# Journal of Radiotherapy in Practice

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## **Case Study**

Cite this article: Yuen AH, Li AK, and Mak PC. (2022) Lower neck organs at risk sparing in nasopharyngeal carcinoma using hybrid volumetric-modulated arc therapy (hybrid-VMAT): a case report. *Journal of Radiotherapy in Practice* 21: 434–445. doi: 10.1017/S1460396920001156

Received: 30 October 2020 Revised: 26 November 2020 Accepted: 27 November 2020 First published online: 23 April 2021

#### **Kev words:**

Hybrid technique; lower neck organs at risk; nasopharyngeal carcinoma; volumetricmodulated arc therapy

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# Lower neck organs at risk sparing in nasopharyngeal carcinoma using hybrid volumetric-modulated arc therapy (hybrid-VMAT): a case report

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#### Abstract

Introduction: Nasopharyngeal carcinoma (NPC) is a prevalent disease in Southern China. Radiation therapy remains the primary treatment modality for NPC due to its high radiation sensitivity. Conventional volumetric-modulated arc therapy (VMAT) can achieve excellent target volume coverage and superior conformal dose distributions while sparing organs at risk (OARs). However, VMAT may also produce substantial volume of low-dose region in the surrounding normal tissue. Our oncology centre has incorporated the concept of anterior cervical field with VMAT in clinical practice of NPC treatment planning. The purpose of this treatment-comparison case study is to demonstrate the lower neck OARs sparing ability of hybrid volumetric-modulated arc therapy (hybrid-VMAT) over conventional VMAT for NPC. Methods: Four patients diagnosed with NPC of different clinical lymph node staging (N staging) were enrolled for this treatment-comparison case study. Planning target volumes and OARs were delineated with reference to Radiation Therapy Oncology Group (RTOG) 0225/0615. Additional OARs from lower neck region, including thyroid, trachea, cervical spine and pharyngeal constrictor muscles (PCMs), were also delineated. Two treatment techniques, hybrid-VMAT and VMAT, were created for each patient's dataset.

Results and findings: Both treatment techniques produced adequate target coverage and reduced radiation dose to the OARs as suggested in RTOG 0225/0615. Hybrid-VMAT plans achieved superior dose reduction in larynx, oesophagus, middle PCM, inferior PCM, cervical spine and trachea comparing with VMAT plans. Hence, the clinical usability and functional outcome of hybrid-VMAT should be further investigated for NPC radiation therapy.

### Introduction

Nasopharyngeal carcinoma (NPC) is characterised by its unique geographic distribution. Southern China has one of the highest incidence rates of NPC in the world. Radiation therapy remains the primary treatment modality for NPC due to its high radiation sensitivity. Radiation Therapy Oncology Group (RTOG) 0225 and 0615 have recommended detailed dose criteria for NPC using intensity-modulated radiation therapy (IMRT) (Table 1). These trials have resulted in excellent loco-regional control and encouragingly low rates of grade 3–4 acute toxicities. <sup>1,2</sup>

Volumetric-modulated arc therapy (VMAT) has gained extensive clinical interest in the field of radiation oncology over the years. It can achieve excellent target volume coverage and superior conformal dose distributions while sparing organs at risk (OARs) through simultaneous variation of gantry rotation speed, treatment aperture shape and dose rate during NPC treatment delivery compared to IMRT.<sup>3,4</sup> However, VMAT may also produce substantial volume of low-dose region in the surrounding normal tissue.<sup>5,6</sup> Since treatment fields of radiation therapy for NPC traditionally encompass the primary disease and involve cervical lymph nodes, as well as the entire draining lymphatic regions to the lower neck, wide distribution of low-dose region to the lower neck OARs (such as larynx, thyroid, cervical spine, pharyngeal constrictor muscles (PCMs), trachea and oesophagus) can be harmful to the patient. Although RTOG 0225/0615 protocol does not provide dosimetric criteria for all of these OARs, radiation-induced toxicity to these structures during radiation therapy has been described in previous publications with negative impact on patients' quality of life.<sup>7-9</sup> Therefore, radiation dose to the lower neck OARs should not be overlooked and should also be considered during radiation therapy planning of NPC. In order to reduce low-dose volume to the lower neck region, our oncology centre has incorporated the concept of anterior cervical field with VMAT in clinical practice of NPC treatment planning.

The purpose of this treatment-comparison case study is to demonstrate the lower neck OARs sparing ability of hybrid volumetric-modulated arc therapy (hybrid-VMAT) over conventional VMAT for NPC.



Table 1. Dose criteria of RTOG 0225/0615 protocol

	Second criteria First criteria: ideal acceptable		
Critical OARs			
Brain stem	D <sub>max</sub> < 54 Gy	1 % volume < 60 Gy	
Optic nerves	D <sub>max</sub> < 54 Gy	1 % volume < 60 Gy	
Optic chiasm	D <sub>max</sub> < 54 Gy	1 % volume < 60 Gy	
Spinal cord	$D_{max}$ < 45 Gy	1 cc volume < 50 Gy	
Temporal lobes	D <sub>max</sub> < 60 Gy	1 % volume < 65 Gy	
Mandible and temporomandibular joint	D <sub>max</sub> < 70 Gy	1 cc volume < 75 Gy	
Brachial Plexus	D <sub>max</sub> < 66 Gy		
Intermediate-risk OARs			
Parotid gland	D <sub>mean</sub> < 26 Gy (at least one gland)	20 cc of both parotid glands < 20 Gy/50% volume < 30 Gy (at least one gland)	
Oral cavity	D <sub>mean</sub> < 40 Gy		
Eyes	D <sub>mean</sub> < 35 Gy	D <sub>max</sub> < 50 Gy	
Lens	D <sub>max</sub> < 25 Gy		
Cochleae	D <sub>mean</sub> < 50 Gy		
Glottic larynx	D <sub>mean</sub> < 45 Gy		
Oesophagus	D <sub>mean</sub> < 45 Gy		
Unspecified OARs	< 5 % volume ≥ 70 Gy	< 1 %/1 cc volume≥ 77 Gy	

Abbreviations: RTOG, Radiation Therapy Oncology Group; OARs, organs at risk;  $D_{max}$ , maximum dose;  $D_{mean}$ , mean dose.

## **Case Description**

# Patient selection and simulation

Four patients diagnosed with NPC of different clinical lymph node staging (N staging) were enrolled for this treatment-comparison case study. Patient demographic, clinical features and treatment prescription were summarised in Table 2. The dose-fractionation scheme was individualised to each patient based on clinical judgement of the attended oncologists in accordance with RTOG 0225/0615 (Table 2).

All patients were simulated in the supine position. TIMO Head & Neck Support Cushions (Med-Tec, Orange City, IA) and thermoplastic mask (Klarity Medical & Equipment Co. Ltd, Guangzhou, China) were used for immobilisation. The computed tomography (CT) simulation images (native, 120 kV, 80 mA, slice thickness 3 mm, in-plane resolution 1 mm) were acquired using dual-source CT scanner (SOMATOM Definition, Siemens Healthcare, Forchheim, Germany). CT simulation images were electronically transferred to the Eclipse™ (Varian Medical System, Palo Alto, CA) version 15.5 treatment planning system for treatment planning.

### Targets and OARs delineation

The delineated targets included the gross tumour volume (GTV), clinical target volume (CTV) and planning target volume (PTV).

**Table 2.** Patient demographic, clinical features (AJCC cancer staging 8th edition) and treatment prescription

	Patient 1	Patient 2	Patient 3	Patient 4
Sex	Female	Male	Male	Female
Age	52	34	62	62
Clinical stage	T1 N0 M0	T2 N1 M0	T2 N2 M0	T4 N3 M0
AJCC prognostic stage groups	Stage I	Stage II	Stage III	Stage IV
Dose prescription				
PTV of gross tumour (PTV <sub>GT</sub> )	70 Gy/33 Frs	70 Gy/33 Frs	70 Gy/35 Frs	70 Gy/ 33Frs
PTV of lymph node (PTV <sub>NL</sub> )	/	66 Gy/33 Frs	70 Gy/35 Frs	70 Gy/ 33Frs
PTV of subclinical region (PTV <sub>SC</sub> )	60 Gy/33 Frs	60 Gy/33 Frs	60 Gy/35 Frs	63 Gy/ 33Frs
PTV of clinically negative neck region (PTV <sub>neg</sub> )	54 Gy/33 Frs	54 Gy/33 Frs	54 Gy/35 Frs	54 Gy/ 33Frs

Abbreviations: PTV, planning target volume.

The GTV covered the visible primary tumour and neck nodes of NPC shown on the image studies. The CTV encompassed the GTV with a  $1.5\,\mathrm{cm}$  margin, the subclinical region and the prophylactic area of neck. The PTV included the CTV with 5-mm extensions in all dimensions to account for patient set-up error and motion uncertainties, except for situations where the GTV or the CTV is adjacent to the brain stem, where the margin can be as small as 1 mm.

The OARs concerned including seven serial-type organs (serial OARs): brain stem, spinal cord, lenses, eyes, optic nerves, chiasm and mandible; and eight parallel-type organs (parallel OARs), for example, parotids, larynx, oesophagus, thyroid, trachea, cervical spine, PCMs and oral cavity.

### Treatment planning

A total of eight treatment plans (four VMAT plans and four hybrid-VMAT plans) were optimised using Eclipse™ (Varian Medical System, Palo Alto, CA) version 15.5 treatment planning system. All plans were scheduled on a Varian TrueBeam™ linear accelerator with a millennium 120-leaf multi-leaf collimator (MLC) (Varian Medical Systems, Palo Alto, CA). Jaw tracking was enabled. The Photon Optimizer (PO, ver.15.5.11, Varian Medical Systems) was used for treatment plans optimisation. For dose calculation, the anisotropic analytic algorithm (AAA, ver.15.5.11, Varian Medical Systems) was used with a dose calculation grid of 1 mm.

## Volumetric-modulated arc therapy (VMAT)

Considering that the shape of NPC target volume is highly irregular based on the unique anatomy of the patient and the extensiveness of disease, the fields arrangement and gantry rotation of VMAT were individualised for each patient through the beam's eye view option available on the treatment planning system. The arc fields were positioned to adequately cover all target volumes. Optimisation constraints and priorities were added to reduce radiation dose to the OARs. The isocentre was placed at the central of all PTVs. The arc fields were scheduled using 6-MV photon beams with maximum dose rate of 600 MU/min (Figures 1–4).

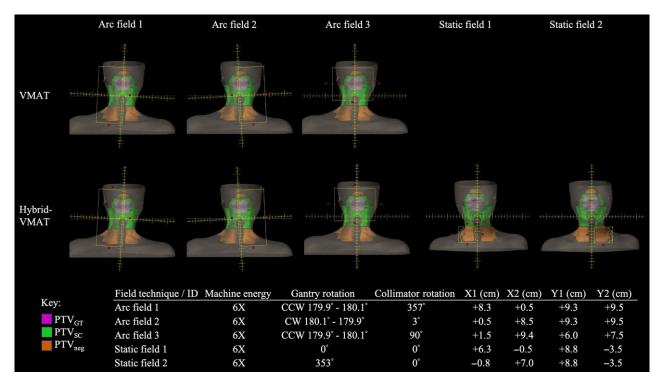


Figure 1. Beam arrangements of VMAT and hybrid-VMAT plans for patient 1.

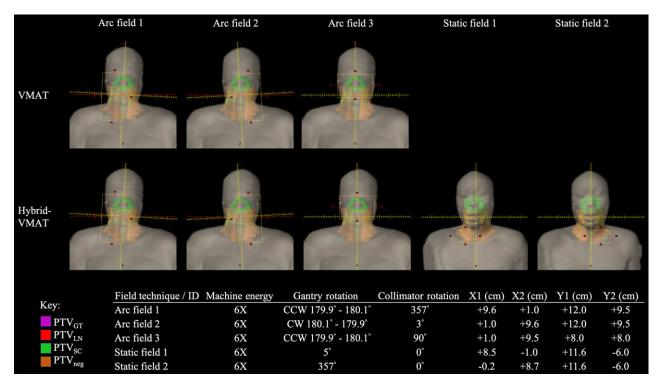


Figure 2. Beam arrangements of VMAT and hybrid-VMAT plans for patient 2.

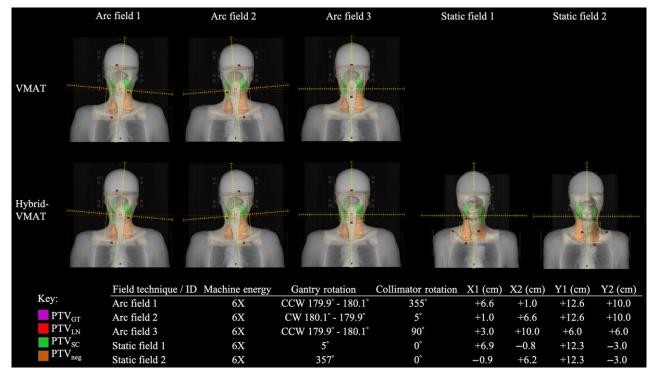


Figure 3. Beam arrangements of VMAT and hybrid-VMAT plans for patient 3.

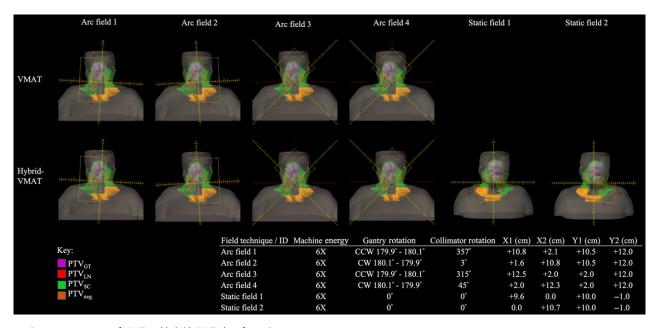


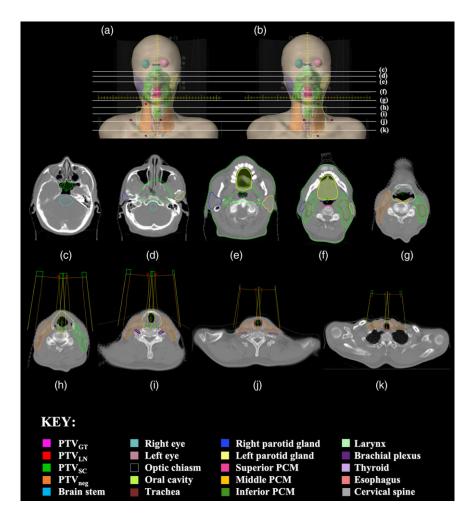
Figure 4. Beam arrangements of VMAT and hybrid-VMAT plans for patient 4.

## Hybrid-volumetric-modulated arc therapy (Hybrid-VMAT)

Hybrid-VMAT plans concurrently combined arc fields and anterior static fields. The beam arrangements of the arc fields were identical to the VMAT plan of each patient. The arc fields were also scheduled using 6-MV photon beams with maximum dose rate of 600 MU/min.

Two additional 3D anterior static fields were added to the lower neck. The 3D static fields were scheduled using 6-MV photon beams with maximum dose rate of 600 MU/min. In static field 1 and 2, X2 and X1 collimator jaws were reduced respectively so that vast majority of the centrally located lower neck OARs were shield, while part of the  $\rm PTV_{SC}$  and  $\rm PTV_{neg}$  was covered. MLCs

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**Figure 5.** (a) & (b) Beam eye views of static field 1 and 2 in patient 3. Lines corresponding to (c)–(k) were superimposed on (a)–(b), showing the delineated target volumes and OARs in these levels.

were used to further minimise the irradiated lower neck OARs volume [Figure 5 (a) & (b)]. The isocentre was placed at the same location as the VMAT plans. Dose splitting between 3D anterior static fields (range from approximately 40 to 50% of the prescribed dose to  $\rm PTV_{neg}$ ) and arc fields (range from approximately 50 to 60% of the prescribed dose to  $\rm PTV_{neg}$ ) were determined by that provided the most optimal combination to maximise the tumour dose and minimise the lower neck OARs dose. The beam weights of the static fields for patient 1–4 were set to deliver 40%, 50%, 45% and 50% of the prescribed dose to the PTV  $_{\rm neg}$ , respectively, by certified medical dosimetrist (Figures 1–4).

The contouring of target volumes and OARs used in the present study were demonstrated in Figure 5. The same contoured structures and margins were used to optimise both treatment plans. To avoid introducing bias, optimisation objectives of major structures were standardised between techniques of each patient.

## **Plan analysis**

In the present case study, a total of eight treatment plans (four VMAT and four hybrid-VMAT) were created for four patients with different clinical N staging. The main goal for treatment planning optimisation was to reduce radiation dose to the OARs (OARs as suggested in RTOG 0225/0615 and additional lower neck OARs

in the present study) while distributing adequate prescribed dose to the target volumes. The dosimetric parameters of all patients using hybrid-VMAT and VMAT were presented in Table 3.

#### Patient 1

Patient 1 had no evidence of cervical lymph node involvement. Due to the less complexity of the target volume, two and a half arc fields were used in VMAT planning. Two static fields were added on VMAT to form the hybrid-VMAT. Both hybrid-VMAT and VMAT plans for patient 1 delivered adequate dose to the target volume. This patient presented a challenge for dose reduction during optimisation in neck OARs due to proximity of PTV<sub>neg</sub> in both sides. Comparing hybrid-VMAT with VMAT, there were resulting mean doses reduction of 5·4%, 15%, 1·4%, 11·9%, 5·8% and 17·9% to larynx, oesophagus, middle PCM, inferior PCM, cervical spine and trachea, respectively. The plan comparison and dose—volume histogram (DVH) analysis of the two treatment techniques were shown in Figures 6 and 7, respectively.

## Patient 2

In patient 2, both treatment techniques have delivered adequate dose to the target volume. Using hybrid-VMAT, dose reduction in OARs as suggested by RTOG 0225/0615 was comparable to

Table 3. Dosimetric parameters comparison of the OARs for VMAT and hybrid-VMAT plans

OARs		Pati	Patient 1		Patient 2		Patient 3		Patient 4	
	Parameters	VMAT	Hybrid- VMAT	VMAT	Hybrid- VMAT	VMAT	Hybrid- VMAT	VMAT	Hybrid- VMAT	
Brain stem*	D <sub>max</sub> (cGy)	5241-3	5182-1	4224-5	4104-0	3977-4	4328-5	6002-2	5952.7	
Spinal cord*	D <sub>max</sub> (cGy)	4429-5	4472-5	2803-6	1562-5	3003-6	2519-4	3946-7	3925-5	
Left optic nerve*	D <sub>max</sub> (cGy)	5235-6	5064-0	2227-0	2171-6	596-9	558-4	5595-3	5539.7	
Right optic nerve*	D <sub>max</sub> (cGy)	5228-7	5207-8	4068-6	4154-7	871-4	660-9	5317-0	5362-4	
Optic chiasm*	D <sub>max</sub> (cGy)	4595-0	4428-9	1061-7	1165-8	592-4	553-3	5542-1	5481.3	
Mandible and temporomandibular joint*	D <sub>max</sub> (cGy)	6416-5	6398-9	7108-6	7186-7	6506-2	6421-1	7529-3	7497-9	
	D <sub>mean</sub> (cGy)	3878-3	3882-1	3584-2	3583-3	3635-8	3629-7	4683-4	4599-2	
Brachial plexus*	D <sub>max</sub> (cGy)	5759-2	5651-1	5762-0	5635-4	5710-6	5781.7	6982-7	7026-7	
Left parotid gland*	D <sub>mean</sub> (cGy)	3056-2	3057-8	2592-0	2592-9	2556-9	2559-7	3759-0	3805-4	
Right parotid gland*	D <sub>mean</sub> (cGy)	2718-8	2740-2	2522-2	2518-3	2083-8	2101-3	3541.4	3598-6	
Oral cavity*	D <sub>mean</sub> (cGy)	3544-2	3513-2	2895-0	2971-2	2804-6	2805-3	4453.7	4484-8	
Left cochlea*	D <sub>max</sub> (cGy)	5286-6	5280-3	4464-1	4554-6	4205-2	4209-5	7012-3	7151-4	
Right cochlea*	D <sub>max</sub> (cGy)	5196-3	5373.6	5738-1	5628-6	3678-7	3879-3	5236-1	5319-2	
Left eye*	D <sub>max</sub> (cGy)	1790-4	1956-0	2100-5	2196-3	710-6	562-0	5269-6	5382.5	
	D <sub>mean</sub> (cGy)	522-0	529-1	402-9	410-6	221.5	194-7	2213-5	2236-6	
Right eye*	D <sub>max</sub> (cGy)	2188-4	2108-8	2102-7	2085-7	1118-7	717-4	3400-1	3534-5	
	D <sub>mean</sub> (cGy)	660-1	695-0	516-9	512-1	271.3	210-8	1181-4	1265-7	
Left lens*	D <sub>max</sub> (cGy)	489-7	512-0	496-1	504-2	277-4	250-1	1092-0	1248-6	
Right lens*	D <sub>max</sub> (cGy)	445-1	513.7	512.8	541.3	339-2	262-3	777-1	836-2	
Larynx*	D <sub>mean</sub> (cGy)	5010-9	4738-4	3851.1	3352-9	3881.8	2464-6	5566-8	4483-2	
Oesophagus*	D <sub>mean</sub> (cGy)	2340-3	1988-3	2135-8	1798-5	3096-6	1814-0	3749-2	3302.7	
Thyroid^	D <sub>mean</sub> (cGy)	5311-3	5241-4	5494-9	5320-8	5365-1	5105-8	5575-3	5237-1	
Superior PCM^	D <sub>mean</sub> (cGy)	6902-5	6884-8	5041.5	5077-4	4049-5	3964-1	7272-4	7247-7	
Middle PCM^	D <sub>mean</sub> (cGy)	5248-3	5172-3	3854-2	3598-2	3995-1	2112-1	5343-3	4694-6	
Inferior PCM^	D <sub>mean</sub> (cGy)	4863-5	4284-2	3713-9	2608-5	3444-2	2128-4	5101-0	3584-9	
Cervical spine^	D <sub>mean</sub> (cGy)	3313-8	3120.6	3103.7	2805.3	3039-9	2593-1	4280-1	4096-9	
Trachea^	D <sub>mean</sub> (cGy)	2452-2	2012-6	4426-1	1795-5	3844-1	2246-8	3604-5	3192-3	

Abbreviations: OARs, organs at risk; VMAT, volumetric-modulated arc therapy; D<sub>max</sub>, maximum dose; D<sub>mean</sub>, mean dose; PCM, pharyngeal constrictor muscles. \* RTOG protocol 0225/0615; ^ additional lower neck OARs.

VMAT plans. Comparing hybrid-VMAT with VMAT, there were resulting mean doses reduction of 12.9%, 15.8%, 6.6%, 29.8%, 9.6% and 59.4% to larynx, oesophagus, middle PCM, inferior PCM, cervical spine and trachea, respectively. The plan comparison and DVH analysis of the two treatment techniques were shown in Figures 8 and 9, respectively.

#### Patient 3

Due to more separation distance between the PTV $_{\rm neg}$  in lower neck, dose reduction of lower neck OARs in this patient was less challenging. In this patient, the resulting mean doses reduction of larynx, oesophagus, middle PCM, inferior PCM, cervical spine and trachea were 36·5%, 41·4%, 47%, 38·2%, 14·7% and 41·6%, respectively. The plan comparison and DVH analysis of the two treatment techniques were shown in Figures 10 and 11, respectively.

#### Patient 4

The treatment plans optimisation of patient 4 were technically demanding due to the enlarged and complex shape of the cervical lymph node. In order to deliver adequate dose coverage to the target volume, four full arcs were used in VMAT plans and arc fields of hybrid-VMAT. In this patient, the PTV did not follow an inverted U shape, instead, the caudal part of the PTV<sub>neg</sub> merged together and formed an O shape PTV. Therefore, the gantry angles of the static fields for hybrid-VMAT were set to 0° so that the static fields can fully cover the caudal part of the PTV. Comparing hybrid-VMAT with VMAT, there were resulting mean doses reduction of 19·5%, 11·9%, 12%, 29·7%, 4·2% and 11·4% to larynx, oesophagus, middle PCM, inferior PCM, cervical spine and trachea, respectively. The plan comparison and DVH analysis of the two treatment techniques were shown in Figures 12 and 13, respectively.

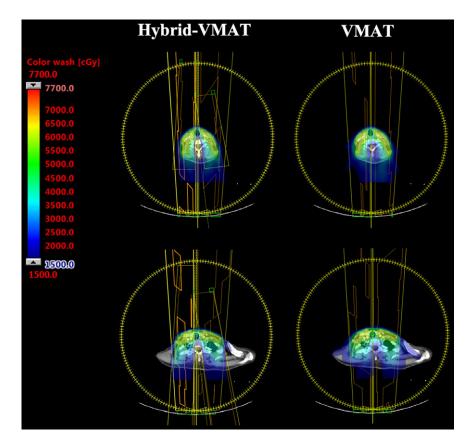
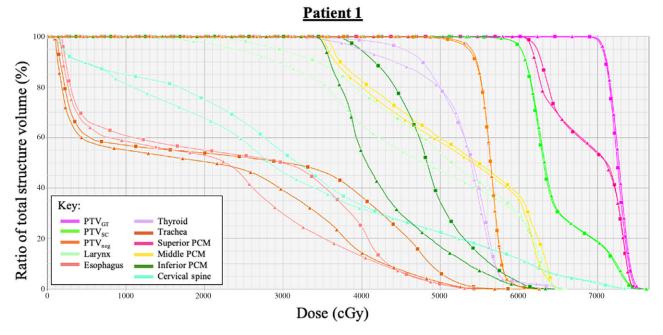


Figure 6. Plan comparison of VMAT and hybrid-VMAT for patient 1



**Figure 7.** Dose–volume histogram analysis of VMAT ( $\blacksquare$ ) and hybrid-VMAT ( $\triangle$ ) for patient 1.

#### **Discussion**

The treatment plans have been evaluated based on the dose criteria of RTOG 0225/0615 and the mean dose to the lower neck OARs. The results of the present study have shown that hybrid-VMAT plans are comparable to VMAT plans in terms of target coverage and doses received by OARs as suggested in RTOG 0225/0615.

In the present study, hybrid-VMAT plans have demonstrated a consistent pattern of dose reduction in mean dose of larynx, oesophagus, middle and inferior PCM, cervical spine and trachea. In hybrid-VMAT plans, with approximately 40%–50% of the prescribed dose to the clinically negative neck region delivered through the 3D anterior static fields, vast majority of these centrally

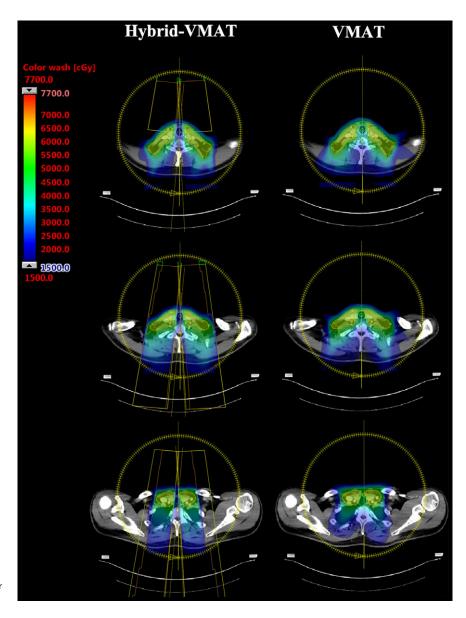


Figure 8. Plan comparison of VMAT and hybrid-VMAT for patient 2.

located lower neck OARs are shielded by the MLC and X jaw, therefore, reducing the integral doses to these OARs. Meanwhile, the remainder of the prescribed dose is delivered through arc fields to maintain a highly conformal plan. Reduction of radiation dose to lower neck OARs can be extremely important in NPC radiation therapy. Extensive previous publications have demonstrated that radiation-induced adverse effect in lower neck OARs after NPC radiation therapy can have devastating impact on patients' quality of life.<sup>7–9</sup> The results have indicated that hybrid-VMAT may be capable to reduce the incidence of acute and/or late toxicity of these organs, such as radiation-induced dysphagia, osteoradionecrosis of cervical spine and radiation-induced chondronecrosis.

Among the four patients in this treatment-comparison case study, patient 1 has demonstrated relatively less dose reduction in lower neck OARs. The underlying reason would be the less weighting (40%) of the static fields that has been used for patient 1. As the proportion of the arc fields weighting increased, wide distribution of low-dose volume was created within the lower neck

region, hence lowering the efficacy of dose reduction to the lower neck OARs in patient 1. Thus, it is recommended that an appropriate weighting of the static fields should be chosen to balance with the target coverage during treatment planning.

Theoretically, VMAT plans are also able to produce radiation dose distribution similar to hybrid-VMAT by modulating the gantry speed, MLC shape and dose rate, and generating a similar treatment delivery sequence (i.e., speed of gantry rotation and MLC slowed at the angles of the anterior cervical static fields, simulating the delivery of the static fields). However, the delivery sequence is solely determined by the optimiser of the treatment planning system during optimisation in accordance with the dose constraints given. In the present study, the treatment planning system has appeared to decline the aforementioned delivery sequence for VMAT plans due to its incapability. Therefore, VMAT plans have delivered radiation dose in simply arc sequence to fulfil the dosimetric requirements. The addition of avoidance sectors or avoidance regions of interest (ROIs) might be a possibility to reduce dose to the lower neck OARs in VMAT. However, invert treatment

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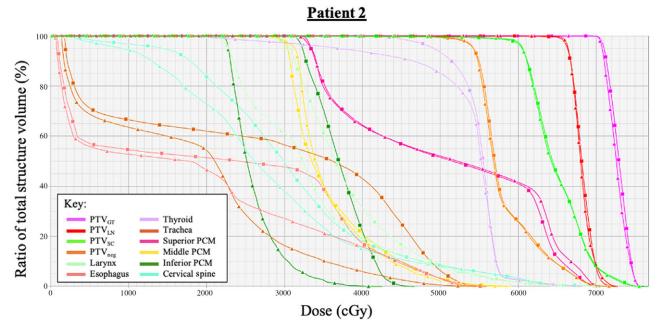
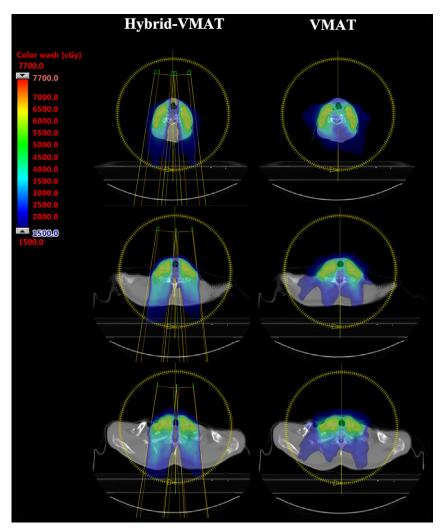


Figure 9. Dose–volume histogram analysis of VMAT ( $\blacksquare$ ) and hybrid-VMAT ( $\triangle$ ) for patient 2.



**Figure 10.** Plan comparison of VMAT and hybrid-VMAT for patient 3.

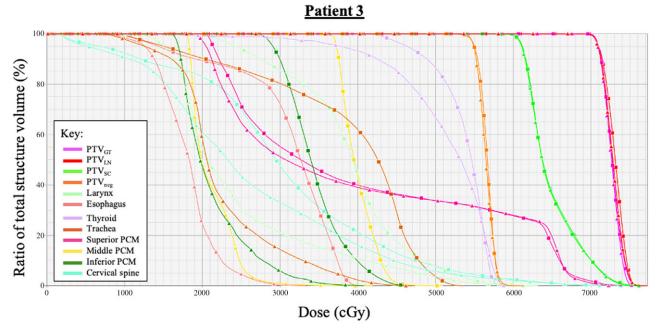


Figure 11. Dose-volume histogram analysis of VMAT ( $\blacksquare$ ) and hybrid-VMAT ( $\triangle$ ) for patient 3.

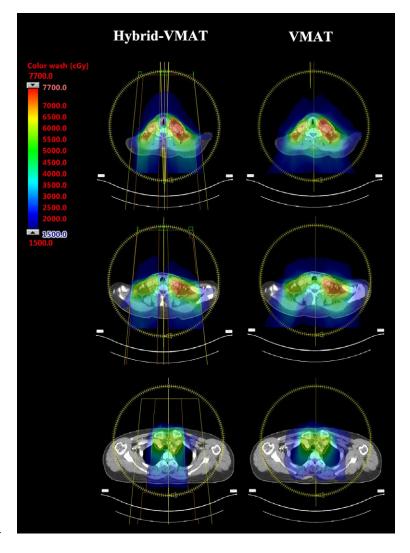


Figure 12. Plan comparison of VMAT and hybrid-VMAT for patient 4.

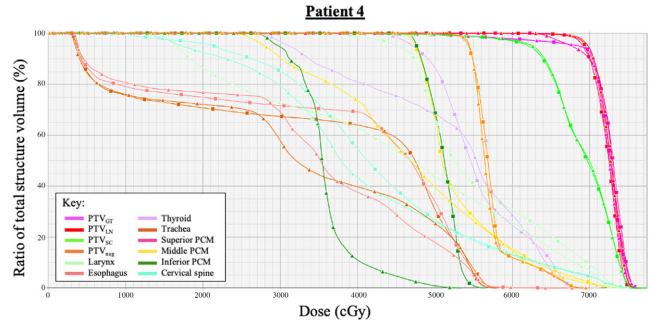


Figure 13. Dose-volume histogram analysis of VMAT (■) and hybrid-VMAT (▲) for patient 4.

planning is strongly user-dependent, <sup>10</sup> substantial experience in treatment planning may be needed to determine the most optimal angles or values for avoidance sectors/avoidance ROIs in order to achieve dose distribution similar as hybrid-VMAT. Therefore, manual beam selection in anterior fields of hybrid-VMAT may be a standard/easy alternative to dosimetrists with varying levels of planning experience to spare lower neck OARs.

The improved dose sparing in lower neck OARs using hybrid-VMAT is at the expense of increased treatment time. The increment in treatment delivery time is primarily attributable to the additional gantry travel time for the static fields. Nonetheless, it is foreseeable that more advanced optimisation system in future may be capable to achieve comparable plan quality with reduced treatment time.

#### Conclusion

Advancements in radiotherapy have enabled better care to be given to patients, thus improving their quality of life. Therefore, consideration of all OARs during treatment planning forms an integral part of the patient's holistic care. Purely from the dosimetric point of view, incorporation of static fields with VMAT planning has been associated with dose reduction in lower neck OARs without compromising plan quality, which is often a challenge to NPC radiation therapy since many of these OARs are in close proximity to the PTV. Hence, the clinical usability and functional outcome of hybrid-VMAT should be further investigated for NPC radiation therapy.

**Acknowledgements.** The authors would like to thank the editor and two anonymous reviewers for their constructive comments. The authors would also like to thank the Oncology Centre, St. Teresa's Hospital (HKSAR), for providing access to the treatment planning system and patient data. Sincere appreciation is also extended to Dr. Gordon Kwok Hung Au and Dr. Thomas Man Cheuk Ng for the comments on dosimetric planning.

**Ethics approval and consent to participate.** All procedures in this study were reviewed and approved by the Oncology Centre, St. Teresa's Hospital (HKSAR).

**Consent for publication.** Publication of this study was approved by the Oncology Centre, St. Teresa's Hospital (HKSAR).

Availability of data and materials. The data that support the findings of this study are available from the Oncology Centre, St. Teresa's Hospital (HKSAR), but restrictions apply to the availability of these data, which were used under permission for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of the Oncology Centre, St. Teresa's Hospital (HKSAR), at the following e-mail address: sthochk@gmail.com.

### **Competing interests.** None

**Funding.** This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

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