Volume 22, No 2 | International Journal of Radiation Research, April 2024

Dosimetric comparison of different radial and longitudinal margins for tomotherapy in esophageal cancer

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► ***Original article***

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Received: May 2023
Final revised: October 2023
Accepted: November 2023

Int. J. Radiat. Res., April 2024; 22(2): 387-393

DOI: 10.61186/ijrr.22.2.387

Keywords: *Esophageal cancer, tomotherapy, margins, radiation dosimetry.*

ABSTRACT

Background: This paper aimed to investigate the radiation dosimetry and dose deposition to the surrounded organs at risk (OARs) with different radial and longitudinal margins based on the normal tissue complication probability (NTCP) and dose-volume histogram (DVH) methods. ***Materials and Methods:*** Fifteen patients with histologically diagnosed esophageal cancer were retrospectively selected. From the clinical target volume (CTV), eight planning target volumes (PTV) were expanded for each patient, with one group of four radial margins (3mm, 5mm, 7mm, 10mm) and the other group of four longitudinal margins (3mm, 5mm, 7mm, 10mm). Then, eight plans with the prescription dose of 50.4Gy were designed in the tomotherapy system. Within each group, doses for the OARs and NTCP-based risk of pneumonitis and pericardial disease were compared. ***Results:*** Almost all the dose parameters in both groups, except for the Dmax (maximum dose) of the spinal cord in the longitudinal direction, showed significant linearly increasing trends with the expansion of margins. For same dose parameters, the increased slopes in the radial direction were larger than those in the longitudinal. Heart V30Gy (the percent volume of receiving 30Gy) grew fastest compared to other clinical constraint indexes in both groups, and the most significant difference in the risk of pneumonitis was observed in the radial group when the margin was expanded from 3 to 10mm. ***Conclusions:*** In order to lower the likelihood of radiation-related toxicity, radial margin expansion should be more strictly controlled in the radiotherapy of esophageal cancer with tomotherapy.

INTRODUCTION

Esophageal cancer is one of most common cancer-related deaths all over the world, presenting a poor survival rate of 21% [1]. Definitive chemoradiotherapy remains the standard treatment modality for patients unfit for surgery [2-4]. In the radiotherapy (RT) of esophageal cancer, organs at risk (OARs) including the spinal cord, heart, and lungs surround the planning target volume (PTV), making an appropriate PTV is necessarily important to ensure locoregional control and lower toxicity [5, 6].

Generally, PTV is expanded from the clinical target volume (CTV) with safety margins to allow for daily set-up variations and organ motions [7-10]. For instance, Boekhoff *et al.* analyzed the dosimetric effects of the tumor's daily translations and suggested the smallest margins of 8mm in posterior and right, 9mm in anterior and superior, and 10mm in left and inferior directions separately [8]. Voncken *et al.* found the largest organ motion amplitude in the cranio-caudal (CC) direction, and suggested an 11 mm expansion margin while the left-right (LR) is 8mm and anterior-posterior (AP) is 7mm, respectively [9]. Hoffmann *et al.* claimed an 8mm margin in radial (LR & AP) direction and 11mm in longitudinal (CC) direction separately to account for organ motions and uncertainties [10]. All these studies demonstrated distinct motion in the longitudinal compared to the radial direction. However, using a uniform larger margin to cover the maximum uncertainty in every direction may result in overexposure to OARs. Differentiated radial and longitudinal expansion margins may reduce the target volume, thereby lowering the radiation-related toxicity.

Helical tomotherapy is a rotational intensity-modulated radiotherapy (IMRT) technology that equipped with daily megavoltage computed tomography (MVCT) imaging with sharp dose gradients [11-13]. Recent research indicated it as a better option of RT for its superior performance to volumetric-modulated arc therapy (VMAT) or IMRT [14-16]. Guo *et al.* found that tomotherapy plans could achieve superior homogeneity and conformity, and led to dose reduction to OARs compared to IMRT plans for cervical cancer [14]. Wang *et al.* claimed that compared with VMAT and IMRT, tomotherapy not only had superior homogeneity and conformity but could also reduce the specified dose parameters for the lungs in esophageal cancer [15]. Gu *et al.* preferred tomotherapy to IMRT plan in esophageal cancer for its better conformity and homogeneity, and dose sparing of lungs V_{20Gy} (the percent volume of receiving 20Gy), heart V_{30Gy} (the percent volume of receiving 30Gy), V_{40Gy} (the percent volume of

[DOI: 10.61186/ijrr.22.2.387]

receiving 40Gy) as well as its max dose of the spinal cord from 41.66Gy to 40.22Gy [16].

Furthermore, the tomotherapy system features three field widths of 1cm, 2.5cm, and 5cm in the longitudinal direction, while the radial direction width can reach up to 40cm and is modulated by multi-leaf collimator (MLC). Based on the field width differences of the machine and the motion amplitude differences of the esophageal cancer target in the longitudinal and radial directions, the dosimetric differences of the target expansion should be separately evaluated in both directions.

To this end, the CTV with different margins was hereby separately expanded in the radial and longitudinal directions, and all plans in the tomotherapy system were optimized. The dosimetric impact and risk of complications of margin expansion in different directions were then assessed. By doing so, not only the margin contributions to the OARs were estimated, but the change trend differences of dose parameters in both directions were also figured out. To our knowledge, this is the first work that analyzed the dosimetric impact of different expanded radial and longitudinal margins in esophageal cancer RT with tomotherapy based on the tomotherapy properties and target motion characteristics. The margin of CTV to PTV derived from this method will better reflect the necessary expansion and could be used for OARs protection.

MATERIALS AND METHODS

Patients and simulation

Herein, fifteen consecutive esophageal cancer patients who were histologically confirmed middle and upper squamous cell carcinoma (SCC) of the esophagus between 2017 and 2022 in our hospital were retrospectively selected. The study was approved by the ethics committee of Chongqing University Cancer Hospital (Ethical code: CZLS2023037-A, date: 28 Feb 2023). Table 1 lists characteristics of all patients. Patients were asked to breathe gently before being scanned head-first with their arms raised above their heads in the supine position. A vacuum pad and thermoplastic mask were used to fix the body. The patients then underwent computed tomography (CT) simulation with the Philips Brilliance™ 16-slice big bore CT scanner (Philips, Amsterdam, Netherlands). At the end of the simulation, we placed three tattoos on the patients' thermoplastic mask approximately at the center of the gross tumor volume (GTV) for patient alignment or isocenter setup. A slice thickness of 3mm CT scan data was adopted for treatment planning.

Delineations

The CT datasets were transferred to a commercial treatment-planning system (Eclipse 13.6, Varian Medical Systems, and Palo Alto, California, USA). The GTV was delineated on the axial CT images by one certified radiation oncologist with the aid of markers and all resources available. The CTV included the GTV as well as 0.8-1.0 cm radial and 3cm (at least) longitudinal margins to the GTV. From the CTV, eight PTVs were expanded for each patient, divided into one group of four radial margins (3mm, 5mm, 7mm, 10mm) and the other group of four longitudinal margins (3mm, 5mm, 7mm, 10mm). In each group, only the margin in this direction was expanded. All the OARs were contoured by the same radiation oncologist. The images and structure sets were then transferred to the tomotherapy planning station following the DICOM-RT protocol.

Table 1. Clinical characteristics of the study population.

Characteristics		Full cohort (n = 15)	
		n	%
Number of patients		15	
Age	Mean	67.73±8.24	
	Range	54-87	
Clinical T stage	T2	2	13.3
	T3	6	40
	T4	7	46.7
Clinical N stage	N0	5	33.3
	N1	4	26.7
	N2	6	40
Clinical M stage	M0	14	93.3
	M1	1	6.7

Abbreviations: TNM= Tumor Node and Metastasis. Classification of the clinical stage was based on the seventh edition of the TNM classification for esophageal cancer.

Treatment planning

All of the plans were optimized in tomotherapy (TomoHD™2.1.2, Accuray, USA) system with the prescription dose of 50.4Gy in 28 fractions for the PTV. 95% of the PTV was covered by the prescription dose at least. All the plans were optimized with modulation factor (3), pitch (0.287), and jaw width (2.5cm). The OARs constraints for all the plans are listed in table 2. Dosimetric parameters of the OARs among different margins were independently compared in each group, and the absolute maximum dose (D_{max}), mean dose (D_{mean}), and relative dose parameters V_{5Gy}-V_{30Gy}, V_{40Gy} were analyzed. V_{5Gy}, V_{10Gy}, V_{15Gy}, and V_{25Gy} were defined as the percent volume of receiving 5Gy, 10Gy, 15Gy, and 25Gy of the lungs as well as heart in all plans, respectively. As for the spinal cord, only the D_{max} was compared.

Table 2. Dose constraints of the OARs.

Organs	Dose constraints
Lungs (left and right included)	V_{5Gy}<60%
	V_{20Gy}<30%
	V_{30Gy}<20%
	D_{mean}<15Gy
Heart	V_{30Gy}<40%
	V_{40Gy}<30%
	D_{mean}<26Gy
Spinal cord	D_{max}<45Gy

Abbreviations: V_{5Gy}, V_{20Gy}, V_{30Gy}, andV_{40Gy} represent percent volume of receiving 5Gy, 20Gy, 30Gy, and 40Gy; Dmean: mean dose; Dmax: max dose.

[DOI: 10.61186/ijrr.22.2.387]

Normal tissue complication probability (NTCP)

In our study, we estimated the complication probability of normal tissue based on the dose-volume histogram (DVH). The widely-used Niemierko NTCP model was hereby adopted, and the clinical effects of the dose differences for lungs and heart in all plans were evaluated [17], as shown in equation (1).

$$NTCP = \frac{1}{1+\left(\frac{TD_{50}}{EUD}\right)^{4\gamma_{50}}} \quad (1)$$

where, the EUD indicates the uniform dose that has the same radiobiological effect as the investigated inhomogeneous dose distribution, TD_{50} denotes the dose to the whole organ (reference volume) which leads to a complication probability of 50% while γ_{50} specifies the dose-response curve slope for the interest of normal tissue or tumor and is unit-less.

Statistics

All the measurement results are listed in the mean±standard deviation (SD) form. The Statistical Package for the Social Sciences version 25.0 (SPSS, IBM Corp, NY, USA) was utilized for statistical analysis. The paired sample t-test was conducted to calculate the *p*-value and assess the differences between PTVs, and $p<0.05$ considered to be significant.

RESULTS

Figure 1 demonstrates an example of dose distribution in the transverse plane of different PTVs for a patient. The adjacent OARs dosimetric parameters (assessed from the plan DVH) and the comparisons are summarized in detail in tables 3 and 4. The scatter plots of the dose parameter change trends with margin expansion and correlation coefficients (R^2) are presented in figure 2. To assess the dosimetric influences of margin expansion, a comparison was conducted within the group.

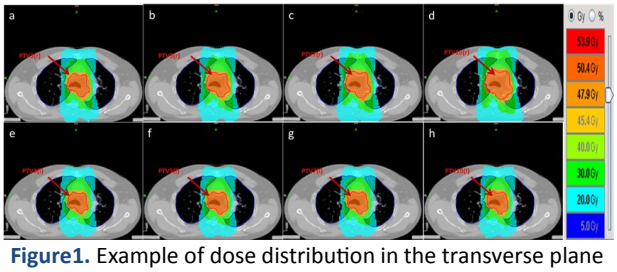

Figure1. Example of dose distribution in the transverse plane of different PTVs for a patient with esophageal cancer using tomotherapy. a-d: PTV3(r), PTV5(r), PTV7(r), PTV10(r), PTV with radial margin expansion of 3mm,5mm,7mm,10mm; e-h: PTV3(l), PTV5(l), PTV7(l),PTV10(l), PTV with longitudinal margin expansion of 3mm,5mm,7mm,10mm.

Radial group

Table 3 shows all of the PTVs and corresponding dose parameters for the spinal cord, lungs, and heart in the radial margins group. The D_{max} of the spinal cord increased as the margin grew, and dose parameters for the lungs and heart (D_{mean}, V_{5Gy}-V_{30Gy}, V_{40Gy}) increased in the same way as the spinal cord.

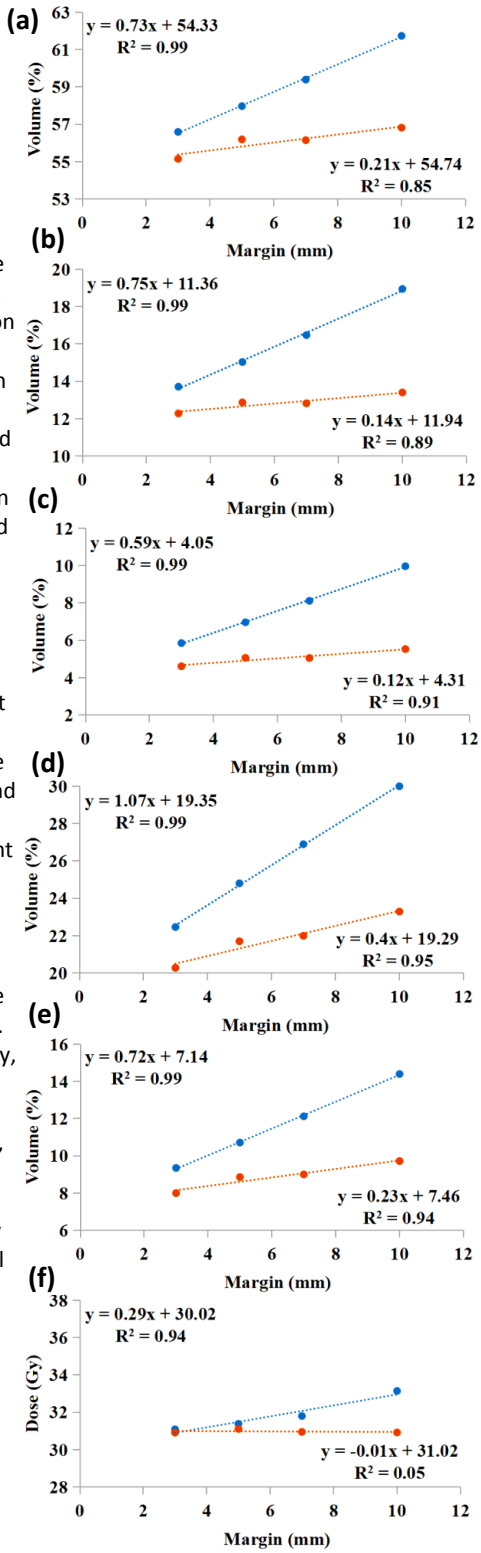

Figure 2. The scatter plots and correlation coefficients (R2) between margin expansion and dose parameters in the radial and longitudinal groups. The blue lines represent radial data (The linear fit results are shown at the upper left.) and the orange lines represent longitudinal data (The linear fit results are shown at the lower right.). **(a)** Lungs V5Gy, **(b)** lungs V20Gy, **(c)** lungs V30Gy, **(d)** heart V30Gy, **(e)** heart V40Gy and **(f)** spinal cord Dmax.

Scatter plots for the lungs V_{5Gy}, V_{20Gy}, V_{30Gy}, heart V_{30Gy}, V_{40Gy} and D_{max} of the spinal cord are depicted in figure 2. Significant positive linear relationship correlations were found between the margin expansion and dose parameters increase ($R^2 \geq 0.94$). The heart V_{30Gy} grew at the fastest rate (k=1.07). V_{5Gy}, V_{20Gy} of the lungs, and V_{40Gy} of the heart all grew at

[DOI: 10.61186/ijrr.22.2.387]

roughly the same rate (k=0.73, 0.75, 0.72). The increased V_{30Gy} slope in the lungs was relatively flat, and k was only 0.59. With k values less than 0.3, the D_{max} of the spinal cord increased the slowest. In general, lower dose-volume parameters grew faster than higher ones. V_{5Gy}>60% was discovered when the margin was expanded to 10mm. According to the changing trend of the dosimetric parameters, larger margins (>10mm) might cause the clinical constraints to be exceeded. When comparing margins 3 to 10mm, a 5% dose increase for the lungs V_{5Gy}, V_{20Gy}, and 7% for the heart V_{30Gy} could be observed. About 2Gy increase could be seen in D_{max} of the spinal cord, D_{mean} of the lungs, and heart. Besides, the dose parameters among each other were compared and all the p<0.05, which suggested the significant influence of margin expansion in the radial direction on the adjacent OARs.

Table 3. Dose parameters for the radial margin group.

	PTV3(r)	PTV5(r)	PTV7(r)	PTV10(r)
Spinal cord				
D_{max}	31.09±1.75	31.38±1.86	31.80±1.72	33.14±2.36
Lungs				
V_{5Gy} (%)	56.59±7.79	57.97±7.61	59.40±8.38	61.73±8.56
V_{10Gy} (%)	37.99±7.87	39.74±7.72	41.43±8.03	44.04±8.06
V_{15Gy} (%)	22.54±6.20	24.23±6.31	26.09±7.24	29.34±7.93
V_{20Gy} (%)	13.71±3.95	15.03±3.95	16.47±4.40	18.94±5.00
V_{25Gy} (%)	9.09±3.01	10.27±3.08	11.49±3.33	13.53±3.69
V_{30Gy} (%)	5.85±2.17	6.96±2.37	8.11±2.57	9.96±3.02
V_{40Gy} (%)	2.24±0.99	2.88±1.16	3.54±1.33	4.82±1.71
D_{mean} (Gy)	10.01±1.74	10.56±1.78	11.14±1.95	12.13±2.12
Heart				
V_{5Gy} (%)	77.89±23.81	78.33±23.87	78.80±23.70	79.39±23.60
V_{10Gy} (%)	68.58±24.38	69.80±24.57	70.87±24.65	72.07±24.65
V_{15Gy} (%)	57.75±22.79	60.14±23.36	62.09±23.85	64.55±24.32
V_{20Gy} (%)	45.47±19.64	48.19±20.15	50.68±20.75	54.07±21.73
V_{25Gy} (%)	32.86±15.14	35.68±15.90	38.07±16.37	41.63±17.61
V_{30Gy} (%)	22.46±10.69	24.80±11.66	26.89±12.19	29.99±13.22
V_{40Gy} (%)	9.35±4.78	10.71±5.42	12.12±5.98	14.39±6.96
D_{mean} (Gy)	19.09±6.83	19.95±7.00	20.74±7.18	21.85±7.48

Abbreviations: V_{10Gy}, V_{15Gy}, V_{25Gy} represent percent volume of receiving 10Gy, 15Gy, 25Gy.

Table 4. Dose parameters for the longitudinal margin group.

	PTV3(l)	PTV5(l)	PTV7(l)	PTV10(l)	p^{3-5}	p^{3-7}	p^{3-10}	p^{5-7}	p^{5-10}	p^{7-10}
Spinal cord										
D_{max}	30.91±1.60	31.11±1.70	30.95±1.61	30.92±1.57	**0.09**	**0.511**	**0.84**	0.023	0.03	**0.363**
Lungs										
V_{5Gy} (%)	55.15±7.46	56.19±7.52	56.15±7.63	56.82±7.62	<0.001	<0.001	<0.001	**0.636**	0.001	<0.001
V_{10Gy} (%)	35.88±7.77	36.92±7.84	36.90±7.95	37.64±7.96	<0.001	<0.001	<0.001	**0.695**	<0.001	<0.001
V_{15Gy} (%)	20.62±5.68	21.41±5.92	21.41±6.05	22.09±6.14	<0.001	<0.001	<0.001	**0.972**	<0.001	<0.001
V_{20Gy} (%)	12.28±3.76	12.87±3.86	12.82±3.88	13.40±3.97	<0.001	<0.001	<0.001	0.035	<0.001	<0.001
V_{25Gy} (%)	7.77±2.81	8.26±2.94	8.24±2.91	8.74±3.03	<0.001	<0.001	<0.001	**0.124**	<0.001	<0.001
V_{30Gy} (%)	4.61±1.94	5.06±2.06	5.05±2.06	5.53±2.20	<0.001	<0.001	<0.001	**0.773**	<0.001	<0.001
V_{40Gy} (%)	1.67±0.84	1.90±0.96	1.89±0.96	2.13±1.07	<0.001	<0.001	<0.001	**0.379**	<0.001	<0.001
D_{mean} (Gy)	9.43±1.66	9.70±1.67	9.70±1.69	9.96±1.70	<0.001	<0.001	<0.001	**0.888**	<0.001	<0.001
Heart										
V_{5Gy} (%)	79.56±23.19	81.62±22.25	82.60±21.61	85.07±20.31	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
V_{10Gy} (%)	69.16±23.75	71.55±23.45	72.72±23.15	75.23±22.65	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
V_{15Gy} (%)	56.63±21.89	59.18±21.96	60.19±21.77	62.98±21.97	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
V_{20Gy} (%)	43.29±18.57	45.63±18.85	46.34±18.77	48.60±19.03	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
V_{25Gy} (%)	30.44±14.06	32.25±14.41	32.70±14.37	34.45±14.60	<0.001	<0.001	<0.001	0.001	<0.001	<0.001
V_{30Gy} (%)	20.28±9.68	21.70±10.06	21.99±10.01	23.29±10.31	<0.001	<0.001	<0.001	0.017	<0.001	<0.001
V_{40Gy} (%)	8.00±4.01	8.86±4.28	9.00±4.28	9.72±4.46	<0.001	<0.001	<0.001	**0.064**	<0.001	<0.001
D_{mean} (Gy)	18.63±6.39	19.41±6.39	19.72±6.22	20.48±6.27	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Abbreviations: 3-5, 3 mm margin vs. 5 mm margin, 3-7, 3 mm margin vs. 7 mm margin, 3-10, 3 mm margin vs. 10 mm margin, 5-7, 5 mm margin vs. 7 mm margin, 5-10, 5 mm margin vs. 10 mm margin, 7-10, 7 mm margin vs.10 mm margin.

Table 5. NTCP of lungs and heart for radial and longitudinal margin groups.

		PTV3	PTV5	PTV7	PTV10	p^{3-5}	p^{3-7}	p^{3-10}	p^{5-7}	p^{5-10}	p^{7-10}
Radial group	Lungs	0.001±0.001	0.002±0.002	0.003±0.003	0.006±0.006	<0.001	0.002	0.001	0.007	0.002	0.001
	Heart	0.001±0.001	0.002±0.001	0.002±0.002	0.004±0.003	0.001	0.001	0.001	0.001	0.001	0.001
Longitudinal group	Lungs	0.001±0.001	0.001±0.001	0.001±0.001	0.001±0.001	0.001	0.001	0.001	**0.132**	0.001	<0.001
	Heart	0.001±0.001	0.001±0.001	0.001±0.001	0.001±0.001	0.001	0.001	0.001	0.009	0.001	0.001

Abbreviations: PTV3, PTV5, PTV7, PTV10 represent PTV with margin expansion of 3mm,5mm,7mm,10mm.

[DOI: 10.61186/ijrr.22.2.387]

Longitudinal group

Dose parameters in the longitudinal groups are showed in table 4. In this group, the spinal cord D_{max} did not necessarily increase with the increase of the margin. Smaller D_{max} values could be observed in larger margins. $p<0.05$ could only be found when comparing 5 and 7mm, 5 and 10mm margins. All the dose parameters for lungs (D_{mean}, V_{5Gy}-V_{30Gy}, V_{40Gy}) increased with the margin growth except for comparing 5 and 7mm margins ($p>0.05$ except V_{20Gy}). All dose parameters increased as the margin grew in the heart.

Figure 2 depicts scatter plots of key dose parameters for the lungs, heart, and spinal cord. In this group, all dose parameters increased more flatly compared with the radial group. Compared to the heart, the lungs dose parameters increased rather slowly, with a maximum k value of 0.21 and less obvious linear relationship correlations ($R^2 \leq 0.91$). The maximum increase was less than 2% when the margin was expanded to 10mm. Similar to the radial group, a significant linear correlation could be observed between heart dose parameters and margin expansion, but the growth trend was flatter, with k values no more than 0.4. The D_{max} of the spinal cord did not follow a linear trend, R^2 was only 0.05, and there existed no obvious change in regularity.

Complications

The most common radiation-related toxicities to the lungs and heart are generally pneumonitis and pericardial disease [18-21]. Table 5 shows the NTCP for the lungs and heart. Significant variations ($p<0.05$) for the likelihood of pneumonitis and pericardial disease with margin expansion in the radial group were observed. Except for the risk of pneumonitis when comparing 5 with 7mm margins ($p=0.132$), a significant tendency to increase the risk of pericardial disease and pneumonitis in the longitudinal group. Meanwhile, the most significant risk of pneumonitis difference could be seen between the 3 and 10mm margins in the radial group.

DISCUSSION

It is widely acknowledged that tomotherapy system has three longitudinal field widths to choose from, while the width can reach up to 40cm and is modulated by MLC in the radial direction. Furthermore, numerous studies have revealed the radial and longitudinal motion amplitude differences for esophageal cancer targets. Based on the properties of the machine and the motion characteristics of the target, the dosimetric differences and dose deposition to the OARs in both directions were hereby separately investigated.

As far as we know, this is the first investigation for dosimetric impact of different radial and longitudinal margins in esophageal cancer RT with tomotherapy. Vošmik *et al.* generated the PTV by expanding the CTV with uniform 10mm margin in the RT of esophageal cancer without considering the motion characteristics of the target, which might be too conservative and thus result in over-irradiation of the OARs [7]. Katsuta *et al.* generated 7 mm margin in AP and LR direction, and a 15 mm margin in the CC direction around CTV to account for organ motions and uncertainties [22]. This very expansion manner was consistent with that proposed in the present study. Münch *et al.* found that the reduction of longitudinal margins could lower the dose deposition to lungs and heart in esophageal cancer significantly [23]. The conclusion was slightly different from what was hereby found, most likely because none of them had a margin difference of less than 1cm.

In the radial margin group, possibly given the target expansion in the radial direction being physically closer to the surrounding OARs or even having more overlaps, almost all the evaluated parameters showed a different level of increase with the expansion of margins. Besides, it should be noted that a 10mm expansion might exceed the clinical constraint, for $V_{5Gy}>60\%$ were observed. Other evaluated parameters were within clinical limits, which could be attributed to the small tumor size and single-direction margin expansion.

Dose parameters in the longitudinal group, on average, had a slower increase rate than those in the radial group. When compared to the lungs, the heart parameters showed more obvious increases, which was most likely attributed to anatomical location. When the margin grew, the PTV reached the lower thorax, and more heart slices were involved and exposed.

At the same time, it should be noted that there was little change in the dose parameters for the lungs when comparing the 5 and 7mm margins. This could result from the target in the radial section hardly changing although the length was expanded. The spinal cord D_{max} did not necessarily increase as the margin increased, which might be attributed to the approximately unchanged distance from the target to the spinal cord during margin expansion. Besides, all the dose parameters could meet the clinical constraints. By comparing the change trends of dose parameters between the two groups, it was found that margin expansion in the radial group had a greater impact on OARs.

Regarding the lungs, V_{20Gy} and D_{mean} are commonly associated with pneumonitis and are used in clinical practice most commonly [24-27]. Inoo *et al.* considered that $V_{20Gy}\geq 20\%$ was associated with radiation pneumonitis [25], while Tonison *et al.* recommend limiting the V_{20Gy} below 23% to keep the risk of symptomatic pneumonitis below 10% [26]. Luna *et al.* demonstrated that lungs $V_{20Gy}>27.4\%$, $D_{mean}>15.4$Gy, $V_{10Gy}>36.3\%$, and $V_{5Gy}>43.6\%$ consistently

[DOI: 10.61186/ijrr.22.2.387]

predicted the presence of radiation pneumonitis [27]. All these studies provided the clinicians with valuable guidance to accept dosimetric cut-offs in plan evaluation to lower pneumonitis development possibility. In this study, dose parameters were found to generally increase with margin expansion, and a larger margin was frequently associated with a higher V_{20Gy}, D_{mean}, etc., which increased the risk of radiation pneumonitis. Fortunately, with routine daily set-up correction by MVCT scan in tomotherapy treatments, it should be reasonable to expand smaller PTV margins. Boekhoff *et al.* concluded that the intrafraction motion were 7.7cm, 2.1cm, and 2.4cm in CC, LR and AP directions, respectively [28]. Smaller margins (3 or 5mm) seemed to be sufficient to cover the tumor, and the risk of pneumonitis could thus be lowered significantly.

Dose parameters correlated with pericardial disease have been reported in several previous researches [29-32]. Goldoost *et al.* found a significant correlation between the cardiac function and heart V_{30Gy} [31]. Wang *et al.* recommend that D_{mean} of the heart, particularly<15Gy, was associated with reduced grade 3 or higher cardiac events [32]. By reducing the longitudinal margin to 5-7mm, dose parameters and the corresponding risk of the pericardial disease could be significantly lowered compared to 10mm.

However, the current study is still subject a few weaknesses. First, the small patient cohort from a single institution may be insufficient to reveal the significance of the comparisons of dosimetric parameters. Second, differences will inevitably be introduced when the plan is re-optimized following the PTV replacement. Although the deviation was not completely controlled during optimization, attempts were made to keep other parameters constant to obtain more accurate results. At last, the patients' movements during treatment or tumor changes over the course were not taken into account. Based on daily MVCT image records, adaptive radiotherapy (ART) was proposed as a feasible next step in this study.

CONCLUSION

In the radiotherapy of esophageal cancer with tomotherapy, radial expansion should be more strictly controlled for higher increase slopes. With routine daily set-up correction by MVCT, smaller margins may be feasible for upper and middle esophageal cancer, thus lowering the risk of pneumonitis and pericardial disease.

ACKNOWLEDGMENT

We would like to thank the patients who contributed to our work.

***Ethical consideration*:** The study was approved by the ethics committee of Chongqing University Cancer Hospital (Ethical code: CZLS2023037-A, date: 28 Feb 2023).

***Founding*:** This work was supported by Natural Science Foundation Project of China [grant number 11575038] and Natural Science Foundation Project of Chongqing [grant number cstc2021jcyj-msxmX0441].

***Conflicts of interest*:** The authors declare no conflicts of interest.

***Author contribution*:** F.J. and X.T. designed the conception of this study; Material and data were collected and analyzed by X.T., Z.S., S.W., X.L. and H.L.; the manuscript was drafted by X.T. and F.J.; and all authors reviewed and approved the final manuscript.

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[DOI: 10.61186/ijrr.22.2.387]