

Oesophageal Cancer: Conformal Radiotherapy vs. Hybrid-VMAT Technique With Two Different Treatment Planning Systems

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Abstract. *Background/Aim: Traditionally, the radiotherapy of oesophageal cancer has been conformal radiotherapy (CRT). We sought to compare dosimetric parameters of conformal radiotherapy (CRT) with those of two treatment planning systems for hybrid-volumetric modulated arc therapy (h-VMAT) for the treatment of oesophageal cancer. Patients and Methods: In 11 patients, we compared: i) planning target volume coverage, ii) dose to organs at risk, and iii) the dose rate (DR) of the three techniques. We evaluated two treatment planning systems: i) Eclipse and ii) RayStation. Results: The Conformity Index of the CRT plan was significantly higher for the h-VMAT plans, compared to all other parameters. Normal lung tissue volumes receiving >5, 13, or 20 Gy were lower with the RayStation plan compared to Eclipse. The volume of cardiac tissue receiving >40 Gy was highest with the CRT plan. The minimum DR in VMAT was lowest for the RayStation plan (49.5 MU/min). Conclusion: The h-VMAT plan using RayStation is the appropriate choice for reducing lung dose.*

Oesophageal cancer is a common cause of cancer death around the world (1). Chemoradiotherapy for oesophageal cancer has better local control and overall survival compared to chemotherapy (2). A cisplatin-based combination is the

standard regimen of chemoradiotherapy for oesophageal cancer (3).

The radiotherapy (RT) technique for oesophageal cancer has commonly been conformal radiation therapy (CRT). This technique is often limited by the dose to the organs at risk (OARs). The National Cancer Institute (NCI) does not permit intensity-modulated radiotherapy (IMRT) for treatments in the thorax of patients in NCI-sponsored trials (4, 5). IMRT generally produces widely distributed but lower doses of radiation to normal tissues surrounding the planning target volume (PTV) compared to CRT. The normal tissue volumes involved during RT for oesophageal cancer are larger compared to those in lung cancer treatment because of the longer cranio-caudal length of the PTV.

Volumetric modulated arc therapy (VMAT) has recently been used for the treatment of oesophageal cancer (6). To reduce the volume of normal tissue that receives these extraneous doses, Mayo *et al.*, (7) have developed a new technique called 'Hybrid-IMRT'. This technique combines static and IMRT beams used concurrently, and has produced results with a better dose conformity and sparing of OARs using VMAT with a shorter treatment time compared to IMRT (8). For this reason, we used volumetric modulated arc therapy (VMAT) instead of IMRT (9). Multiple commercial treatment planning systems (TPSs) have become available. Lafond *et al.*, (10) have compared the dosimetric parameters of two VMAT treatment planning systems for prostate cancer, whereas Langner *et al.*, (11) have compared point doses between Eclipse and Raystation (Eclipse Version 13.7.29; Varian Medical Systems, Palo Alto, CA, USA and RayStation version 4.7.4.4, RaySearch Medical Laboratories AB, Stockholm, Sweden) for proton therapy. The result of calculation is difficult between TPSs, because the calculation algorithm was different. Comparison of hybrid-VMAT (h-VMAT) techniques using two treatment planning systems has not been done before.

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The aim of this study was to compare dosimetric parameters of CRT with those of two h-VMAT plans from two different treatment planning systems for the treatment of oesophageal cancer.

Patients and Methods

Patients. Subjects were 11 cases of oesophageal cancer patients treated with h-VMAT technique at our institute between 2017 and 2018. Patient characteristics are summarized in Table I. This study was approved by our ethics committee (No. 42718).

Treatment planning. For the computed tomography (CT) simulation, patients were immobilized with a vacuum pillow (Vac-Lock, Civco Medical Solutions, Iowa, USA) in the supine position with the arms raised. CT images were acquired using the Revolution HD (GE Medical Systems, Milwaukee, WI, USA). The parameters for CT acquisitions were: i) 2 mm slices, ii) 512x512 matrix, and iii) 50 cm field of view. These images were transferred to the Eclipse TPS (Eclipse Version 13.7.29; Varian Medical Systems).

The CRT plan used only Eclipse. The h-VMAT plans used both Eclipse and RayStation. The dose calculation used the analytical anisotropic algorithm (AAA), while the h-VMAT plan from RayStation was recalculated by the AAA of Eclipse.

Target volumes and OARs (e.g., the lung, heart, and spinal cord) were contoured by radiation oncologists. The gross tumour volume (GTV) consisted of identified masses and clinical target volumes (CTV) for boosting and was created by adding potential volumes of tumour extension to GTV. CTV for elective treatment included lymph node regions at potential risk of occult metastasis. The PTV was created by adding an isotropic margin of 5 mm to the CTV. In all cases, high-risk planning target volume (PTVboost) was based on the primary and clinical lymph node metastases, while PTVelective included elective dose areas.

The dose prescriptions were 40 and 20 Gy for the PTVelective and PTVboost (2 Gy/fraction), respectively. For the CRT plan, doses were delivered to the isocentre. For the h-VMAT plans, doses were prescribed to the mean dose to the PTV. The CRT plan consisted of opposite anterior-posterior (AP) fields to deliver PTVelective and opposite oblique fields to deliver PTVboost to the isocentre. The h-VMAT plans used two full arcs in VMAT and opposite AP fields. The prescription dose of the h-VMAT plan was delivered at 50% with VMAT, and 50% in the AP direction. The following dose constraints were used for OARs: i) maximal dose (Dmax) to the spinal cord at ≤ 45 Gy, ii) V_5 for the lung at $\leq 65\%$, and iii) V_{20} for the lung at $\leq 35\%$. While maintaining dose constraints of PTV coverage and spinal cord, the three plans had added constraints to minimize lung dose.

The typical field arrangements and isodose distribution from 5 Gy to max dose of the three treatment techniques are illustrated in Figure 1.

The following dosimetric parameters were analysed: i) D_{98} , ii) D_{95} , iii) D_2 , iv) conformity index (CI) for PTV, v) homogeneity index (HI) for PTV, vi) Dmax to the spinal cord, vii) V_5 , viii) V_{13} , ix) V_{20} , x) V_{30} and xi) mean of lung-PTVelective (MLD), xii) V_{40} and xiii) mean to heart. Dx% indicates the dose that includes x% of the target and $V_x\%$ indicates the volume% of the target receiving x% of the prescribed dose. CI was determined by dividing the volume receiving the prescribed dose by the target volume. HI was evaluated as the difference between D_2 and D_{98} of PTV divided by

Table I. Patient characteristics.

		Patients (n=11)
Age	Median	66
	Range	38-89
Gender	Male	9
	Female	2
Histology	Squamous cell carcinoma	11
	Primary site	
	Ut	3
	Ut-Mt	3
	Mt	2
	Mt-Lt	1
	Lt	2
Stage	I	2
	II	1
	III	4
	IVA	2
	IVB	2
PTVelective Volume (cc)	Median	532.5
	Range	284.8-912.1
PTVboost Volume (cc)	Median	225.7
	Range	105.6-328.4
PTVelective CCL (cm)	Median	23.9
	Range	13.4-31.2
PTVboost CCL (cm)	Median	15.82
	Range	9-24.4

Ut: Upper thoracic; Mt: middle thoracic; Lt: lower thoracic. PTV: planning target volume; CCL: craniocaudal length.

D_{50} of PTV. The Dx of PTVboost was calculated adding plans of PTVelective and PTVboost. The dose rates (DR:MU/minute) of the two arc beams of two h-VMAT plans were compared.

Data analysis. Results are expressed as mean \pm standard deviation. Paired Student's *t*-tests were used to compare the dosimetric parameters. A value of $p < 0.017$ was defined as having statistical significance using the Bonferroni's method.

Results

Target coverage. Table II shows the dosimetric parameters of PTV for CRT and the two h-VMAT plans. D_{95} of PTVelective and PTVboost were not significantly different and $>95\%$ of the prescribed dose. The D_{50} of PTVelective for the Eclipse plan was not significantly different from that of the RayStation plan. The D_{50} for PTVboost of the Eclipse plan was significantly different from that of the RayStation plan ($p < 0.01$). The CI for PTVelective of the CRT plan was significantly higher compared to that of the Eclipse and RayStation plans ($p < 0.001$). The CI for PTVboost of the Eclipse plan was also significantly lower compared to that of the RayStation plan ($p < 0.001$).

Organs at risk. Table II shows OAR doses. The V_5 for lung-PTVelective of the Eclipse plan was significantly

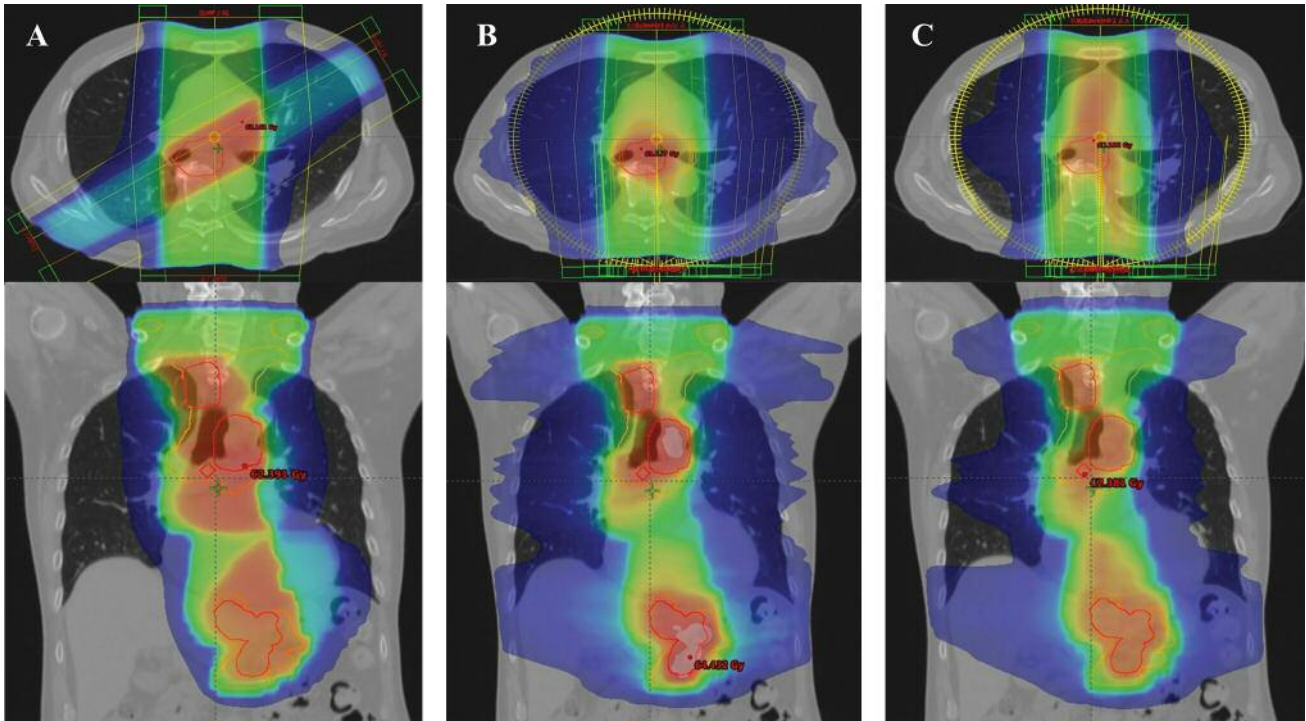


Figure 1. Axial (upper) and coronal (lower) dose distribution of >5 Gy for the three planning techniques for one patient. (A) CRT plan, (B) h-VMAT plan using Eclipse, (C) h-VMAT plan using RayStation. The color of dose distribution is >5 Gy (blue), >20 Gy (light blue), >30 Gy (green), >45 Gy (yellow), >55 Gy (orange).

higher compared to those of the CRT and RayStation plans ($p < 0.001$ and 0.01 , respectively). The V_{13} for lung-PTVelective of the RayStation plan was significantly lower compared to that of the CRT plan ($p = 0.005$). The V_{20} for lung-PTVelective of the RayStation plan was significantly lower compared to that of the CRT plan ($p < 0.001$). The V_{30} for lung-PTVelective of the CRT plan was not significantly different from those of the Eclipse and RayStation plans. The mean dose for lung-PTVelective of the CRT plan was significantly different from those of the Eclipse and RayStation plans. The maximum spinal cord dose of the CRT plan was significantly higher than that of the Eclipse and RayStation plans ($p = 0.026$ and 0.035 , respectively).

Dose rate. The mean DR of the RayStation plan was significantly higher compared to that of the Eclipse plan ($p < 0.001$). The minimum DR of the RayStation plan was lower compared to that of the Eclipse plan (49.53 MU/min vs. 62.06 MU/min). The beams of the CRT plan and AP beams of the h-VMAT plan were 600 MU/min stably. Figure 2 shows an example of DR for h-VMAT plans between Eclipse and RayStation.

Discussion

In this study, we compared the dosimetric parameters of CRT and of two h-VMAT plans using two treatment planning systems in 11 oesophageal cancer patients. The two h-VMAT plans showed a significant improvement in CI compared to CRT. The h-VMAT plan using RayStation in CI showed good coverage compared to Eclipse plans. In normal lung, the RayStation plan provided lower low-dose volumes except for the V_5 of the CRT plan. The heart V_{40} was highest in CRT compared the other plans. The D_{max} to spinal cord was not significantly different among all methods. The minimum of DR was lowest for the RayStation plan (49.5 MU/min), though the RayStation plan had a wider range of DR compared to the Eclipse plan.

Previous publications on IMRT/VMAT have recognized some advantages compared to CRT (12-14). However, the IMRT/VMAT plans give a higher lung dose compared to the CRT plans (V_5 , V_{10} , V_{20} , MLD) (15). To reduce the volume of normal lung for V_5 , V_{13} , V_{20} , V_{30} , MLD, the h-VMAT plan offered better conformity and lower low-dose volumes except for the V_5 of the lung (9). It is generally understood that V_{20} and mean lung dose (MLD) are major predictors for

Table II. Dose parameters of PTV coverage, OARs.

	CRT	EC	RS	p-Value		
				CRT vs. EC	CRT vs. RS	EC vs. RS
PTV						
PTV _{el}						
D98 (%)	36.61±0.70	36.96±0.56	36.39±0.98	0.11	0.56	0.11
D95 (%)	37.41±0.62	37.75±0.48	37.74±0.48	0.16	0.21	0.94
D50 (%)	39.98±0.62	40.15±0.14	40.26±0.11	0.39	0.15	0.04
D2 (%)	42.14±0.88	41.92±0.65	41.55±0.33	0.52	0.05	0.11
PTV _b						
D98 (%)	54.54±3.65	56.61±1.05	56.33±1.54	0.09	0.15	0.62
D95 (%)	56.63±2.00	57.59±0.85	57.65±1.04	0.85	0.76	0.89
D50 (%)	60.39±1.50	60.32±0.17	60.56±0.21	0.87	0.71	<0.01
D2 (%)	62.04±1.63	62.45±0.82	61.95±0.54	0.74	0.88	0.38
CI						
PTV _{el}	2.65±1.14	0.58±0.07	0.7±0.12	<0.001	<0.001	<0.001
PTV _b	1.42±1.50	0.66±0.07	0.83±0.13	0.11	0.2	<0.001
HI						
PTV _{el}	0.14±0.02	0.12±0.03	0.13±0.03	0.7	0.37	0.16
PTV _b	0.12±0.06	0.09±0.03	0.09±0.03	0.16	0.16	0.99
Lung-PTV_{el}						
V5 (%)	48.81±15.40	75.25±17.61	56.38±9.88	<0.001	0.19	<0.01
V13 (%)	30.68±11.41	23.09±6.96	18.76±5.58	0.07	0.005	0.12
V20 (%)	23.92±9.06	12.32±4.02	11.86±4.22	<0.001	<0.001	0.8
V30 (%)	10.22±3.97	7.07±3.28	7.52±3.39	0.06	0.1	0.76
Mean (%)	29.43±3.38	10.8±2.16	9.58±1.89	0.6	0.13	0.17
Heart						
V40 (%)	40.54±26.77	22.88±17.63	29.43±20.03	0.08	0.28	0.42
Mean (%)	26.77±11.69	25.24±9.88	25.93±9.97	0.74	0.86	0.87
Spinal cord						
Dmax (Gy)	44.64±0.49	43.25±1.85	43.55±1.51	0.026	0.035	0.67

PTV: Planning target volume; Dx: the percentage of the prescribed dose covering x% volume of PTV; CI: conformity index; HI: homogeneity index; Vx: the percentage of organ receiving ≥x Gy; EC: Eclipse; RS: Raystation;

radiation pneumonitis (RP). A critical review of the dose-volume effect in the lung recommends limiting V₂₀ to ≤30-35% and MLD to 20-23 Gy (16). Schallenkamp *et al.*, (17) have reported results from a study that examined MLD, V₁₀, V₁₃, V₁₅, V₂₀, V₃₀, and effective lung dose for the treatment of a series of 99 lung cancer patients. They concluded that larger volumes of lung exposed to lower doses (V₁₃) may be more predictive of complications compared to V₂₀ or V₃₀. V₅ may also be important (18). Wu *et al.*, (19) have compared CRT, IMRT, and VMAT in oesophageal cancer patients, and have demonstrated that all plans were able to meet the prescription and there was no clear distinction on PTV coverage. VMAT can decrease the high dose area but delivers more volume of the low dose area. The h-VMAT plan using RayStation compared to CRT and Eclipse successfully lowered the V₂₀ and mean lung dose, however, the low dose was similar to that of the CRT plan, together with an improvement in CI. Regarding the cardiac dosimetry, the RTOG 0617 clinical trial reported that the heart V₅ and V₃₀

are important predictors of patient survival (20). In this study, the heart V₄₀ was extremely high with the CRT plan. This was due to the presence of oblique beams used to reduce the lung dose. The heart V₄₀ remains significantly associated with OS in the multivariable analysis (21).

CI_s to PTV_{el} were significantly higher for the CRT plan. For this reason, a lung volume receiving >20 Gy of the CRT plan was significantly higher than that of the Eclipse and RayStation Plans. Chan *et al.* have compared the CI_s of three treatment techniques: i) CRT, ii) VMAT, and iii) h-VMAT for locally-advanced non-small cell lung cancer. They have described that the CI_s of VMAT (1.13±0.07) and h-VMAT (1.13±0.05) plans were lower than that of CRT (1.42±0.17) (9). Similarly, in our study, the CI_s of PTV_{el} and PTV_{boost} for the CRT plan were higher compared to the other plans. A wide distribution of low dose to the surrounding normal tissues can be harmful for the patients (18). The differences in DRs for the h-VMAT plan between the two treatment systems have not been compared

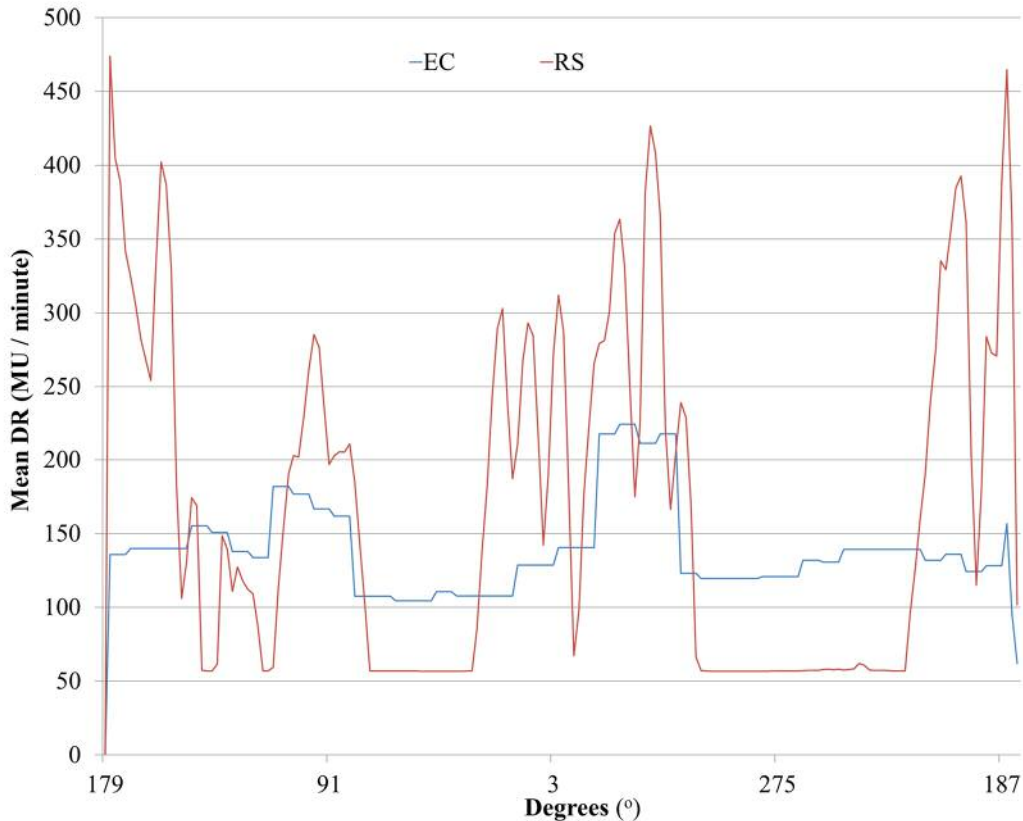


Figure 2. Example of DR for h-VMAT plan between Eclipse (blue) and RayStation (red).

yet. Lafond *et al.*, (10) have compared the DR between two treatment planning systems [Monaco (Elekta, Crawley, UK) and Pinnacle (Philips Medical Systems, Best, the Netherlands)] for VMAT in prostate cancer. The average DR was higher with Monaco (230 MUs/min) compared to Pinnacle (160 MUs/min).

In that study, the VMAT treatment plans obtained with Monaco and Pinnacle offered clinically acceptable dose distributions for prostate cancer (10). The DR of the RayStation plan compared to that of the Eclipse plan was wider and had a lower mean in our study. Due to a wide range of DR, the RayStation plan was a steep distribution compared to the Eclipse plan.

Some limitations exist in this study. First, the V_5 of lung for the CRT and h-VMAT plan using RayStation were not significantly different. The lung dose of the h-VMAT plan may be reduced by changing the ratio of the A-P beam and VMAT. Second, this study was calculated using AAA. AAA can be suboptimal in low density tissues, such lung, where it may overestimate the dose. Inaccuracy of dose calculation may be reduced by using Monte Carlo (22) or a commercial software (Acuros XB, Varian Medical Systems) (23).

The CI of the h-VMAT plan was significantly lower compared to that of the CRT plan for PTVelective. For this reason, lung doses except for V_5 were significantly higher with CRT compared to the h-VMAT plan. The V_5 mean of Lung-PTVelective of the h-VMAT plan using RayStation was significantly lower compared to that of the Eclipse plan. The h-VMAT plan using RayStation is an approach for reducing the lung volume receiving a low dose volume during the treatment of oesophageal cancer.

Conflicts of Interest

No actual or potential conflicts of interest exist.

Authors' Contributions

All Authors contributed to data collection, and participated in the writing and final approval of the manuscript.

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