual operation time and computer processing time, were statistically reduced by 26.3%, from 144mins to 106mins ($P<0.05$).

3.D Stratified analysis by the overall stage

The locally advanced NPC patients were divided into two groups, accoradiing to the overall stage. Then the differences in selected dosimetric characteristics between APs and MPs for the targets and OARs were calculated separately for the two groups, as shown in Table 4. It seems that the dose difference for the targets was indepentent of overall stage as the values were quite similar and without statistically difference (not lsited in Table 4).

Table 4. Differences in dosimetric parameters between manual and automatic VMAT for the OARs stratified by overall stage (mean ± SD)

OARs	Index	Stage 3		Stage 4	
		△	p-value	△	p-value
Left lens	D_{max} (Gy)	-0.04±0.74	0.929	0.10±0.85	0.646
Right lens	D_{max} (Gy)	0.34±0.69	0.155	-0.97±1.56	0.139
Left optic nerves	D_{max} (Gy)	2.02±6.92	0.091	1.79±7.21	0.093
Right optic nerves	D_{max} (Gy)	1.39±4.78	0.062	1.48±3.39	0.017
Optic chiasm	D_{max} (Gy)	1.69±3.27	0.033	0.78±4.87	0.541
Brain stem	D_{max} (Gy)	1.17±2.41	0.110	0.79±2.23	0.285
Brain stem	V_{50} (%)	2.20±2.13	0.024	0.44±1.77	0.005
Spinal cord	D_{max} (Gy)	-1.46±1.83	0.028	-0.59±1.00	0.043
Parotid left	D_{mean} (Gy)	0.46±1.92	0.248	0.64±2.02	0.169
	V_{30} (%)	1.28±5.25	0.424	1.95±5.63	0.333
Parotid right	D_{mean} (Gy)	-0.37±3.97	0.657	0.74±1.78	0.139
	V_{30} (%)	-2.09±12.26	0.929	1.78±4.64	0.241
TM joint	D_{2cc} (Gy)	0.96±2.35	0.220	1.05±2.64	0.333
Mandible	D_{2cc} (Gy)	1.41±1.90	0.050	0.67±0.94	0.074
Temporal lobes	D_{2cc} (Gy)	0.21±1.29	0.534	0.11±1.12	0.646
Oral cavity	D_{mean} (Gy)	0.67±2.56	0.285	2.39±3.08	0.013
Thyroid	V_{40} (Gy)	4.93±8.12	0.050	-1.77±6.54	0.386

In both groups, APs might provide superior dose sparing for most OARs than MPs, except for spinal cord. The improvement tended to be greater for optic chiasm and brain stem in Stage III, and for parotid grands in Stage IV, although most of them were without significant difference. Notablely, V_{50} of brain stem in APs reduced more evidently for stage III (2.2% vs 0.4%, $P<0.05$). On the contrary, V_{30} and D_{mean} of parotid grands reduced more evidently for stage IV, without significant difference. Nevertheless, the max dose of spinal cord was lower in MPs for both groups, and the difference was greater in stage III (both $P<0.05$).

4. Discussion

As the previous researches indicated, there are quite a number of clinical IMRT plans could be futher optimized and improved, espically for those designed by novice physicists.[24] Recently, automatic IMRT planning was developed fastly and possible to improve the plan quailty and effiency. For example, the Auto-Planning module in the Pinnacle TPS would attempt to adjust optimization parameters and generate an acceptable plan automatically, based on an optimization algorithm[14]. In this study, we validated the feasibility and efficiency of Auto-Planning module in the VAMT planning for locally advanced NPC.

For both APs and MPs, the dose criteria of targets and OARs were not fully met because some of the OARs were close to or even partial overlapped with the targets. In general, the targets dose coverage of APs was similar to that of MPs. It was notable that the dose uniformity for GTV-T-P was superior in the MPs. APs provided better brainstem sparing and it might cause more of hot-dose regions in GTV-T-P. The pass rates for targets were similar, with APs equal to or slightly higher than MPs.

For most of the OARs, the dosimetric parameters of APs were superior to that of MPs, while the pass rates were usually higher than or equal to MPs, as also concluded by Yang et al[25] and Wang et al[26]. APs could automatically generate a number of auxiliary structures for the dose limiting, which was difficult to accomplish manually. However, the average D_{max} of spinal cord for MPs was 1.03Gy lower than that of APs ($P < 0.05$). For particular organs such as the spinal cord, the physicalist was paticulary concerned and would spend more time on its dose limiting. Then a better balance between the particular OAR and targets might be reached by repeatedly adjusting the related parameter settings.[14]

For locally advanced NPC, dose differences for most OARs were similar between the two types of plans and independent of stage. However, the APs provided better brain stem sparing in patients with stage III. As shown in Fig. 1.A and 1.B, there might be enough gaps for dose fall-off around brain stem in patients with stage III, due to relatively small volume of GTV-T-P and a lagerer anatomic distance between the brainstem and targets. Zhang et al have reported that automatic plan would be more conducive to sparing the brain-stem if the anatomic distance between targets and the pons was greater than 5mm.[27] In addition, the parotid glands sparing in patients with stage IV seemed to be superior for the automatic plan. However, when focus on paticular patients with stage IV, the parotid glands were easy to be overprotected in the APs, at the cost of dose coverage for GTV-NL-P and GTV-NR-P. It was known that the parotid glands were overlaped with the target to varying degrees, especially serious in Stage IV. The dose distubiton for a stage IV patient was showed in Fig. 1.C and 1.D. The parotid glands were clearly better protected in the AP, but there was a significant underdose in the overlapping region between targets and parotid glands. Nevertheless, in this case, the automatic plan could still not meet the dose criteria for parotid glands, which was usually not acceptable by the clinicist. In general, the balance between parotid glands and target dose was quite difficult for the Auto-Planning program, especially in S4 patients. In our study, when specific dose distrubiton and dosimetric parametres were considered, the plan quality of APs was superior or equal to MPs in most cases, and inferior to MPs in several patients with stage IV.

Overall, the design of a conventional VMAT radiotherapy for locally advanced NPC could benefit from the automatic planning. In most cases, automatic plan can achieve a similar or better plan quality. However, in several stage IV patients, automatic planning may over-protect particular OARs such as the parotid glands. It might be related to the template parametre setting and need more attention by the physicist. In addition, automatic planning could improve the planning efficiency. The overall planning time was decreased by 26% in the automatic planning, consistent with previous studies.[21,28] In fact, the increasement of planning efficiency was even much greater. Because the physicist can continue to work on other patients or tasks while the automatic planning is going on. As a disadvantage of this study, the template parametres setting was lack of individuality and almost unanimously among these patients. As we known, the dose distrubiton was closely related to the individual anatomy. During recent years, artificial intelligence-based automatic planning has also been developing rapidly and they usually could take the individual anatomy into account.[29–32] Bai et al has developed a neural network-based IMRT treatment planning technique for locally advanced NPC.[32] Then automatic IMRT plan could be generated based on the individual's anatomy, with comparable dosimetric qualities to manual plan.[32] However, these automatic plannings were usually difficult to integrate into commercial TPS and required high quality database or computer skills for the physicist. Conversely, the Auto-Planning module was more convenient and simple in the pratical work.

5. Conclusion

For locally advanced NPC, Auto-Planning module could generate VMAT plans with similar or superior plan quality comparing to manual VMAT plans in most cases. However, manual plans could be preferred choices in paticular patients with stage IV, due to a better balance between the OARs and targets. In general, automatic VMAT could greatly improve the physicist's efficiency and might be another option for the implementation of locally advanced NPC VMAT treatment planning after careful confirmation.

Declarations

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Author contributions

P.B. and X.Z. participated in the design of the study. J.C. and Y.C performed the experiments. K.C. and Y. D assisted statistical analysis. J.C. drafted and wrote the manuscript. All authors read and approved the final manuscript.

Competing interests

No conflicts of interest.

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Figures

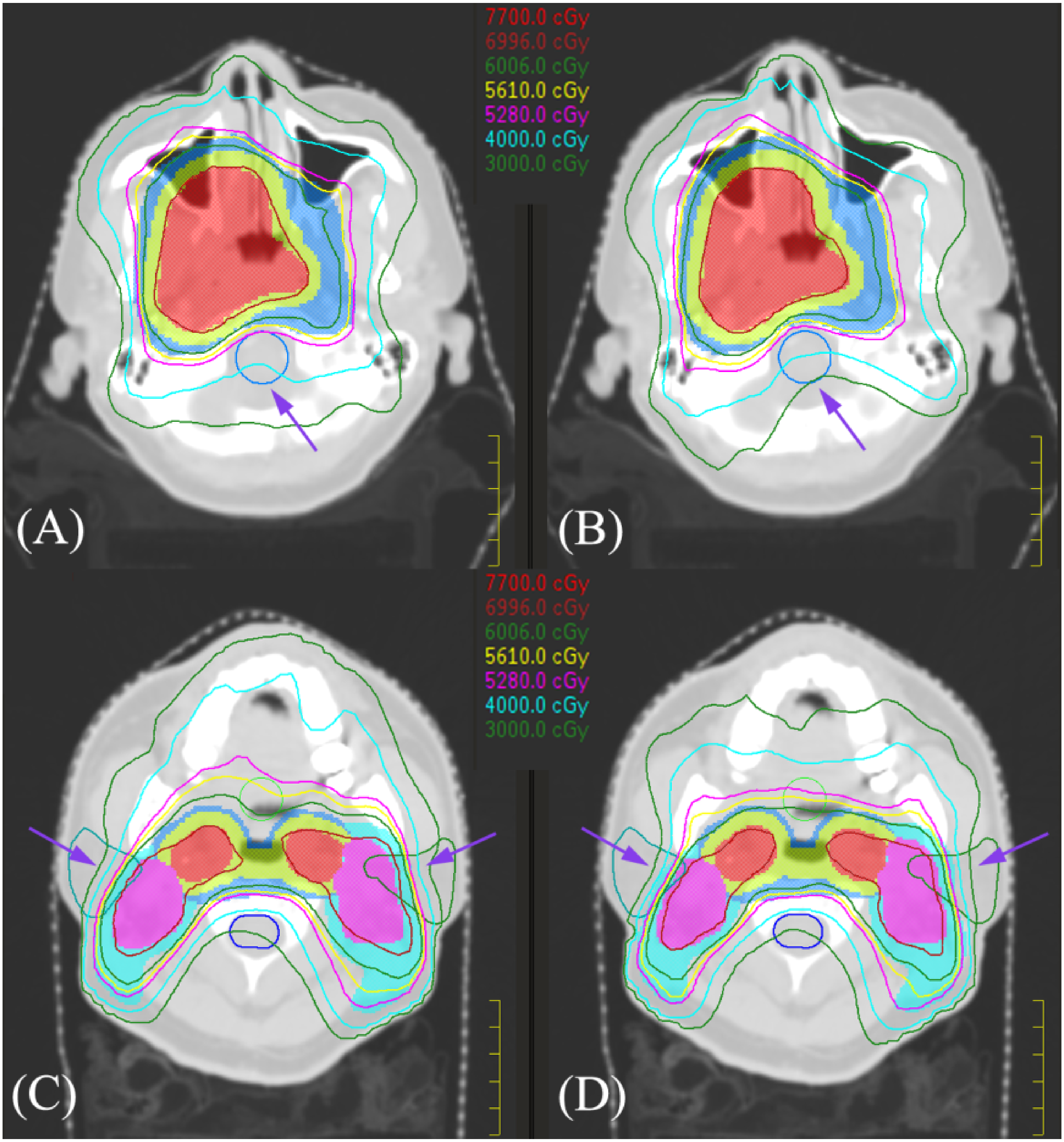

Figure 1

The dose distributions for two representative NPC patients were displayed. (A): manual plan, (B): automatic plan for a patient with stage III (T3N2M0); (C): manual plan, (D): automatic plan for a patient with stage IV (T4N3M0).