Comparison of nodal irradiation dose using radiotherapy for patients with thoracic esophageal cancer

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Abstract. The present study aimed to compare incidental nodal irradiation (INI) doses using volume-modulated arc therapy (VMAT), 5-field intensity-modulated radiotherapy (5F-IMRT) and 3D-conformal radiotherapy (3D-CRT) treatment plans for patients with thoracic esophageal cancer (EC). A total of 15 patients with thoracic EC were selected for participation between October 2016 and July 2017 at the Hangzhou Cancer Hospital. Regional lymph nodal stations were contoured according to 3D CT-based images of the Japan Esophageal Society Guidelines. All patients were treated with 60 Gy using VMAT, 5F-IMRT and 3D-CRT plans. Dose-volume histograms of planning target volume (PTV), lung, heart, spinal cord and incidental nodal irradiation were compared between the three plans. 5F-IMRT was superior in PTV_$V_{95\%}$ (the volume of the PTV receiving 95% of the prescription dose, P=0.003) and the VMAT plan was best in terms of conformal index (P=0.005). V_{20} and V_{30} were reduced by 10.7-22.6% (P=0.002) and 12.8-21% (P=0.026), respectively, in normal lung tissue using the VMAT plan. 5F-IMRT demonstrated the lowest maximum dose (D_{max}) for the spinal cord (P=0.037). For the INI, 3D-CRT exhibited the highest equivalent uniform dose (EUD) values for 106pre (P=0.014) and 106tb-L (P=0.03) in upper-thoracic EC. The mean EUD of all lymph nodal regions in middle-thoracic EC were >40 Gy in VMAT and 5F-IMRT plans; the VMAT plan had higher EUD values in lower-thoracic EC compared with 5F-IMRT, 3D-CRT plans for INI. VMAT were comparable to the 5F-IMRT plan with respect to dosimetric characteristics for planning and INI doses to thoracic nodal levels NO 105-112 are considerable for thoracic EC.

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Introduction

Thoracic esophageal cancer (EC) has a high mortality rate and can be difficult to treat (1). The incidence of EC has increased rapidly compared with that of other cancer types and the symptoms often present at a late stage of disease, resulting in a 17% 5-year survival rate for all stages combined (1).

Esophageal resection is currently the only curative treatment for EC; however, this surgical procedure is associated with considerable mortality risk and associated complications (2). Other treatment options include chemo-radiotherapy, which is the standard approach for treating local advanced EC (3,4), aiming to achieve optimal tumor control while improving quality of life. Radiotherapy (RT) is also used to treat EC, with the aim of effectively covering the target volume while minimizing irradiation of the surrounding normal tissue. Even with curative RT, long-term survival rates remain poor due to a high frequency of lymph node metastasis and regional recurrence (5,6). Muijs *et al* (7) demonstrated that the overall survival rate of patients with EC was considerably low due to the presence of microscopic tumors outside of the clinical target volume, even after conformal radiation therapy (CRT). Furthermore, Ji *et al* (8) reported that 3D-CRT may deliver considerable doses of incidental radiation to elective regions in thoracic EC, which has a substantial impact on the control of micro-metastases.

In recent years, the clinical application of technology has increased with the development of new hardware and software designed to treat cancer. For example, VMAT is a novel radioactive technique that has been demonstrated to generate dosimetrically equivalent plans with intensity modulated radiation therapy (IMRT) (9-11). Using VMAT, RT technology has dynamic parameters, including variations in dose rate, gantry position, gantry rotation speed and leaf motion speed. The ability to alter these parameters generates superior results in target conformity and in sparing organs at risk (OARs). Despite this, low-dose irradiation of tissues surrounding the target volume is unavoidable when using advanced RT technology. The purpose of the present study was to determine whether advanced RT technology generates incidental irradiation doses for lymph nodes and to compare three RT techniques (VMAT, IMRT and 3D-CRT) with respect to the treatment of patients with thoracic EC.

Materials and methods

Patient selection, ethical approval and computed tomography (CT) simulation. A total of 15 patients between the ages of 46 and 81 years (mean age, 66.5 years) with early-stage EC [Tumor $(T)_{1\text{-}3}$ Node $(N)_0$ Metastasis $(M)_0$], who were previously treated with VMAT at the Hangzhou Cancer Hospital (Hangzhou, China), were recruited between October 2016 and July 2017. Each patient was retrospectively re-planned for IMRT and 3D-CRT techniques on the Pinnacle treatment planning system (TPS, ADAC Pinnacle V9.1, Philips Medical System, USA) with a 6 MV photon beam from Elekta Axesse equipped with a Millennium MLC with 160 leaves. The present study was approved by the Medical Ethics Committee of Hangzhou Cancer Hospital (Hangzhou, China) and written informed consent was obtained from all patients. Patient characteristics are summarized in Table I.

A CT simulator was used to determine target volume. Patients were placed in the supine position with arms extended above the head and the CT images were obtained at 3-mm slices. Target volume was visualized on the CT images and using an endoscopic extension. The gross tumor volume and clinical target volume were contoured by the radiation oncologist according to the International Commission On Radiation Units and Measurements report 62 (12) and a margin was placed to form a planning target volume (PVT). The prescription dose was 2.0 Gy x 30 fractions, for a total dose of 60 Gy.

Principles of lymph nodal station (LNS) delineation. LNS were delineated and termed according to the Japan Esophageal Society Guidelines (1314), presented in Table II. Delineation focused on thoracic lymph nodes NO. 105-112. The LNSs were grouped into upper-thorax, middle-thorax and lower-thorax categories. The delineation of NO.105-112 was performed using a mediastinal CT window (400 HU width, at +40 HU level) to identify the segmental bronchi for limits of visibility (15). All LNSs were contoured by the same radiation oncologist. On completion of LNS delineation, an experienced pathologist and radiation oncologist each verified the LNS contours on the CT images.

Treatment plan. VMAT technology aims to improve target area coverage and spare normal tissues (16). The advantage of VMAT is shorter treatment times compared with conventional IMRT technology. Patients were treated with a single full arc with clockwise rotation of the gantry with start and stop angles of 182 and 178. The maximum dosage was 600 MU/min and the maximum gantry rotation velocity was 3 deg/min. Dose distribution optimization was performed inversely using dose-volume objectives with instantaneous dose rates, MLC leaf positions and gantry rotational speeds (17,18).

A 5-coplanar field arrangement was used for the IMRT plans. The PVT conformity was defined using a right-posterior oblique field with gantry angle 210, an anterior oblique field with gantry angle 0 and a left-posterior oblique field with gantry angle 150 to minimize exposure of the lung. The other two beams included the right-anterior oblique field at gantry angle 315 and left-anterior oblique field at gantry angle 45 This was used to compensate for the dose gradients of the target volume due to anterior and posterior fields. A direct machine parameter optimization algorithm was applied to optimize the treatment plans. The minimum field size and monitor unit (MU) of the subfield were restricted to 2 cm^2 and 5 MU.

3D-CRT with 4-field beam arrangements were generated using the Pinnacle treatment planning system. Treatment plans for a tumor located in the lower-thorax had an antero-posterior-posteroanterior, and two right and left lateral field beam arrangement. Two parallel-opposed oblique fields and anteroposterior-posteroanterior were always used in the treatment plans for upper- and middle-thoracic EC to avoid exposure of the spinal cord. Typical oblique angles were 150° and 210° from the posterior side.

Plan evaluation. Three types of plan were transferred to TPS for analysis. The cumulative dose volume histograms were generated for evaluation and comparison. For each target volume, $D_{2\%}$ and $D_{98\%}$ (dose corresponding to 2% and 98% of the target volume), $V_{95\%}$, and $V_{110\%}$ (volume of the target receiving 95% and 110% of the prescription dose), conformal index (CI), and homogeneity index (HI) were tabulated and reviewed. The following were selected for evaluation: The mean dose (D_{mean}) and the percentage of the lung that received 5 Gy (V_5), 20 Gy (V_{20}) and 30 Gy (V_{30}), the mean dose (D_{mean}) and the percentage of the heart that received 20 and 30 Gy (V_{20} and V_{30}, respectively), and the maximum dose (D_{max}) to the spine. The percentage volume that received >40 Gy (V_{40}) for each nodal region was calculated and the equivalent uniform dose (EUD) was also calculated for each contoured nodal region. The CI, HI and EUD are described below.

CI and HI were defined to describe the quality of the target as follows: $CI=(V_{T.ref}/V_T) \times (T_{T.ref} \times V_{ref})$, where V_T represents the target volume, $V_{T.ref}$ represents the target volume wrapped by the reference isodose curve face, and V_{ref} represents the total volume wrapped by the reference isodose curve face. A higher CI value, ranging from 0 to 1, represents better conformity. $HI=(D_{2\%}-D_{98\%})/D_{mean}$. Where $D_{2\%}$ represents the dose corresponding to 2% of the target volume, as shown in DVH, and can be deemed the maximum dose; $D_{98\%}$ represents the dose corresponding to 98% of the target volume, and can be deemed the minimum dose. EUD is the absorbed dose that is biologically equivalent to the non-homogenous dose, when given homogenously, and was calculated using the following formula:

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

Where N is the number of voxels in the structure of interest, D_i is the dose in the *i*th voxel and *a* is the tumor-specific parameter for cold spots of interest in the tumor target volume, reflected by the value of EUD when the value is <1.

Statistical analysis. The results between the three plans were analyzed using one-way analysis of variance and Tukey's test was used to further determine differences in pairwise comparisons. Multiple parameter regression analysis was conducted to assess the incidental nodal irradiation (INI). All statistical analyses were performed using SPSS v.19.0 software (IBM Corp., Armonk, NY, USA). $P<0.05$ was considered to indicate a statistically significant difference.

Table I. Patient characteristics.

Patient	Age, years	Sex	Location	TNM stage	Length, cm	PTV, cc
1	60	M	Ut	$T_2N_0M_0$	3	279.6
2	68	M	Ut	$T_2N_0M_0$	5	417.4
3	60	M	Ut	$T_3N_0M_0$	10	568.6
4	63	F	Ut	$T_2N_0M_0$	5	195.4
5	57	M	Ut	$T_3N_0M_0$	6	362.8
6	81	M	Mt	$T_2N_0M_0$	13.3	446.3
7	56	M	Mt	$T_3N_0M_0$	8	589.8
8	71	M	Mt	$T_2N_0M_0$	10	474.0
9	79	F	Mt	$T_2N_0M_0$	5	273.5
10	76	M	Mt	$T_3N_0M_0$	7	348.2
11	78	F	Lt	$T_2N_0M_0$	3	377.8
12	70	M	Lt	$T_2N_0M_0$	7	380.5
13	46	M	Lt	$T_3N_0M_0$	6	276.7
14	54	M	Lt	$T_2N_0M_0$	7	213.1
15	81	M	Lt	$T_2N_0M_0$	4.2	241.8

M, male; F, female; Ut, upper thorax; Mt, middle thorax; Lt, lower thorax; TNM, tumor-node-metastasis; PTV, planning target volume.

Table II. Classification of lymph nodal station in Japan Esophageal Society Guidelines.

Region	Numbering	Japan Esophageal Society
Upper-thorax	105	Upper thoracic paraesophageal nodes
	106tb-R	Right tracheobronchial lymph nodes
	106pre	Pretracheal lymph nodes
	106tb-L	Left tracheobronchial lymph nodes
	106recL	Left recurrent nerve lymph nodes
	106recR	Right recurrent nerve lymph nodes
Middle-thorax	107	Subcarinal lymph nodes
	108	Middle thoracic paraesophageal lymph nodes
	109R	Right main bronchus lymph nodes
	109L	Left main bronchus lymph nodes
Lower-thorax	110	Lower thoracic paraesophageal lymph nodes
	111	Supradiaphragmatic lymph nodes
	112	Posterior mediastinal lymph nodes
	112ao	Thoracic paraaortic lymph nodes
	112pul	Pulmonary ligament lymph nodes

Results

Comparison of PTV and OAR sparing for all plans. The target coverage and OAR sparing are summarized in Table III. The 5F-IMRT plan was superior in target coverage, as indicated by the PTV_$V_{95\%}$ (P=0.003); 3D-CRT was inferior in terms of target coverage, as indicated by $V_{95\%}$ (P=0.003) and $V_{110\%}$ (P=0.012). The VMAT plan was superior in terms of CI (P=0.005); all plans demonstrated no significant statistical difference in HI (P=0.120). V_{20} and V_{30} were reduced by 10.7-22.6% (P=0.002) and 12.8-21% (P=0.026), respectively, for normal lung tissue using the VMAT plan. 5F-IMRT was superior regarding the D_{max} for the spinal cord (P=0.037).

INI dose 60 Gy prescription for thoracic EC treatment. Tables IV-VI compare the three treatment plans based on the dosimetric parameters of INI in thoracic EC, the EUD, DVHs and P-values for each of the thoracic lymph nodes. In the three plans, the mean EUD was >40 Gy in the majority of the upper-thoracic lymph nodal regions, except for 106pre and 106tb-L levels of the VMAT plans. 3D-CRT demonstrated the highest EUD for 106pre (P=0.014) and 106tb-L (P=0.030). V_{40} of 106pre in 3D-CRT was the highest compared with VMAT and 5F-IMRT (P=0.023). For middle-thoracic EC, the mean EUD of all lymph nodal regions was >40 Gy in the VMAT and 5F-IMRT plans, and 108 and 110 levels in the 3D-CRT plan demonstrated poor results. The VMAT plan exhibited the

Table III. Comparison of PTV and organs at risk sparing for all plans.

Variable	VMAT[a]	5F-IMRT[a]	3D-CRT[a]	P-value
PTV_$V_{95\%}$	97.3±1.2	99.2±1.3	95.1±1.5	0.003
PTV_$V_{110\%}$	1.6±1.1	2.4±1.7	3.3±1.4	0.012
PTV_D_2	62.4±0.6	62.7±0.3	64.2±1.6	0.061
PTV_D_{98}	57.6±1.5	58.4±0.8	55.3±1.4	0.074
PTV_HI	0.1±0.01	0.15±0.02	0.22±0.05	0.120
PTV_CI	0.85±0.08	0.70±0.07	0.63±0.03	0.005
Lung_V_5	48.5±3.2	43.4±2.1	47.3±5.4	0.065
Lung_V_{20}	22.6±3.7	25.3±2.8	29.2±3.6	0.002
Lung_V_{30}	14.3±2.2	16.4±1.7	18.1±2.6	0.026
Lung_D_{mean}(Gy)	10.3±1.2	11.2±2.5	11.8±1.4	0.074
Heart_V_{20}	23.5±2.6	22.7±1.3	24.6±2.8	0.056
Heart_D_{mean}(Gy)	15.7±5.3	16.4±6.2	17.3±7.5	0.077
Spinal Cord_D_{max}(Gy)	43.5±1.8	40.3±2.5	44.2±1.4	0.037

[a]Data are presented as the mean ± standard deviation. PTV, planning target volume; VMAT, Volume-Modulated Arc Therapy; 3D-CRT, 3D conformal radiotherapy; IMRT, Intensity-Modulated Radiotherapy; $V_{95\%}$, volume of the target receiving 95%; V110%, volume of the target receiving 110%; D_2, dose corresponding to 2% of the target volume; D_{98}, dose corresponding to 98% of the target volume; V_5, percentage that received 5 Gy; V_{20}, percentage that received 20 Gy; V_{30}, percentage received 30 Gy; D_{mean}, mean dose; D_{max}, maximum dose; CI, conformal index; HI, homogeneity index (HI).

greatest EUD and a V_{40} value of 107 (P=0.004 and 0.006); and 5F-IMRT demonstrated superior values of 108 and 110 in EUD and V_{40} (P=0.017, 0.008; P=0.025, 0.036, respectively). There was a significant difference between the three treatment plans in 112ao, 112pul-R and 112pul-L levels for lower thoracic EC. The VMAT plan exhibited the highest values of EUD and V_{40} in these lymph nodal stations (P=0.001, 0.001; P=0.002, 0.004; P=0.015, 0.008, respectively). Comparisons of INI doses for the three different treatment plans for each statistically significant lymph node station are further illustrated in Figs. 1-3. Fig. 1 illustrates that the 3D-CRT plan resulted in higher EUD values for INI. Fig. 2 shows that the 5F-IMRT and VMAT plans resulted in relatively higher EUD values compared with the 3D-CRT plan in INI. Fig. 3 highlights the VMAT plan exhibited higher EUD values compared with the 5F-IMRT and 3D-CRT plans in INI. A boxplot graph demonstrates the level of dispersion within the lymph nodal dataset and the EUD values of INI for the three different treatment plans.

Discussion

VMAT, IMRT and 3D-CRT are important RT approaches for the treatment of thoracic EC in both definitive and neo-adjuvant settings. The dose distribution and dosimetric parameters of the three treatment plans were acceptable according to established clinical criteria. The VMAT plan generated the greatest CI in three technical studies, and decreased the percentage exposure of the normal lung tissue to 20 and 30 Gy radiation. The use of 5F-IMRT resulted in the best $V_{95\%}$ and the smallest percentage of 5 Gy and 20 Gy dose incidental irradiation of the lung and heart, respectively. Finally, of the three plans, 5F-IMRT also demonstrated the lowest D_{max} in the spinal cord.

Fenkell *et al* (19) suggested that IMRT plans provide improved target volume coverage and conformity compared with 3D-CRT plans, with decreased irradiation of normal structures in cervical EC. Yin *et al* (20) reported that the rapid-arc approach achieved similar coverage to f-IMRT, and effectively spared OARs in cervical EC. This is similar to the findings of Benthuysen *et al* (21), which revealed that VMAT plans had OAR sparing and PTV coverage similar to that of IMRT in distal EC. The present study suggests that VMAT may be equivalent to IMRT, and even slightly more effective than 3D-CRT from a dosimetric perspective, which is consistent with the literature.

Numerous studies have reported that the poor long-term survival of patients with EC is associated with a high incidence of lymph node metastasis and local recurrence of thoracic EC (22-24). Therefore, the predominant clinical recommendation is elective nodal irradiation for patients with EC (25-27). Zhao *et al* (28) suggested that incidental radiation doses to lymph nodes were considerable for early stage non-small-cell lung cancer (NSCLC) without intentional elective nodal irradiation and that these doses were likely to reach a level that may achieve a modest clinical benefit. This may account for the lower incidence of regional failure. Kepka *et al* (29) performed a study with 220 patients with NSCLC, which suggested that incidental nodal irradiation was able to eradicate some subclinical metastases in regional lymph nodes. The present study demonstrated that RT technologies generate considerable incidental irradiation doses to lymph nodal stations in thoracic EC. The mean EUD of all thoracic lymph nodes NO. 105-112 irradiated using 3D-CRT, 5F-IMRT or VMAT was >40 Gy.

In upper-thoracic EC, the 3D-CRT plan resulted in higher EUD values in incidental irradiation doses for 106Pre and 106tb-L, compared with 5F-IMRT and VMAT (Fig. 1). In middle- and lower-thoracic EC, the majority of the lymph

Table IV. Incidental nodal irradiation dose for upper-thoracic EC.

	105		106tb-R		106pre		106tb-L		106recR		106recL	
Variable	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %
VMAT	58.8±0.6	100±0	57.6±0.1	97±1	35.7±1.4	45±14	38.6±2.5	52±23	45.8±1.2	53±24	52.4±1.6	80±31
5F-IMRT	60.2±0.3	100±0	58.8±0.6	100±0	44.8±0.8	65±21	43.4±1.3	54±15	47.3±0.9	54±17	50.3±2.4	78±24
3D-CRT	62.5±0.2	100±0	60.2±0.4	100±0	50.3±1.2	80±18	47.5±2.1	57±8.0	45.2±1.8	53±13	53.2±1.5	81±26
P-value	0.230	1.000	0.350	0.870	0.0140	0.0230	0.030	0.062	0.140	0.630	0.380	0.270

Data are presented as the mean ± standard deviation EC, esophageal cancer; VMAT, volume-modulated arc therapy; 3D-CRT, 3D conformal radiotherapy; 5F-IMRT, 5-field intensity-modulated radiotherapy; EUD, equivalent uniform dose; V_{40}, percentage volume that received >40 Gy.

Table V. Incidental nodal irradiation dose for middle-thoracic EC.

	105		106tb-R		106pre		106tb-L		106recR		106recL	
Variable	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %
VMAT	61.3±0.4	100±0	59.3±0.2	100±0	62.8±1.2	100±0	54.8±3.1	65±26	49.6±2.2	58±22	46.3±2.9	50±27
5F-IMRT	62.2±0.6	100±0	60.5±0.6	100±0	60.2±0.4	100±0	50.4±2.4	56±13	53.4±1.6	65±11	49.6±3.1	53±31
3D-CRT	59.1±0.3	100±0	58.2±0.1	100±0	59.4±1.5	100±0	42.8±2.6	42±21	36.6±1.4	42±19	33.8±1.2	42±18
P-value	0.340	1.000	0.570	1.000	0.640	1.000	0.004	0.006	0.017	0.008	0.025	0.036

Data are presented as the mean ± standard deviation EC, esophageal cancer; VMAT, volume-modulated arc therapy; 3D-CRT, 3D conformal radiotherapy; 5F-IMRT, 5-field intensity-modulated radiotherapy; EUD, equivalent uniform dose; V_{40}, percentage volume that received >40 Gy.

Table VI. Incidental nodal irradiation dose for lower-thoracic EC.

	110		112ao		112pul-R		112pul-L	
Variable	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %	EUD, Gy	V_{40}, %
VMAT	54.3±0.8	86±13	60.6±0.5	97±11	50.3±0.4	72±23	46.9±0.5	62±16
5F-IMRT	53.8±0.4	84±14	52.8±0.9	88±23	42.3±0.3	58±14	37.2±0.3	38±21
3D-CRT	53.4±0.3	83±27	44.2±1.0	65±17	35.3±0.2	40±20	30.5±0.7	33±12
P-value	0.640	0.870	0.001	0.001	0.002	0.004	0.015	0.008

Data are presented as the mean ± standard deviation EC, esophageal cancer; VMAT, volume-modulated arc therapy; 3D-CRT, 3D conformal radiotherapy; 5F-IMRT, 5-field intensity-modulated radiotherapy; EUD, equivalent uniform dose; V_{40}, percentage volume that received >40 Gy.

Figure 1. Lymph nodal stations received incidental irradiation doses in upper-thoracic EC for three treatment plans. The 3D-CRT plan resulted in higher EUD values for incidental nodal irradiation. EC, esophageal cancer; VMAT, volume-modulated arc therapy; 3D-CRT, 3D conformal radiotherapy; 5F-IMRT, 5-field intensity-modulated radiotherapy; EUD, equivalent uniform dose.

Figure 2. Lymph nodal stations received incidental irradiation doses in middle-thoracic EC for the three plans. The 5F-IMRT and VMAT plans resulted in relatively higher EUD values compared with the 3D-CRT plan in incidental nodal irradiation. EC, esophageal cancer; VMAT, volume-modulated arc therapy; 3D-CRT, 3D conformal radiotherapy; 5F-IMRT, 5-field intensity-modulated radiotherapy; EUD, equivalent uniform dose.

Figure 3. Lymph nodal stations received incidental irradiation doses in lower-thoracic EC for the three plans. The VMAT plan exhibited higher EUD values compared with the 5F-IMRT and 3D-CRT plans in incidental nodal irradiation. EC, esophageal cancer; VMAT, volume-modulated arc therapy; 3D-CRT, 3D conformal radiotherapy; 5F-IMRT, 5-field intensity-modulated radiotherapy; EUD, equivalent uniform dose.

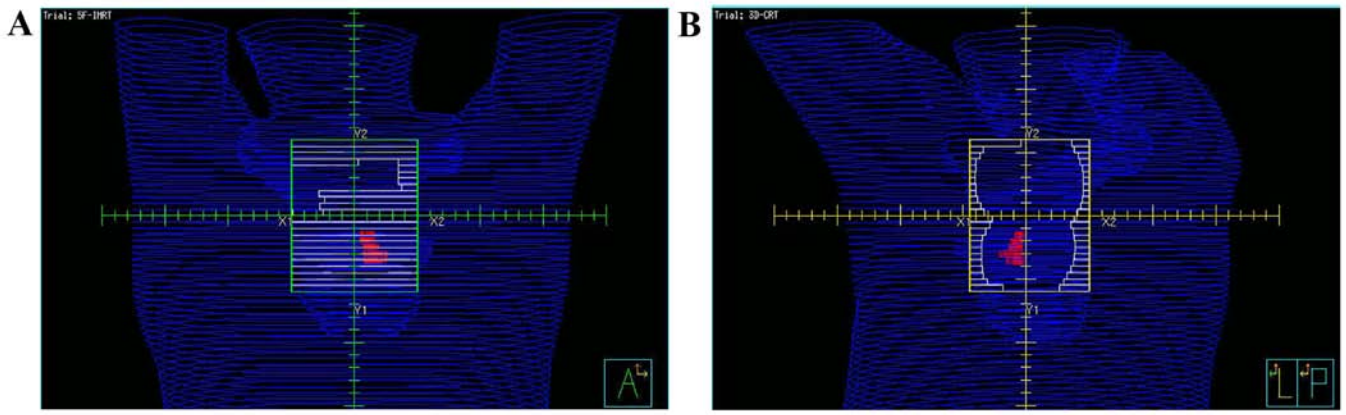

Figure 4. Segments of 3D slices. Segments of 3D slices in the (A) 5F-IMRT and (B) 3D-CRT plans. 5F-IMRT used multiple segments to generate a steeper fall-off dose and 3D-CRT used conventional conformal fields. The red structure indicates the NO 106Pre node. 3D-CRT, 3D conformal radiotherapy; IMRT, 5-field intensity-modulated radiotherapy.

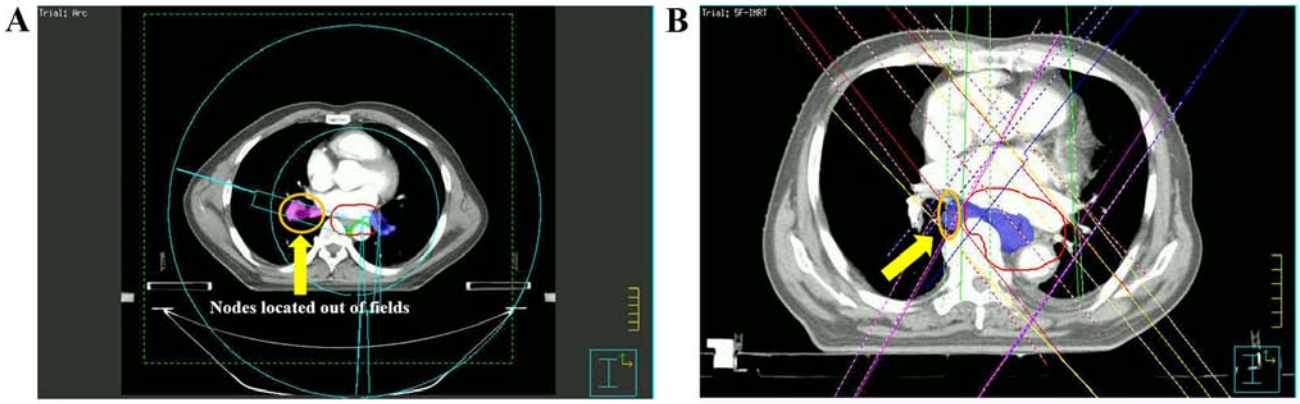

Figure 5. Nodes located outside of the fields. Nodes located out of fields received incidental nodal irradiation using (A) VMAT and (B) 5F-IMRT techniques. The red structure is the planning target volume, and the blue and pink structures are nodes. VMAT, volume-modulated arc therapy; 5F-IMRT, 5-field intensity-modulated radiotherapy.

nodes are out of the field of irradiation and using conventional conformal beams does not obtain the desired incidental irradiation dose (Figs. 2 and 3). This may be explained by the fact that IMRT and VMAT use multiple segments and therefore, doses delivered to lymph nodes are lower compared with those delivered by 3D-CRT due to the steeper dose fall-off achieved with IMRT or VMAT. Due to the location of NO 105 and 106 they are in the field of radiation, therefore the modulated method of 3D-CRT has an advantage for incidental irradiation dose in upper-thoracic EC (Fig. 4). The 5F-IMRT and VMAT plans demonstrated almost equal mean EUD values in middle-thoracic EC, and the VMAT plan resulted in greater incidental nodal irradiation in lower-thorax EC.

The incidental nodal irradiation dose is associated with treatment technique, beam arrangement, number of beams and esophageal tumor length, volume and location. Using different treatment units may influence its contribution to incidental nodal irradiation (Fig. 5). Reports also demonstrate that the larger the area of thoracic EC, the higher the risk of lymph node metastasis (30,31). In the present study, the length of tumors was 3.00-13.3 cm and lymph nodes received relatively high incidental irradiation doses. Further studies are required to determine if controlling metastasis or recurrence in nodal regions is influenced by the effect of incidental irradiation in the treatment of thoracic EC.

The present study was a retrospective analysis of patients with $T_{1\text{-}3}N_0M_0$ stage thoracic EC receiving treatment at the Hangzhou Cancer Hospital. All of the dosimetric metrics for target volume, OARs and incidental nodal irradiation were collected from DVHs. The true dose distribution for patients during irradiation may be different from simulation on TPS, due to organ motion, scattering and leaking of radiation from leaf pairs. IMRT and VMAT should be performed with caution in the course of treatment, particularly for out-of-field lymph nodes. The incidental nodal radiation generated by IMRT or VMAT warrants further investigation and discussion.

In summary, the present study demonstrated that VMAT was comparable to 5F-IMRT in regards to the dosimetric characteristics of planning. Further, incidental nodal irradiation doses to thoracic nodal levels NO 105-112 are considerable for thoracic EC, which may have an impact on the control of metastasis and recurrence in nodal regions.

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Availability of data and materials

The data sets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

NZ, SXW and JHW contributed to the conception of this study and performed preliminary experimentation. NZ and MG were responsible for enrolling patients in the study, performing clinical diagnoses and collecting clinical data. All authors participated in the statistical analysis, contributed to the interpretation of the results and manuscript writing. All authors reviewed the data and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Medical Ethics Committee of Hangzhou Cancer Hospital (Hangzhou, China) and written informed consent was obtained from all patients.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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