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Scientific Article

Esophageal motion characteristics in thoracic esophageal cancer: Impact of clinical stage T4 versus stages T1-T3

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Abstract

Purpose: The main purpose was to investigate the differences of the esophageal motion (EM) and the internal target volume (ITV) margins for the esophagus between clinical T1-T3 (cT1-T3) and cT4 cases, using 4-dimensional computed tomography. A secondary purpose was to assess the metastatic lymph nodal motion (NM) and the ITV margins for lymph nodes (LNs) using the datasets of patients with nodal involvement pathologically defined.

Methods and materials: We analyzed patients with thoracic esophageal cancer consecutively treated with definitive chemoradiation, measuring the EM and the ITV margins in the left-right, anteroposterior, and superoinferior directions. All esophageal contours were divided at the carina. The EM and NM were measured from the displacement of the centroid point between 0% images (at the end of inhalation) and 50% images (at the end of exhalation). The ITV margins were defined as the maximum distance in each direction from the clinical target volume at the 4-dimensional computed tomography average images to the intersection of the clinical target volume at the 0% and 50% images of complete coverage in each patient.

Results: The EM below the carina in cT4 was significantly smaller than that in cT1-T2 in all directions ($P < .01$) and than that in cT3 in all directions (left-right: $P = .03$, anteroposterior and superoinferior: $P < .01$). The EM in the case of a cT4 tumor located below the carina was smaller than that in the case of cT4 tumor located above the carina. The NM of abdominal-LNs was much larger than that of cervicothoracic-LNs and the EM below the carina. These tendencies were similar in the ITV measurements.

Conclusions: The EM and the ITV margins in cT4 were significantly smaller than those in cT1-T3. The NM and the ITV margins of abdominal LNs were much larger than those of cervicothoracic LNs and the esophagus. In clinical radiation therapy planning for esophageal cancer, we should take cT stage into consideration.

Conflicts of interest: None.

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Introduction

In chemoradiation therapy (CRT) for esophageal cancer, the accurate definition of radiation treatment (RT) fields is crucial because the esophagus is a typical intrathoracic mobile organ because of the physiological motion caused by respiration, cardiac activity, and esophageal peristalsis.[1] CRT plays an important role in definitive and preoperative treatments for esophageal cancer.[2,3] Unnecessarily large radiation therapy (RT) fields increase the risk of radiation pneumonitis and pericarditis in esophageal cancer treated with CRT.[4] When needlessly large margins are added to the clinical target volume (CTV) for patients with large primary tumor such as in clinical T4 (cT4) cases, high-grade radiation toxicities may be induced by CRT. However, a definition of the minimum necessary margins for esophageal cancer treated with CRT has not been established.

In RT planning for esophageal cancer, the CTV is often defined as esophageal tumor and the partial esophagus with a possible subclinical spread, but these are not clearly distinguished from each other by gastroesophageal endoscopy, fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT), and other image inspections. The tendencies of esophageal cancer for submucosal skip metastases or multicentric focal disease result from tumor spread to the intramural lymphatic plexuses, which is lacking in the superficial mucosa.[5] In 52% of a series of patients with advanced esophageal cancer, the length of the primary esophageal tumor was >5 cm.[2] In RT planning for esophageal cancer, the margins in the superoinferior (SI) direction were often defined as 5 cm from primary tumor.[2,6] The length of the RT fields is frequently longer than at least 15 cm. The length of the thoracic esophagus is approximately 22 cm as described in the International Union Against Cancer classification (6th edition), and thus the length of the RT field is commonly more than one-half of the thoracic esophagus in many locally advanced cases. For these reasons, we investigated the characteristics of the esophageal motion (EM) and the internal target volume (ITV) margins for the esophagus in a field that is sufficiently long. Cohen et al[7] also evaluated the inter-/intrafraction EM of esophageal cancer patients to account for microscopic tumor spread and skip metastases.

The ITV is defined as the CTV plus the ITV margins to account for physiological motion induced by respiration and cardiac activity.[8] The RT fields are determined by the planning target volume, which is defined as the ITV plus the setup margin.[8] Image guided radiation therapy has technically achieved minimization of the setup margin, and thus the optimization of the ITV margin is an important factor in the determination of the planning target volume. Four-dimensional CT (4DCT) is one of the most important techniques to determine the ITV margin for RT planning.[9] Several studies that reported on esophageal tumor motion using 4DCT have been published.[10-16] In those studies, however, the influence of esophageal tumor invasion was not discussed.

Patel et al[11] recommended that different ITV margins should be applied between esophageal tumor and lymph nodes (LNs). Although they used the images of FDG-PET/CT to diagnose metastatic LNs, the positive predictive value of FDG-PET/CT was approximately 60%.[17] Because enlarged thoracic LNs may be induced by either malignancy, infection, and/or inflammatory conditions, we retrospectively analyzed the lymph nodal motion (NM) using enlarged LNs that were pathologically confirmed by planned surgical resection performed within a couple of months after CRT. Siewert et al[18] summarized the prevalence rates of 722 patients with LN metastasis for both esophageal adenocarcinoma and esophageal squamous cell carcinoma (ESCC). Their analysis revealed that the rates of LN metastasis in stages T3 and T4 were 74% and 100%, respectively, using a database of 414 cases of ESCC. Therefore, the optical information about physiological motion of the esophagus and LNs are important to treat esophageal cancer. It is also necessary to consider whether to set the ITV margins to the esophagus and metastatic LNs individually.

Our hypothesis in the present study was that the EM—especially in stage cT4 cases—may be smaller than that in stage cT1-T3 cases because of the influence of tumor invasion to the adjacent structures. The main purpose of this study was thus to assess the EM and the ITV margins for the esophagus according to cT stage and primary tumor location. A secondary purpose was to assess the NM and the ITV margins for metastatic LNs, because lymphatic metastases are generally treated with CRT in locally advanced esophageal cancer with or without elective lymphatic irradiation. For the assessments of the NM and the ITV margins for LNs, we used the pretreatment datasets of patients with nodal involvement pathologically defined after planned surgical resection following CRT.

Methods and materials

Patients

All 4DCT datasets were acquired at pretreatment. For the measurements of EM, we selected 33 patients with pathologically confirmed thoracic ESCC. For the

measurements of NM, we selected 20 patients with metastatic regional LNs that were pathologically confirmed by planned surgical resection performed within a mean of 5.1 weeks (range, 3.0-8.4 weeks) after CRT. All patients were treated with concurrent CRT between November 2011 and April 2015 at our institute. The patient characteristics are listed in Table 1. All patients were diagnosed based on enhanced CT, esophagogastroduodenoscopy, contrast roentgenography, and FDG-PET/CT. The depth of primary tumor invasion was diagnosed using magnetic resonance imaging and/or endoscopic ultrasound before treatment. Clinical TNM classification was defined using the International Union Against Cancer classification, 6th edition. In the EM measurements, cT4 stage was determined by the invasive depth of primary tumor. This study was approved by the institutional ethics board in November 2011.

4DCT scanning

The 4DCT scans were performed on all patients from the laryngeal level to the celiac trunk level using an Optima CT scanner (GE Medical Systems, Milwaukee, WI). The 4DCT datasets were obtained at 2.5-mm slice thickness under free breathing. All patients were scanned in the supine position with both arms laid parallel to the body. The Varian Real-time Position Management system (Varian Medical System, Palo Alto, CA) was used to monitor respiratory signals. The 4DCT datasets were sorted into 10 images (0%-90%) by Advantage 4D software (GE Medical Systems).

Table 1 Patient characteristics

Variable	Esophageal motion	Nodal motion
Age (y), mean (range)	69.2 (59-82)	65.2 (46-82)
Gender (n)		
Male	27	16
Female	6	4
Tumor stage (n)		
T1	6	1
T2	2	0
T3	11	6
T4	14	13
Nodal stage (n)		
N0	9	0
N1	24	20
Primary tumor length (cm)		
Mean (range)	6.5 (2-15)	NA
Primary tumor sites (n)		
Upper thoracic	12	3
Middle thoracic	10	11
Lower thoracic	11	6
Duration between RT and Op (weeks)		
Mean (range)		5.1 (3.0-8.4)
Metastatic lymph nodal area (n)	NA	
Cervical and thoracic		11
Abdominal		9
Nodal invasion to adherent structures (n)		1

NA, not applicable; Op, operation; RT, radiation therapy.

Measurements of EM and NM

The 4DCT datasets were transferred to the Pinnacle[3] treatment planning system, version 9.6 (Philips Medical Systems, Andover, MA). We used images at 2 respiratory phases (0% and 50%) to measure the EM and NM. The 0% image represented the end of inhalation; the 50% image represented the end of exhalation. The methods that we used to measure the centroid motion are indicated in Fig 1A. For the EM measurements, the adventitia of the esophagus was contoured from the cricoid bone (inlet of the esophagus) to the esophagogastric junction in the 2 selected images by 1 radiation oncologist and 1 medical physicist. All esophageal contours were divided at the carina. The centroid points were set to the esophagus above the carina and below the carina in the 0% and 50% images, respectively. The EM was measured in the left-right (LR), anteroposterior (AP), and SI directions by the difference between the centroid points of the 0% image and those of the 50% image. We evaluated each difference in the EM according to cT stage and primary tumor location. For the NM measurements, the outlines of lymph nodal metastasis were contoured in the 0% and 50% images. The NM values at the cervicothoracic and the abdominal region were also measured from the centroid motion, respectively. The 95th percentile values from cumulative distribution were determined in all directions.

Assessments of the ITV margins

The centroid motion could approximately reflect the ITV margins if a solid tumor is being investigated. However, the centroid motion would be insufficient to represent the shape change of the esophagus such as the expansion and contraction. For this reason, we used different methods to measure the EM and the ITV margins. The ITV margins were measured using the ROI expansion tool of the Pinnacle[3]. Although the 4DCT-average images approximately include the information of internal motion for each patient, those images are still insufficient to completely delineate the edge of the ITV. In this study, we defined the ITV margins in each patient as the maximum distance in each direction from the CTV at the 4DCT-average images (CTV4Dave) to the intersection of the CTV at the 0% and 50% images (ITV_{0+50}) of the complete coverage in the Pinnacle[3]. An example of

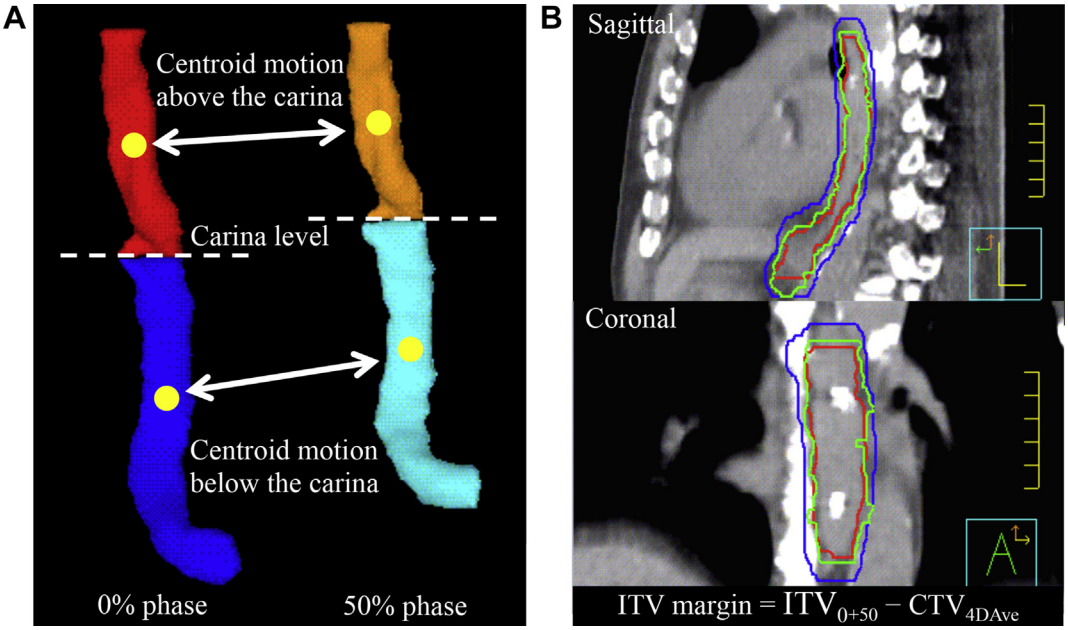

Figure 1 (A) The method used to measure the esophageal motion. The centroid points were set to the esophagus above the carina and below the carina in the 0% phase (the end of inhale) and 50% phase (the end of exhale) images, respectively. The esophageal motion was measured by the difference between the centroid points of the 0% image and those of the 50% image. (B) The measurement method used for the internal target volume (ITV) margin. The red lines represent the clinical target volume (CTV) on the 4DCT-average images (CTV_{4Dave}). The green lines represent the ITV_{0+50} (the CTV at the 0% + the CTV at the 50%). The blue lines represent the CTV_{4Dave} + the ITV margins. In this study, we determined the maximum distance in each direction from the CTV_{4Dave} to the ITV_{0+50} of the complete coverage as an ITV margin in the Pinnacle[3].

ITV measurements is shown in Fig 1B. The thoracic esophagus above and below the carina were defined as the provisional CTV, respectively. The 95th percentile values were used to define the ITV margins for clinical practice in this study.

Statistical analysis

We used the Kruskal-Wallis test and the Mann-Whitney *U* test for statistical analysis in this study. Values of $P < .05$ were considered significant. All statistical analyses were performed using SPSS software, version 22 (Chicago, IL).

Results

The EM characteristics

The EM results for each cT stage are shown in Fig 2A. There were significant differences in the mean EM values below the carina among cT stages (all directions, $P < .01$). The mean EM below the carina in cT4 was significantly smaller than that in cT1-T2 (LR: 0.3 vs 0.9 mm, $P < .01$; AP: 0.7 vs 1.7 mm, $P < .01$; SI: 3.0 vs 6.7 mm, $P < .01$) and than that in cT3 (LR: 0.3 vs 1.0 mm, $P = .03$; AP: 0.7 vs 2.1 mm, $P < .01$; SI: 3.0 vs 6.9 mm, $P < .01$). Because there was no significant difference in the EM between cT1-T2 and cT3, we combined the cT1-T2 and cT3 datasets. We labeled the patient datasets with primary cT4 tumor located in the esophagus above the carina "cT4/above the carina" and labeled the patient datasets with primary cT4 tumor located in the esophagus below the carina "cT4/below the carina."

Figure 2B shows the EM results according to primary tumor location. The significant mean EM values in the comparison of cT1-T3 and cT4/below the carina (cT4/below the carina vs cT1-T3) were 0.2 versus 0.7 mm in the AP direction ($P = .03$) in the esophagus above the carina, 0.4 versus 1.0 mm in the LR ($P = .03$), 0.6 versus 1.9 mm in the AP ($P < .01$), and 2.2 versus 6.8 mm in the SI ($P < .01$) in the esophagus below the carina. The mean EM values below the carina in cT1-T3 and cT4/above the carina (cT4/above the carina vs cT1-T3) were 0.2 versus 1.0 mm in the LR ($P < .01$), 1.0 versus 1.9 mm in the AP ($P = .04$), and 4.5 versus 6.8 mm in the SI ($P = .05$). We also found that on the CT images, the EM in cT4/below the carina was much smaller than that in cT1-T3 (Fig 3). The mean EM below the carina in cT4/below the carina was significantly smaller than that in cT4/above the carina (SI: 2.2 vs 4.5 mm, $P < .01$). The details of the mean and the 95th percentile values of the EM are summarized in Table 2. From these results, we found that the EM including respiratory and other random motion differs according to cT stage and primary tumor location.

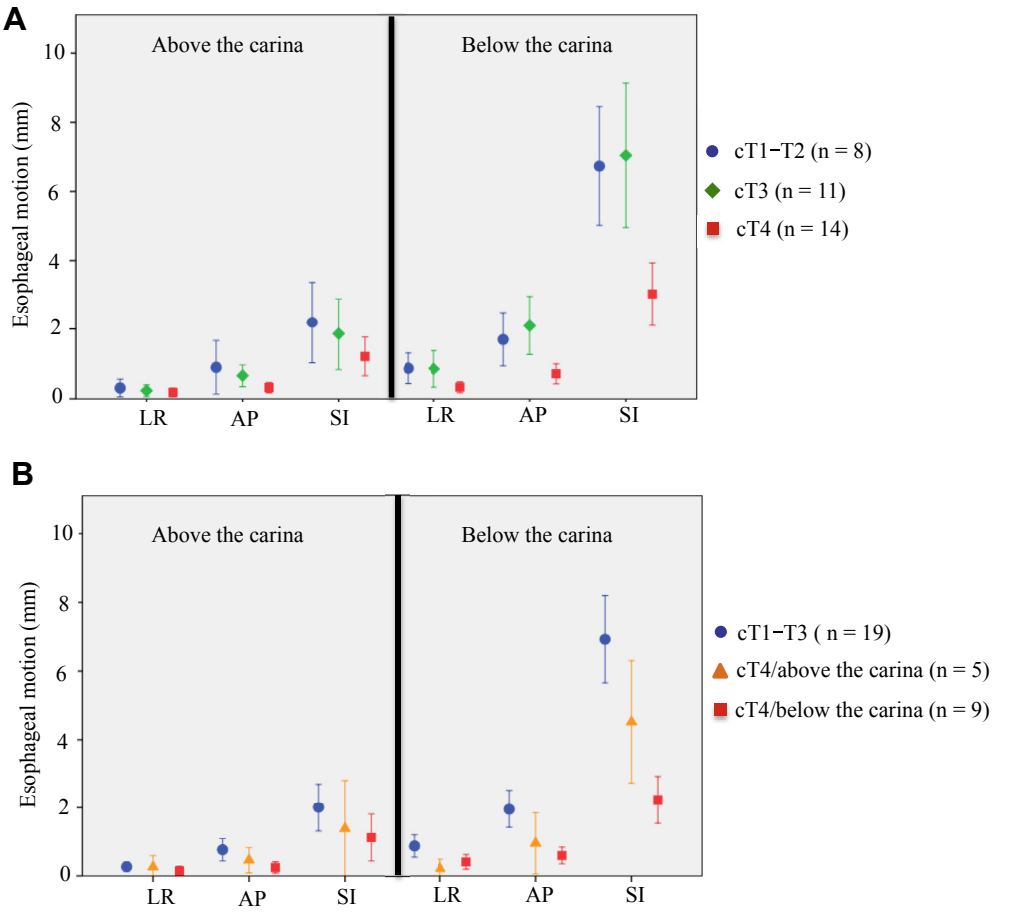

Figure 2 (A) The esophageal motion characteristics according to cT stage (cT1-T2 in blue, cT3 in green, cT4 in red). (B) Comparison of the esophageal motion according to primary tumor location (cT1-T3 in blue, cT4/above the carina in orange, cT4/below the carina in red). cT4/above the carina, the datasets of patients with primary cT4 tumor located in the esophagus above the carina; cT4/below the carina, the datasets of patients with primary cT4 tumor located in the esophagus below the carina.

The NM characteristics

The NM results are also summarized in Table 2. The mean NM at the abdominal region in all directions was significantly more mobile than that at the cervicothoracic region (LR: 0.7 vs 1.5 mm, $P = .04$; AP: 0.6 vs 5.0 mm, $P < .01$; SI: 1.2 vs 8.6 mm, $P < .01$). The mean NM at the abdominal region was also significantly larger than the mean EM below the carina in cT1-T3 (AP: 1.9 vs 5.0 mm, $P < .01$), the cT4/above the carina (LR: 0.2 vs 1.5 mm, $P < .01$; AP: 1.0 vs 5.0 mm, $P < .01$; SI: 4.5 vs 8.6 mm, $P < .01$), and the cT4/below the carina (LR: 0.4 vs 1.5 mm, $P = .01$; AP: 0.6 vs 5.0 mm, $P < .01$; SI: 2.2 vs 8.6 mm, $P < .01$).

Assessments of the ITV margins

The mean and the 95th percentile values of the ITV margins are summarized in Table 3. The ITV margins in cT4/below the carina were significantly smaller than those in cT1-T3 (above and below the carina, all directions: $P < .01$). The ITV margins in cT4/above the carina were smaller than those in cT1-T3 (above the carina; SI: $P < .01$). Much larger ITV margins were necessary for LNs at the abdominal region compared with those for LNs at the cervicothoracic region and for the esophagus below the carina.

Discussion

To our knowledge, this is the first study to report the EM characteristics and the ITV margins for the esophagus according to cT stage and primary tumor location in esophageal cancer. In the comparison of our results with those of previous studies, the EM and the ITV margins in our cT1-T3 cases were similar to or slightly smaller than those studies' values, and those in our cT4 cases were much less than the reported values. Most of the previous studies quantified the motion and the ITV margins for esophageal cancer investigated only in primary solid tumor. In clinical RT planning for advanced esophageal cancer, however, we need to include the partial esophagus

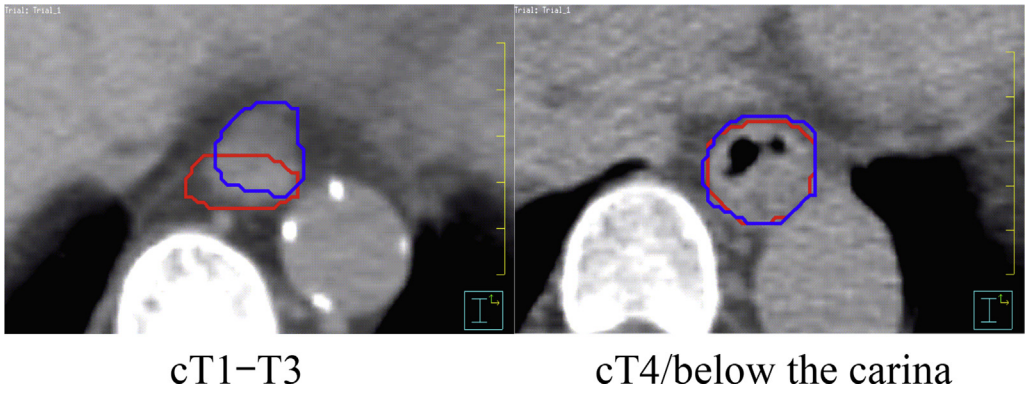

Figure 3 Example of the esophageal motion (EM) comparisons between cT1-T3 and cT4/below the carina (primary cT4 tumor located in the esophagus below the carina). These axial CT images are at the abdominal level. The clinical target volumes are represented in red lines (at the 0% phase) and blue lines (at the 50% phase).

at a certain distance from primary tumor in the RT field. Cohen et al[7] found that the mean absolute values of the inter-/intrafractional esophageal motion was 4.2 mm or less using CT-on-rails imaging in patients with thoracic esophageal cancer.

There are several studies that investigate the esophageal tumor motion using 4DCT. Yaremko et al[10] reported that the mean tumor motion at the distal esophagus using 4DCT in the LR, AP, and SI directions were 1.3 mm, 2.3 mm, and 7.1 mm, respectively. Patel et al[11] reported that the mean esophageal tumor motion in the LR, AP, and SI directions were 2.2 mm, 2.8 mm, and 8.0 mm, respectively. In the present study, the mean EM values below the carina in cT1-T3 (LR: 1.0 mm, AP: 1.9 mm, SI: 6.8 mm) were almost the same as the values of these previous studies. Jin et al[14] also reported tumor motion using fiducial markers and 4DCT in esophageal cancer. They recommended the setting region-dependent ITV margins. In addition to this effect of tumor region, our present findings newly indicated that cT stage influences the EM.

Significant variations in the EM according to cT stage and primary tumor location were revealed in the present study. We found that the EM below the carina in cT4 was significantly smaller compared with that in cT1-T3. In cT4/below the carina, the EM below the carina was more reduced than that in cT4/above the carina. We suspect that the cause of the EM reduction in cT4 cases is the adhesion

Table 2 The esophageal and lymph nodal motion

Esophageal motion	Above the carina (mm)			Below the carina (mm)		
	Mean	SD	95th percentile	Mean	SD	95th percentile
cT1-T3						
LR	0.3	0.3	0.8	1.0	0.7	2.4
AP	0.7	0.7	1.4	1.9	1.2	4.0
SI	1.9	1.5	4.2	6.8	2.8	11.1
cT4/above the carina						
LR	0.3	0.3	0.6	0.2	0.2	0.5
AP	0.5	0.3	0.8	1.0	0.7	1.9
SI	1.2	0.8	2.2	4.5	1.4	6.1
cT4/below the carina						
LR	0.1	0.2	0.5	0.4	0.3	0.8
AP	0.2	0.2	0.6	0.6	0.3	1.0
SI	1.1	0.9	2.3	2.2	0.9	3.4
Nodal motion	Cervicothoracic region (mm)			Abdominal region (mm)		
	Mean	SD	95th percentile	Mean	SD	95th percentile
LR	0.7	0.6	1.6	1.5	1.2	3.5
AP	0.6	0.5	1.3	5.0	2.7	8.9
SI	1.2	0.9	2.4	8.6	3.3	14.2

AP, anteroposterior; cT4/above the carina, the datasets of patients with primary cT4 tumor located in the esophagus above the carina; cT4/below the carina, the datasets of patients with primary cT4 tumor located in the esophagus below the carina; LR, left to right; SD, standard deviation; SI, superoinferior.

Table 3 The ITV margins for the esophagus and lymph nodes

Esophagus	Above the carina (mm)			Below the carina (mm)		
	Mean	SD	95th percentile	Mean	SD	95th percentile
cT1-T3						
LR	2.4	0.5	3.0	4.9	0.9	6.0
AP	2.3	0.6	3.0	5.1	1.0	6.2
SI	3.4	1.2	5.0	7.0	3.2	12.8
cT4/above the carina						
LR	1.8	0.4	2.0	4.4	0.9	5.0
AP	1.8	0.4	2.0	4.6	1.1	5.8
SI	1.0	1.4	2.5	7.5	1.8	9.5
cT4/below the carina						
LR	1.6	0.5	2.0	2.7	0.7	3.6
AP	1.3	0.5	2.0	2.7	0.8	3.8
SI	0.6	1.1	2.5	3.1	1.7	5.0
Lymph nodes	Cervicothoracic region (mm)			Abdominal region (mm)		
	Mean	SD	95th percentile	Mean	SD	95th percentile
LR	1.8	0.4	2.0	4.1	1.5	5.6
AP	1.8	0.4	2.0	5.6	3.1	9.2
SI	1.7	1.2	2.5	9.0	4.3	15.0

cT4/above the carina, the datasets of patients with primary cT4 tumor located in the esophagus above the carina; cT4/below the carina, the datasets of patients with primary cT4 tumor located in the esophagus below the carina; ITV, internal target volume; SD, standard deviation.

of cT4 primary tumors to the adjacent structures. Similar to our findings, Yu et al[19] also indicated that lung tumor motion of locally advanced-stage cancer was smaller than that of early-stage cancer. In this study, the EM above the carina was much smaller in comparison to that below the carina. An earlier investigation also showed that regarding primary tumors, the motion in lower locations was larger than that in upper locations.[13,14] There was no meaningful difference because of cT stage in the EM above the carina in the present study.

Several studies reported the ITV margins for primary esophageal tumor. Qiu et al[15] evaluated the displacement differences of markers between proximal and distal ends of tumor and investigated whether the ITV margins should be determined separately in patients with mid-upper thoracic ESCC. The ITV margins that covered 95% of their datasets in the LR, AP, and SI directions were 2.9, 2.4, and 5.0 mm, respectively. These values were the same as the ITV above the carina in cT1-T3 cases in our study. Patel et al[11] also indicated that the ITV margins for esophageal primary tumors were 7.5 mm (LR), 7.5 mm (AP), and 15.0 mm (SI), respectively. Their ITV margins were greater than those in the present study, especially in cT4.

The ITV margins for the esophagus should be changed according to cT stage and primary tumor location. The ITV margins with 95% coverage in our datasets in each case were: in cT1-T3, the ITV margins in the LR, AP, and SI directions were 3.0 mm, 3.0 mm, and 5.0 mm for the esophagus above the carina, and 6.0 mm, 6.2 mm, and 12.8 mm for the esophagus below the carina; in cT4/above the carina, the ITV margins in the LR, AP, and SI directions were 2.0 mm, 2.0 mm, and 2.5 mm for the esophagus above the carina, and 5.0 mm, 5.8 mm, and 9.5 mm for the esophagus below the carina; in cT4/below the carina, the ITV margins in the LR, AP, and SI directions were 2.0 mm, 2.0 mm, and 2.5 mm for the esophagus above the carina, and 3.6 mm, 3.8 mm, and 5.0 mm for the esophagus below the carina.

Our study indicated that the ITV margins for cT4 cases could be set smaller than those in cT1-T3 cases. If the generalized ITV margins are determined independently from clinical factors such as cT stage and tumor location, we must be careful to avoid excessive ITV margins. By using the ITV margins (ie, LR: 3.6 mm; AP: 3.8 mm; SI: 5.0 mm; Table 3) for cT4 patients treated with definitive CRT, radiation toxicities such as radiation pneumonitis and pericarditis would be reduced.

Previous studies indicated that the esophageal tumor motion is variable according to several factors such as the region of the esophagus or the direction of motion.[10-16] In addition to these factors, our present findings revealed that cT stage also influenced the esophageal motion and the ITV margin in esophageal cancer. If the patient-specific ITV is to be used, the ITV margin should be determined using the several 4D phase images of each patient. Chen et al[16] recommended that the ITV should be created from the three phase images (0%, 50%, and 80%; the middle of the inhalation) to account for regular breathers or 4-phase images (0%, 50%, 60%, and 80%) to adjust for irregular breathers. Compared with their method, the ITV determination in the present study (CTV at 4D average + defined ITV margin for each cT stage) enabled us to

perform efficient RT planning. Our results can be used to guide margins in future clinical trials at any institution, as a safe and generalized ITV margin for each cT stage.

NM information is an important factor for the determination of clinical ITV margins for esophageal cancer. Patel et al[11] demonstrated that the mean NM of the celiac region in the LR, AP, and SI directions were 1.9 mm, 4.6 mm, and 9.2 mm, respectively. They used the datasets of metastatic LNs diagnosed by not only pathological examination but also PET-positive images; the present study is the first to investigate the NM using only datasets with pathological confirmation. The mean NM values at the abdominal region observed in the present study were 1.5 mm (LR), 5.0 mm (AP), and 8.6 mm (SI), and these values are almost the same as those reported by Patel et al.[11] In the present study, the NM at the cervicothoracic region in all directions was much smaller than that at the abdominal region.

The ITV margins for the LNs in our dataset were 2.0 mm (LR), 2.0 mm (AP), and 2.5 mm (SI) at the cervicothoracic region, and 5.6 mm (LR), 9.2 mm (AP), and 15.0 mm (SI) at the abdominal region. If we determine the RT fields for elective lymphatic irradiation, these critical values regarding the ITV margins should be considered. If the esophageal ITV margins are applied for LNs at the abdominal region, the irradiated dose to the involved LNs would be insufficient to cover the essential area. Patel et al[11] also reported that the ITV margins for the celiac-region lymph nodes were larger than those for esophageal tumor.

Our study has several limitations. We could not assess random motion including cardiac and peristaltic motion by using 4DCT. Delineation errors may occur due to the uncertainty of 4DCT images. Although we found the tendencies of the EM and ITV margins characteristics according to cT stage and primary tumor location, the study's limited sample size made it difficult to provide a recommendation of exact values.

Conclusions

Both the EM and the ITV margins in cT4 were significantly smaller than those in cT1–T3. In cT4/below the carina, these values were more reduced than those in cT4/above the carina. In clinical RT planning for esophageal cancer, cT stage should be taken into consideration. If smaller ITV margins can be used for cT4 cases than those generally used, radiation toxicities induced by definitive CRT would be reduced. The NM and the ITV margins at the abdominal region would be larger than those at the cervicothoracic region and the esophagus below the carina.

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