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TECHNICAL NOTE

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Hybrid split-arc partial-field volumetric modulated arc therapy: an improved beam arrangement for linear accelerator-based hippocampal-avoidance whole brain radiation therapy

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ABSTRACT

Background: This technical note aims to verify the hippocampus and adjacent organs at risk (OARs) sparing ability of an improved beam arrangement, namely hybrid split-arc partial-field volumetric modulated arc therapy (VMAT) (Hsapf-VMAT) during whole brain radiation therapy (WBRT).

Materials and methods: Computed tomography simulation images of 22 patients with brain metastases were retrieved in this retrospective planning study. The hippocampus was manually delineated according to the criterion of RTOG 0933. Plans delivering 30 Gy in 10 fractions were generated for each patient using split-arc partial-field VMAT (sapf-VMAT) and Hsapf-VMAT. The sapf-VMAT plans consisted of 4 arc fields of 179.9° each with reduced field size. The Hsapf-VMAT consisted of 4 arc fields similar to sapf-VMAT in addition to 2 lateral opposing static fields. Statistical comparisons between treatment plans of both techniques were performed using the paired t-test at 5% level significance.

Results: The results demonstrated that Hsapf-VMAT can achieve superior dose sparing in hippocampus which is comparable to sapf-VMAT ($p > 0.05$). In both eyes, Hsapf-VMAT had significantly lower D_{mean} and D_{max} compared to sapf-VMAT ($p < 0.005$). Decrease in D_{max} of both lenses using Hsapf-VMAT ($p < 0.005$) were statistically significant when compared to sapf-VMAT. Hsapf-VMAT demonstrated significant reduction of D_{mean} and D_{median} to the optic nerves ($p < 0.05$). Whole brain planning target volume (PTV) coverage was not compromised in both techniques.

Conclusion: The present study adopts a hybrid technique, namely Hsapf-VMAT, for hippocampal sparing WBRT. Hsapf-VMAT can achieve promising dose reduction to the hippocampus, both eyes and lenses. Therefore, Hsapf-VMAT can be considered an improved version of sapf-VMAT.

Key words: hippocampal sparing; static-field; partial-field; split-arc; volumetric modulated arc therapy; whole brain radiation therapy; neurocognitive deficit

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Introduction

Radiation Therapy Oncology Group (RTOG) 0933, a phase II clinical trial, studies the effectiveness of hippocampal sparing during whole brain radiation therapy (WBRT) and has demonstrated promising results in preserving memory function using the dose criteria in the protocol (Supplementary File — Tab. S1) [1]. Recently, our oncology centre has employed both split-arc and partial-field techniques together to eliminate scatter radiation and overcome multileaf collimator (MLC) limitations in WBRT volumetric modulated arc therapy (VMAT) planning [2]. This technique has shown to be more advantageous in sparing hippocampus compared with conventional dual-arc VMAT, while the target coverage has not been compromised.

However, owing to the relatively low total prescription dose (30 Gy in 10 fractions) of WBRT, potential radiation-induced toxicity to organs at risk (OARs), in addition to hippocampus, can be overlooked and underestimated. In fact, radiation-induced toxicity to the adjacent OARs, including the eyes and lenses, during WBRT have been described in previous publications with negative impact on patients' quality of life [3–6]. Previous publications have reported that radiation retinopathy can be induced with radiation dose as low as 18 Gy in patients with presence of comorbidities (such as compromised chorioretinal circulation) [7] or with exposure to radiation sensitizers (such as chemotherapy) [8]. In the meantime, radiation dose as low as 2 Gy may result in abnormalities of lens fibers, subsequently cataract [9]. Jeganathan et al. [10] have reported that there is a 66% risk of cataract progression if the lens receives radiation doses exceeding 6.5 Gy with a latency of 4 years. Therefore, radiation dose to the adjacent OARs, in addition to hippocampus, should also be considered and minimized during treatment planning of WBRT.

Using VMAT alone has been reported to produce a large volume of low dose region in the surrounding normal tissue [11–13]. In the meantime, the study of Wang et al. [14] has shown better eyes and lenses sparing using lateral opposing static fields. We, therefore, hypothesize that a hybrid technique, the combination of split-arc partial-field VMAT (sapf-VMAT) with lateral opposing static fields for hippocampal sparing WBRT may provide further improvement in OAR sparing while keeping enough dose coverage to the whole brain target volume.

This technical note has proposed an improved version of the split-arc partial-field VMAT (sapf-VMAT), namely hybrid split-arc partial-field VMAT (Hsapf-VMAT), for hippocampal sparing WBRT. The present study aims to compare the dosimetric parameters of Hsapf-VMAT with sapf-VMAT to verify its sparing ability to the hippocampus as well as to adjacent OARs during WBRT.

Materials and methods

Patient selection and computed tomography simulation

In the present retrospective planning study, 22 patients, who were previously treated with WBRT in 2012–2020, were randomly selected. During computed tomography (CT) simulation scan, patients were immobilized in a supine position on a dual-source CT scanner (SOMATOM Definition, Siemens Healthcare, Forchheim, Germany). Immobilization was achieved using Head & Neck Support Cushions and thermoplastic mask. The CT simulation images were transferred to the Eclipse™ (Varian Medical System, Palo Alto, CA) version 15.5 treatment planning system for WBRT planning.

Targets and OARs delineations

Six OARs were defined, including the eyes, lenses, optic nerves, optic chiasm, brainstem and hippocampus. To accurately identify the hippocampus as suggested by Gondi et al. [1], all patients underwent T1-weighted spoiled gradient-recalled echo magnetic resonance (MR) imaging, standard axial and fluid attenuation recovery (FLAIR) sequence and T2-weighted sequence. Automatic rigid registration was performed between CT simulation and MR images. Target and OARs delineations were made on CT simulation images based on co-registered T1-weighted cranial magnetic resonance images. To minimize inter-observer variability, the hippocampus was manually delineated by a radiation oncologist according to the criterion of RTOG 0933 (available at: http://www.rtog.org) (Supplementary File — Fig. S1).

The planning target volume (PTV) for optimization (whole brain PTV) was defined as the whole

brain volume subtracting the hippocampal planning risk volume. The hippocampal planning risk volume was generated by volumetrically isotropic 5mm expansion of hippocampus volume using the in-built expansion function of the planning system.

Dose prescription

The treatment prescription to the whole brain PTV was 30 Gy in 10 fractions. According to RTOG 0933, the minimum dose ($D_{100\%}$) and maximum dose (D_{max}) to the hippocampus were limited to 9 Gy and 17 Gy, respectively. The D_{max} to the optic chiasm and optic nerves were limited to 37.5 Gy.

Treatment planning

Treatment plans were scheduled using Varian TrueBeam™ (Varian Medical Systems, Palo Alto, CA), Millennium 120-leaf MLC, jaw tracking, and 6-MV photon beams with a maximum dose rate of 600 MU/min. All treatment plans were normalized such that at least 97% of the whole brain PTV received 95% of the prescribed dose. To avoid bias, the present study standardized the optimization objectives between patients of each technique. The optimization objectives of major structures were illustrated in Supplementary File — Table S2. The anisotropic analytic algorithm (AAA, ver.15.5.11, Varian Medical Systems) was used for dose calculation with calculation grid of 1 mm.

Split-arc partial-field VMAT (sapf-VMAT)

The sapf-VMAT plans were created with reference to previous publication of our oncology centre [2]. Four VMAT arc fields of 179.9° were employed with collimator angle of 85°, 95°, 15° and 345°, respectively. Reduced field size was employed in each beam arc to spare the hippocampus while not sacrificing the whole brain PTV coverage. Detailed description of the sapf-VMAT beam arrangement was illustrated in Supplementary File — Figure S2A.

Hybrid split-arc partial-field VMAT (Hsapf-VMAT)

The Hsapf-VMAT consisted of 4 arc fields of 179.9° each and 2 lateral opposing static fields. The isocentre was the same as the sapf-VMAT plans. The beam arrangement of the static fields was in lateral opposing directions where the vast majority of whole brain PTV were covered by the beam axis. Collimator angles of 60° and 120° were chosen for the 2 static fields, so that both eyes were shielded by the X1 collimator jaw. MLC were used to minimize the irradiated hippocampus volume. The beam arrangement of lateral opposing static fields was illustrated in Supplementary File — Figure S3. The lateral opposing static fields plan was set to deliver 30% of the prescribed dose.

Using the lateral opposing static fields plan as a base plan, the 4 arc fields were optimized to sculpture the optimal conformity and organ sparing. The arc fields were arranged similarly to sapf-VMAT. Detailed description of the Hsapf-VMAT beam arrangement was illustrated in Supplementary File — Figure S2B.

Treatment planning evaluation and quality assurance

Dosimetric parameters of both techniques were extracted from the dose–volume histogram (DVH). Homogeneity index (HI) of whole brain PTV was evaluated [15] (Equation 1):

$$HI = \frac{(D_{2\%} - D_{98\%})}{D_{median}} \quad \text{(Equation 1)}$$

MobiusCalc dose calculation verification system (version 2.1, Mobius Medical Systems, LP, Houston, TX) was used for quality assurance (QA) of treatment plans. All treatment plans were required to achieve a gamma value > 95% with tolerance for distance to agreement as 3 mm and dose difference as 3%.

Statistical analyses

Statistical comparisons between treatment plans of both techniques were performed using the paired t-test at 5% level significance.

Results

All treatment plans have achieved good correlation in QA. Dosimetric parameters were summarized as mean ± standard deviation (SD) (Tab. 1). DVH of the dosimetric parameters using sapf-VMAT and Hsapf-VMAT were compared (Fig. 1A). The average hippocampus volume was 3.80 cm^3 (ranged from 2.82–4.72 cm^3), the average hippocampal planning risk volume was 26.50 cm^3 (ranged from 23.06–30.03 cm^3), and the average whole brain PTV was 1232.05 cm^3 (ranged from 1050.93–1471.00 cm^3).

Table 1. Averaged results and comparison of dosimetric parameters using split-arc partial-field VMAT (sapf-VMAT) and hybrid split-arc partial-field volumetric modulated arc therapy (Hsapf-VMAT). Each value was calculated based on the data from 22 patients and was expressed as mean ± standard deviation (SD)

Structures	Dosimetric parameters	sapf-VMAT	Hsapf-VMAT	p-value
Whole brain PTV	V_{30Gy} (%)	94.79 ± 0.12	94.69 ± 0.15	0.358
	$D_{2\%}$ [Gy]	33.14 ± 0.33	33.28 ± 0.24	0.145
	$D_{98\%}$ [Gy]	25.87 ± 0.31	25.62 ± 0.22	0.868
	HI	0.23 ± 0.01	0.24 ± 0.02	0.516
	D_{median} [Gy]	31.33 ± 0.14	31.39 ± 0.08	0.322
	D_{mean} [Gy]	31.16 ± 0.13	31.14 ± 0.09	0.751
Hippocampus	$D_{100\%}$ [Gy]	7.88 ± 0.04	7.92 ± 0.09	0.677
	D_{max} [Gy]	13.26 ± 0.45	13.31 ± 0.32	0.681
	D_{median} [Gy]	9.03 ± 0.13	9.11 ± 0.09	0.184
	D_{mean} [Gy]	9.17 ± 0.10	9.21 ± 0.12	0.686
Left optic nerve	D_{max} [Gy]	30.69 ± 0.45	30.55 ± 0.56	0.785
	D_{median} [Gy]	25.29 ± 1.49	20.90 ± 2.33	< 0.005**
	D_{mean} [Gy]	24.12 ± 1.01	20.20 ± 1.71	< 0.005**
Right optic nerve	D_{max} [Gy]	30.37 ± 0.77	30.41 ± 0.57	0.324
	D_{median} [Gy]	24.21 ± 2.93	20.89 ± 2.37	< 0.05*
	D_{mean} [Gy]	23.36 ± 1.96	20.23 ± 2.02	< 0.005**
Optic chiasm	D_{max} [Gy]	32.50 ± 0.71	32.37 ± 0.28	0.461
	D_{median} [Gy]	31.10 ± 0.40	31.39 ± 0.27	0.153
	D_{mean} [Gy]	31.11 ± 0.42	31.34 ± 0.27	0.073
Left eye	D_{max} [Gy]	17.23 ± 0.56	12.26 ± 1.48	< 0.005**
	D_{median} [Gy]	9.87 ± 0.41	6.95 ± 0.14	< 0.005**
	D_{mean} [Gy]	9.55 ± 0.41	7.18 ± 0.17	< 0.005**
Right eye	D_{max} [Gy]	17.18 ± 0.24	12.35 ± 1.05	< 0.005**
	D_{median} [Gy]	9.90 ± 0.51	7.01 ± 0.19	< 0.005**
	D_{mean} [Gy]	9.27 ± 0.33	7.38 ± 0.56	< 0.005**
Left lens	D_{max} [Gy]	7.37 ± 0.26	5.82 ± 0.19	< 0.005**
	D_{median} [Gy]	5.72 ± 0.20	5.26 ± 0.17	< 0.005**
	D_{mean} [Gy]	5.75 ± 0.19	5.28 ± 0.17	< 0.005**
Right lens	D_{max} [Gy]	7.43 ± 0.38	5.77 ± 0.16	< 0.005**
	D_{median} [Gy]	5.86 ± 0.26	5.22 ± 0.13	< 0.005**
	D_{mean} [Gy]	5.90 ± 0.26	5.25 ± 0.11	< 0.005**
Total MU		1087.58 ± 158.57	1093.78 ± 122.15	0.599
Beam-on time [min]		3.06 ± 0.23	3.31 ± 0.16	0.157
Delivery time [min]		3.64 ± 0.24	4.80 ± 0.17	< 0.005**

*p < 0.05; **p < 0.005 (paired t-test); PTV — planning target volume; V_{30Gy} — percentage volume of whole brain PTV receiving dose at least 30 Gy; $D_{2\%}$ — dose to 2% of the whole brain PTV; $D_{98\%}$ — dose to 98% of the whole brain PTV; HI — homogeneity index; D_{max} — maximum dose; D_{mean} — mean dose; D_{median} — median dose; MU — monitor unit

Target coverage and dose homogeneity

The isodose line diagram from 20 Gy to 37.5 Gy of both treatment techniques was illustrated in Figure 1B. All treatment plans were capable of achieving adequate target coverage. The maximum dose of whole brain PTV was less than 37.5 Gy in accordance to the RTOG 0933 protocol. With regard to the whole brain PTV coverage, Hsapf-VMAT provided an average V_{30Gy} of 94.69%, which was comparable to sapf-VMAT (94.79%). No significant differences (p > 0.05)

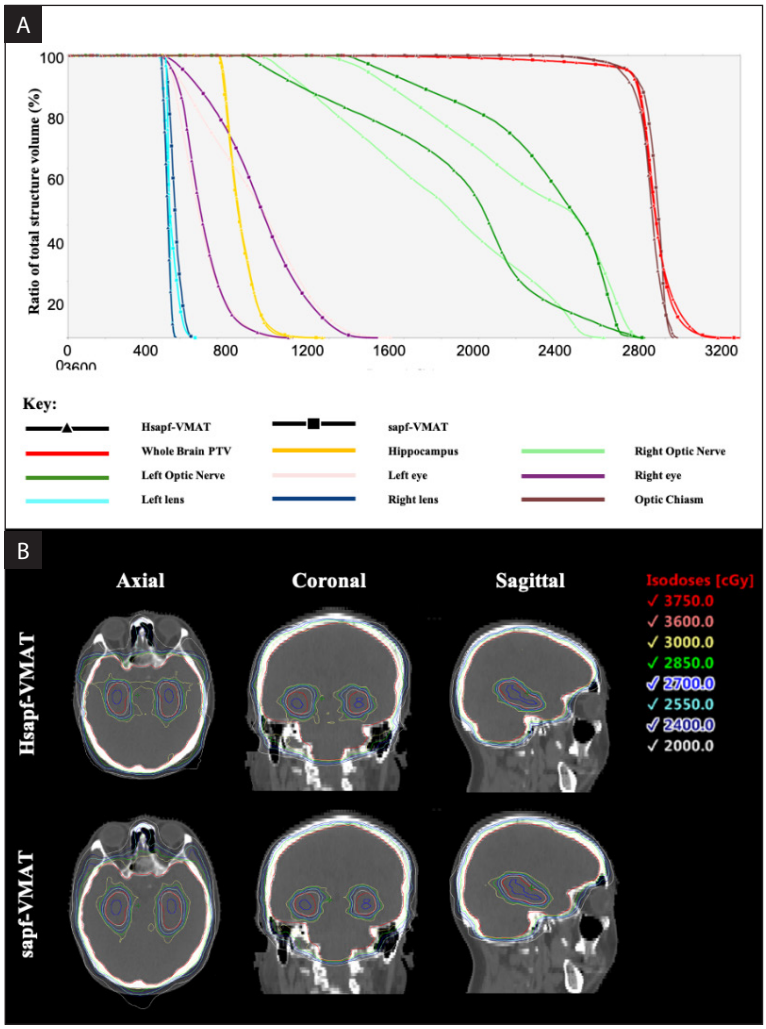

Figure 1. A. Dose volume histogram of whole brain planning target volume (PTV) and organs-at-risk: split-arc partial-field VMAT (sapf-VMAT) (square) compared to Hsapf-VMAT (triangle); **B.** Isodose line diagrams of sapf-VMAT and hybrid split-arc partial-field volumetric modulated arc therapy (Hsapf-VMAT)

were found between Hsapf-VMAT vs. sapf-VMAT in V_{30Gy}. Mean HI of Hsapf-VMAT and sapf-VMAT were 0.24 and 0.23, respectively. No significant differences ($p > 0.05$) were found between both techniques.

Hippocampus

Hsapf-VMAT (7.92 Gy, $p > 0.05$) had a comparable average $D_{100\%}$ to sapf-VMAT (7.88 Gy). There were also no significant differences ($p > 0.05$) between Hsapf-VMAT vs. sapf-VMAT in terms of hippocampus D_{max}, D_{median} and D_{mean}.

Optic chiasm, optic nerves, eyes and lenses

The average D_{max} to the optic chiasm in sapf-VMAT and Hsapf-VMAT was 32.50 Gy and 32.37 Gy, respectively ($p > 0.05$). Hsapf-VMAT was comparable to sapf-VMAT ($p > 0.05$) in averaged D_{max} for both optic nerves. However, Hsapf-VMAT demonstrated significantly lower D_{median} and D_{mean} to the optic nerves compared to sapf-VMAT ($p < 0.05$). In both eyes, Hsapf-VMAT demonstrated significantly lower D_{mean} and D_{max} compared to sapf-VMAT ($p < 0.005$). Hsapf-VMAT also had significantly lower lenses D_{max} compared to sapf-VMAT ($p < 0.005$).

Total monitor unit, beam on time and delivery time

The average total MU in Hsapf-VMAT (1093.78, $p > 0.05$) is comparable to sapf-VMAT (1087.58). The averaged beam-on time was 3.06 minutes and 3.31 minutes for sapf-VMAT and Hsapf-VMAT,

respectively. No significant differences ($p > 0.05$) were found between both techniques in beam-on time. The averaged treatment delivery time was 3.64 minutes and 4.80 minutes, respectively. Significant differences ($p < 0.005$) were found between both techniques in delivery time.

Discussion

In the present study, a hybrid technique named Hsapf-VMAT has been employed. This technique has consistently produced comparable hippocampus dose to sapf-VMAT and is less than the cutoff value of radiation induced neurocognitive deficit onset [1].

The RTOG 0933 protocol does not provide dosimetric criteria for both eyes and lenses. Several studies have reported that damages to eyes and lenses can be induced by radiation dose as low as 18 Gy [7, 8] and 6.5 Gy [10], respectively. Meanwhile, a previous study has shown that higher mean dose to the optic nerves is also associated with higher occurrence of ocular complications [16]. These data provide further support for the minimization of dose to the ocular and orbital organs in patients receiving WBRT. The results from the present study have revealed that Hsapf-VMAT, compared to sapf-VMAT, has demonstrated significant dose reduction to both eyes and lenses, in addition to the hippocampus. Such reduction is achievable since the eyes and lenses have been shielded by the X1 collimator jaw in the pair of static fields in which the beam weights were set to deliver 30% of the prescribed dose (Supplementary File — Fig. S3). It indicates that Hsapf-VMAT may be capable of lowering the risk of radiation induced ocular and orbital morbidity as described in previous publications. This technique is especially important when the patient has existing comorbidity or exposure to radiation sensitizers [7, 8].

The beam arrangement of non-coplanar intensity modulated radiation therapy (nc-IMRT) recommended by the RTOG protocol have included seven or eight non-coplanar beams with the average treatment delivery time of 19 minutes [17]. In fact, intensity modulated radiation therapy itself has required significantly longer treatment delivery time and higher MU when compared to VMAT in brain tumor radiotherapy [18]. Meanwhile, the application of non-coplanar beams may further increase the treatment delivery time [19]. The associated increased treatment time can potentially lead to the possibility of intra-fraction motion. As treatment times are compounded daily, the potential intra-fractional error needs to be weighed against the benefit to the individual patient. In the present study, six coplanar treatment fields (4 arc fields and 2 static fields) were used for Hsapf-VMAT with an average treatment delivery time of 4.8 minutes. Although properties of nc-IMRT has not been compared to Hsapf-VMAT in the present study, Hsapf-VMAT seemingly required less treatment delivery time, since non-coplanar beam has not been used. Extension of this research could examine the dosimetric and treatment properties, including treatment delivery time and intra-fractional error, of Hsapf-VMAT and nc-IMRT.

Admittedly, using Helical Tomotherapy (HT) with a complete directional block technique might achieve lower eyes and lenses dose than Hsapf-VMAT in the present study. However, the improved eyes and lenses doses are also at the expense of substantial increased treatment time [20]. Meanwhile, due to the high machine procurement and maintenance cost [21], HT may not be extensively available as a linear accelerator. Therefore, delivery of Hsapf-VMAT using linear accelerator is still an efficient and cost-effective option for many clinical settings.

There have been no previous reports that examined the optimal proportion for static fields/arc fields during hybrid-VMAT WBRT. In the present study, the preferable weighting proportion of static fields and VMAT in Hsapf-VMAT for WBRT is 30% and 70%, respectively. Increased proportion of static fields during trial have shown to reduce the conformity and homogeneity of the treatment plans, while increased proportion of arc fields have demonstrated reduced dose sparing in the optic nerves, eyes and lenses. Further knowledge on the relationship of static fields/arc fields weighting may allow the application of Hsapf-VMAT to other brain tumors.

Limitation

Manual delineation of the hippocampus poses technical challenges for oncologists, medical physicists, dosimetrists and radiation therapists with

high inter-observer variability [22, 23]. In our oncology centre, to minimize hippocampus contouring uncertainty during treatment planning, hippocampal volume must be delineated by oncologists with at least 5 years of post-specialization experience. To prevent inter-observer variability arising in the present study, the hippocampus was manually delineated by only a single radiation oncologist with more than 10 years of post-specialization experience.

Dose reduction in the optic nerves, eyes and lenses using Hsapf-VMAT may prevent undesirable ocular and orbital morbidity; however, the biological effect of this technique has not been studied in the present technical report. In the future, meta-analysis will be crucial to confirm the clinical usability and functional outcome of Hsapf-VMAT. In the meantime, the benefit of Hsapf-VMAT is at the cost of increased time required for treatment delivery. In the present study, the averaged treatment delivery time of Hsapf-VMAT plans is around 70 seconds longer than the sapf-VMAT plans. The increased treatment time is primarily due to the additional gantry travel time for the lateral opposing static fields. Nonetheless, a more advanced optimization system in the future may be capable of achieving comparable plan quality with reduced treatment time.

Conclusion

The present study adopts a hybrid technique, namely Hsapf-VMAT, for hippocampal sparing WBRT. This technique has taken advantage of both lateral opposing static fields and sapf-VMAT. Hsapf-VMAT has demonstrated comparable hippocampus dose to sapf-VMAT, while achieving dose reduction in the eyes and lenses. Therefore, Hsapf-VMAT can be considered an improved version of sapf-VMAT.

Ethics approval and consent to participate

All procedures in this study were reviewed and approved by the University of Hong Kong and the Oncology Centre, St. Teresa's Hospital (HKSAR).

Consent for publication

Publication of this study was approved by the University of Hong Kong and 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.

Conflict of interests

None declared.

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The authors declare no competing financial interests.

Authors' contributions

Conception and design of the study — AHLY, AKLL; acquisition of data — AHLY, AKLL, PCYM; analysis and interpretation of data — AHLY, PCYM; drafting and revising the article — AHLY; final approval of the manuscript — AKLL, PMW, AHLY

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