

## RESEARCH ARTICLE

## Influence of Intravenous Contrast Medium on Dose Calculation Using CT in Treatment Planning for Oesophageal Cancer

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### Abstract

**Objective:** To evaluate the effect of intravenous contrast on dose calculation in radiation treatment planning for oesophageal cancer. **Methods:** A total of 22 intravein-contrasted patients with oesophageal cancer were included. The Hounsfield unit (HU) value of the enhanced blood stream in thoracic great vessels and heart was overridden with 45 HU to simulate the non-contrast CT image, and 145 HU, 245 HU, 345 HU, and 445 HU to model the different contrast-enhanced scenarios. 1000 HU and -1000 HU were used to evaluate two non-physiologic extreme scenarios. Variation in dose distribution of the different scenarios was calculated to quantify the effect of contrast enhancement. **Results:** In the contrast-enhanced scenarios, the mean variation in dose for planning target volume (PTV) was less than 1.0%, and those for the total lung and spinal cord were less than 0.5%. When the HU value of the blood stream exceeded 245 the average variation exceeded 1.0% for the heart V40. In the non-physiologic extreme scenarios, the dose variation of PTV was less than 1.0%, while the dose calculations of the organs at risk were greater than 2.0%. **Conclusions:** The use of contrast agent does not significantly influence dose calculation of PTV, lung and spinal cord. However, it does have influence on dose accuracy for heart.

**Keywords:** Contrast medium - oesophageal cancer - dose calculation - radiation therapy

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### Introduction

Currently, oesophageal cancer is the eighth most frequent tumour in the world and ranks sixth among various cancers in mortality because of its extremely aggressive nature and poor survival rate (Kamangar et al., 2006; Eslick et al., 2009). Radiotherapy is one of the main treatment modalities in oesophageal cancer, contributing to both its cure and palliation. Modern radiotherapy technologies, such as three-dimensional conformal radiation therapy (3D CRT) and intensity modulated radiation therapy (IMRT), have the potential to provide a dose distribution to the target with a much steeper dose gradient, which increases the dose to the target and minimises the irradiated volume of normal tissue. Therefore, it is important to contour accurately the target volume and the organs at risk (OARs) on computed tomography (CT) images. Intravenous contrast media have the ability to improve the visualisation of normal organs and malignant tissues on a CT scan. For this reason, intravenous contrast media have been extensively used for treatment-planning CT. However, there are concerns that the contrast may introduce errors in dose calculation because of the highly electron-dense material in the

contrasted vessels.

The impact of contrast media on dose calculation is concentration-dependent. Clinical studies on brain, head-and-neck, prostate, and lung cancers have shown that contrast media have little effect on dose calculations for these tumours because of the relatively lower concentration in the clinical setting (Weber et al., 2001; Lees et al., 2005; Liauw et al., 2005; Choi et al., 2006; Létourneau et al., 2008; Shi et al., 2010), while a phantom study (Ramm et al., 2001) indicated that contrast agents do influence the dose calculation when high concentrations are used. Shibamoto et al. (2007) evaluated the influence of contrast materials on dose calculation in radiation planning for tumours at various anatomic regions including the brain, head and neck, mediastinum, and pelvis. The results showed that the use of contrast medium did not obviously influence the dose calculation for these tumours. In that study, 5 mediastinum patients were recruited including 2 lung cancer patients, 2 thymoma patients and 1 patient with thymic cancer. Because the locations of these tumours were not in full accordance with oesophageal cancer and the case number was few, the results could not be applied indiscriminately to oesophageal cancer.

The target of oesophageal cancer, particularly for

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a target in the thorax, usually is closely encompassed by the great vessels and the heart. Meanwhile, the dose differences increase linearly with the expansion of the contrast medium (Ramm et al., 2001). Thus, oesophageal cancer may suffer the most influence from contrast enhancement. The purpose of this study was to determine whether using intravenous contrast in CT planning for oesophageal cancer would result in clinically important errors in the radiation dose calculation.

## Materials and Methods

### Patient population

From February 2012 to September 2012, a total of 22 patients with oesophageal squamous cell carcinoma, treated with palliative radiation therapy or radio-chemotherapy, were included in this study. These 22 patients included 15 males and 7 females, with a median age of 55 years (range, 45–76 years). The tumours were staged according to the 2002 American Joint Committee on Cancer staging system. All of the patients recruited into this study were treated with 3D CRT or IMRT. The patients were staged from II a to IV (II a: 4, II b: 1, III: 12, IV: 5). According to PTV (planning target volume) scope, the patients were divided into 3 groups: Group 1: patients (n=4) whose PTV covered the cervical and upper thoracic region, Group 2: patients (n=13) whose PTV covered the upper and middle thoracic region ( $\pm$  cervix), Group 3: patients (n=5) whose PTV covered the whole thorax ( $\pm$  upper abdomen). The study was approved by the Research Ethics Committee at Shandong Cancer Hospital and Institute. All patients signed informed consents before entry into the study.

### Radiation simulation

The patient was immobilised with an individually moulded whole-body vacuum cushion in the supine position. The radiation simulation setup conventionally

used wall lasers aligned to three marks on the skin of the patient. In every patient, a free-breathing, unenhanced axial CT scan (Brilliance Big Bore CT, Philips Medical Systems, Inc. Cleveland, OH, USA) was taken, followed by a contrast-enhanced scan, for the neck, whole chest, and upper abdomen. Nonionic IV contrast (Ioversol Injection, 320 mg I/ml, molecular formula: C<sub>18</sub>H<sub>24</sub>I<sub>3</sub>N<sub>3</sub>O<sub>9</sub>) was injected as a bolus at a rate of 2 ml/s for a total of 100 ml through the antecubital vein or a catheter in the subclavian vein 45 s before the enhanced scan. The rotation time of the CT gantry was 1.4 s. The CT scan was performed as contiguous slices of 3-mm thickness.

### Treatment planning

The non-contrast and contrast-enhanced CT images were transferred to the Eclipse treatment planning system (TPS, Varian Medical Systems, Palo Alto, CA, USA). The gross tumour volume (GTV) and OARs were contoured on the contrast-enhanced images. The GTV included the primary tumour and metastasis lymph nodes, and the OARs included the total lung, spinal cord and heart. Depending on the tumour location and TNM staging, the clinical target volume (CTV) was created. The CTV was then uniformly expanded by 5 mm to generate the PTV. The enhanced blood stream in the great vessels (diameter, > 8 mm) and heart was divided into 5 parts artificially according to the order of enhancement: the superior vena cava, the right atrium and ventricle, the pulmonary artery, the left atrium and ventricle, and the aorta. The average Hounsfield unit (HU) values for each part were calculated for the non-contrast and contrast-enhanced images (Tables 1). The grid size of the matrix for the mean HU value calculation was set to 8  $\times$  8 pixels in the centre of the vessels. Statistical analysis for the HU value difference among the five non-contrast groups was done using a one-way ANOVA with a post hoc LSD test. The results demonstrated that there was no significant difference among the five groups ( $p < 0.001$  for each index).

**Table 1. HU Values of Non-contrast and Contrast-enhanced Blood Streams**

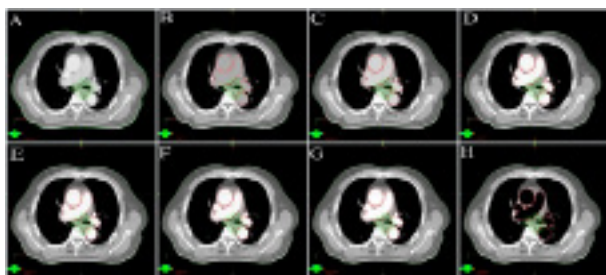
	Non-contrast image (n=22)				Contrast-enhanced image (n=20)			
	Min	Max	Mean	SD	Min	Max	Mean	SD
Superior vena cava	36	53	43.86	4.3	150	465	279.3	84.51
Right atrium and ventricle	35	53	45.18	4.63	128	215	165.8	26.32
Pulmonary artery	31	53	44.27	5.78	126	221	163.2	29.58
Left atrium and ventricle	38	57	45.18	4.83	132	242	175.3	29.57
Aorta	32	58	44.82	5.7	128	287	196.95	42.89
Total	31	58	44.66	5.01	126	465	196.11	63.89

Min, the minimum HU value; Max, the maximum HU value; SD, standard deviation

**Table 2. Dose Variation Between the Simulated Non-contrast Scenario (45 HU) and the Other Contrast Scenarios for PTV**

	HU value	D99 (%difference)*		D95 (% difference)			D90 (% difference)			D80 (% difference)			D50 (% difference)			
		Mean $\pm$ SD	Min	Max	Mean $\pm$ SD	Min	Max	Mean $\pm$ SD	Min	Max	Mean $\pm$ SD	Min	Max	Mean $\pm$ SD	Min	Max
Primary contrast		-0.04 $\pm$ 0.09	-0.19	0.23	-0.02 $\pm$ 0.11	-0.22	0.37	0.00 $\pm$ 0.12	-0.18	0.42	-0.03 $\pm$ 0.10	-0.16	0.35	0.00 $\pm$ 0.07	-0.08	0.29
Simulated contrast	145	-0.02 $\pm$ 0.06	-0.13	0.09	0.00 $\pm$ 0.07	-0.13	0.15	-0.02 $\pm$ 0.07	-0.13	0.19	-0.02 $\pm$ 0.06	-0.15	0.14	-0.01 $\pm$ 0.03	-0.09	0.08
	245	-0.04 $\pm$ 0.15	-0.25	0.3	-0.02 $\pm$ 0.13	-0.24	0.37	-0.03 $\pm$ 0.14	-0.25	0.44	-0.04 $\pm$ 0.12	-0.27	0.35	0.00 $\pm$ 0.07	-0.15	0.22
	345	-0.06 $\pm$ 0.24	-0.43	0.59	-0.05 $\pm$ 0.22	-0.41	0.59	-0.07 $\pm$ 0.22	-0.46	0.69	-0.08 $\pm$ 0.19	-0.48	0.56	-0.02 $\pm$ 0.11	-0.27	0.34
Extreme scenario	445	-0.11 $\pm$ 0.35	-0.62	0.85	-0.11 $\pm$ 0.31	-0.65	0.79	-0.13 $\pm$ 0.03	-0.7	0.92	-0.13 $\pm$ 0.26	-0.69	0.71	-0.04 $\pm$ 0.14	-0.38	0.43
	1000	-0.65 $\pm$ 0.94	-1.99	2.36	-0.58 $\pm$ 0.86	-2.17	2.04	-0.59 $\pm$ 0.76	-2.11	1.89	-0.50 $\pm$ 0.68	-1.76	1.86	-0.08 $\pm$ 0.38	-0.77	1.24
	-1000	-0.61 $\pm$ 1.45	-3.35	2.77	-0.87 $\pm$ 1.33	-3.65	2.24	-0.83 $\pm$ 1.27	-3.58	2.31	-0.57 $\pm$ 1.14	-2.73	2.67	0.09 $\pm$ 0.76	-0.68	3.11

\*D99 (%difference) is the percent variation of the dose that 99% of the planning target volume (PTV) receives between the simulated non-contrast scenario (45 HU) and the other contrast scenarios, and so on for D95–D50



**Figure 1. HU Value Override on Axial CT Slices.** The contrast-enhanced blood stream was contoured with a red line. The volume encompassed by the red line was the HU override region. The green mesh indicates the PTV. Figure 1A: primary contrast image; Figure 1B: 45 HU; Figure 1C: 145 HU; Figure 1D: 245 HU; Figure 1E: 345 HU; Figure 1F: 445 HU; Figure 1G: 1000 HU; Figure 1H: -1000 HU

Therefore, the HU value of the non-contrast blood stream was approximately 45 HU ( $44.66 \pm 5.01$  HU, mean  $\pm$  SD;  $n = 22$ ).

Even though the contrast-enhanced images were acquired immediately following non-contrast scans on the same couch, we observed a slight discrepancy in organ positions and isocentres between the two sets of images due to the difference in scan timings, which was especially obvious when the CT scan was performed without breath holding (Shibamoto et al., 2007). To simulate the non-contrast scenario without errors introduced by the scan timing and the breathing motion, we overrode the HU value of the enhanced blood stream with 45 HU on the contrast-enhanced CT image to create the “simulated non-contrast CT image”, which was used to generate the primary plan. For the primary plan, an IMRT plan was implemented when a 3D CRT plan could not meet the treatment planning goals. It was designed using a combination of 5 to 7 coplanar beams. The prescription dose was uniformly set to 60 Gy at 2.0 Gy per fraction. The treatment planning goals were for 95% of the PTV to receive the prescription dose, a mean lung dose (MLD) less than 17.5Gy, a total lung V20 less than 30%, a total lung V30 less than 20%, a heart V40 less than 40%, and a 45 Gy dose to the spinal cord  $< 0.1$  ml. The algorithm for the dose calculation was the analytical anisotropic algorithm.

#### HU value modification

In this study, we artificially assigned the CT value of the enhanced blood stream with 145 HU, 245 HU, 345 HU, 445 HU, -1000 HU, and 1000 HU in the primary plan, and then the dose calculations were performed. The dose variations obtained by the comparison of the simulated non-contrast scenario and the several “contrast-enhanced” scenarios were analysed to evaluate the influence of intravenous contrast medium on dose calculations. The range of 145 HU–445 HU was in accordance with the actual measured values (range, 126 HU–465 HU, see Table 1). The -1000 HU and 1000 HU scenarios served as two non-physiologic extremes to evaluate the effect of the CT value change on the dose calculation. The primary contrast images (no HU value manipulation to the blood stream) were also analysed by comparison with the simulated non-contrast images. Figure 1 demonstrates how each of

these HU overrides would appear on the axial CT slices. Usually, CT images were displayed at fixed settings, such as the mediastinum window centre, 40 HU, and the mediastinum window width, 400 HU. Therefore, the presence or absence of certain visual characteristics in the region beyond the window would make no difference. As is also shown in Figure 1, the capability of recognising the contrast medium did not increase continuously in the mediastinum window when the HU value of the enhanced blood stream was greater than 245 HU. The predefined look-up table stored in the TPS correlating the HU value with the relative electron density showed that the relative electron density values corresponding to 45 HU, 145 HU, 245 HU, 345 HU, 445 HU, -1000 HU, and 1000 HU were 1.068, 1.117, 1.166, 1.234, 1.301, 0, and 1.668, respectively.

In clinical treatment techniques, the monitor unit (MU) is calculated for a required dose in the target volume. Thus, the variation of MU number needed to compensate for the HU value modification was assessed in this study. The influence of intravenous contrast medium on the target was quantified by calculating the percent change of the dose to the PTVs. To evaluate the effect of contrast medium on OARs, the mean lung dose (MLD), total lung volume that received at least 20 Gy (lung V20), total lung volume that received at least 30 Gy (lung V30), dose to 0.1 ml of the spinal cord (D0.1), and heart volume that received at least 40 Gy (heart V40) were extracted from the dose-volume histograms (DVHs) for all plans.

## Results

A total of 22 patients, 13 with an IMRT plan and 9 with a 3D CRT plan, were included in our study. All primary plans met the guidelines for PTV coverage and normal-tissue tolerance as described above, except for 2 patients with total lung V20 of 38.97% and 42.37%, respectively.

#### CT value differences

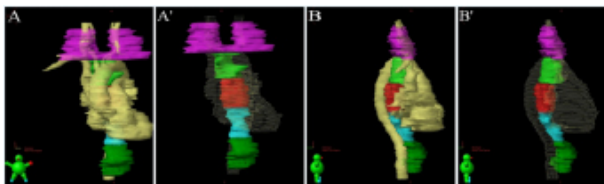
The non-contrast or contrast-enhanced blood stream was divided into 5 parts in turn of enhancement. The mean HU values for each part are summarised in Table 1. As mentioned above, there was no significant difference among the five groups in the unenhanced blood stream. Because the superior vena cava of 2 patients were not enhanced due to the central venous catheters being inserted into the subclavian veins, the statistical analysis for the HU value differences of the 5 contrast-enhanced groups was performed for the other 20 patients with a one-way ANOVA and Dunnett’s post hoc test. There was a significant difference between the superior vena cava group and every other group ( $p < 0.005$  for each index), while there was no significant difference among these other four groups ( $p > 0.05$  for each index). This may be because the contrast in superior vena cava had not dissolved completely when the CT images were acquired. The HU value of the contrast-enhanced blood stream was  $196.11 \pm 63.89$  HU (mean  $\pm$  SD; range, 126–465;  $n = 20$ ), and the mean HU values for the five parts of the contrast-enhanced blood stream of the 20 patients ranged from 137.6 HU to 273 HU (median, 190.7 HU).



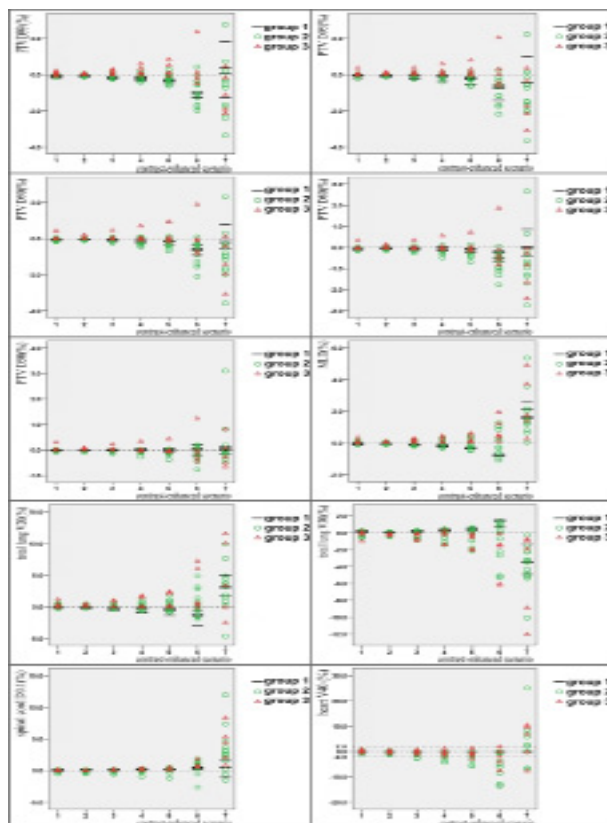
**Table 3. Variations Between the Simulated Non-contrast Scenario (45 HU) and the Other Contrast Scenarios for OARs**

	HU value	V20 (% difference)			V20 (% difference)			MLD (% difference)			Spinal cord D0.1 (% difference)			Heart V40 (% difference)		
		Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	Min	Max	Mean±SD	Min	Max
Primary contrast		0.10±0.32	-0.3	1.14	-0.08±0.32	-1.01	0.33	0.03±0.11	-0.15	0.35	0.01±0.16	-0.51	0.17	-0.07±0.54	-1.27	0.82
Simulated contrast	145	0.02±0.20	-0.25	0.45	-0.05±0.20	-0.45	0.17	-0.01±0.07	-0.11	0.1	0.00±0.15	-0.49	0.21	-0.34±0.49	-1.39	0.49
	245	0.06±0.41	-0.54	1.03	-0.13±0.41	-0.87	0.3	0.00±0.14	-0.2	0.28	0.03±0.19	-0.59	0.26	-0.81±0.98	-2.72	0.73
	345	0.11±0.70	-0.94	1.72	-0.21±0.70	-1.41	0.48	0.00±0.23	-0.33	0.45	0.08±0.27	-0.93	0.41	-1.29±1.46	-4.26	1.05
	445	0.16±0.98	-1.36	2.34	-0.36±1.00	-2.09	0.63	0.00±0.33	-0.48	0.61	0.13±0.36	-1.24	0.55	-1.88±2.04	-5.86	1.3
Extreme scenario	1000	0.67±2.64	-3.07	7.23	-1.17±2.71	-6.14	1.55	0.08±0.86	-1.1	1.93	0.61±0.90	-2.61	1.84	-4.80±4.83	-13.59	1.93
	-1000	3.45±3.87	-4.67	11.55	-4.02±3.01	-12	-0.25	1.96±1.36	0.03	5.38	2.85±3.20	-1.56	11.96	4.39±8.90	-7.79	25.17

V20 (% difference) is the percent variation of total lung V20, and the same for V30 (% difference); MLD, mean lung dose; spinal cord D0.1 (% difference) is the percent variation of the dose to 0.1 ml of the spinal cord; Heart V40 (% difference) is the percent variation of Heart V40 (9 of the 22 patients had heart V40 = 0)



**Figure 2. Schematic Diagram for the Relationship Between PTV and the Blood Stream in the Thorax.** Yellow: blood stream; magenta: cervix target; green: upper thoracic target; red: middle thoracic target; cyan: lower thoracic target; dark green: upper abdominal target. Figure 2A and 2A': anterior direction; Figure 2B and 2B': lateral direction (the great vessels and heart in A' and B' were delineated with contouring). The oesophagus target is closely encompassed by the great vessels and heart, particularly the thoracic segment



**Figure 3. Distribution of the Variations in the Different Contrast-enhanced Scenarios.** Contrast-enhanced scenario 1: the primary contrast scenario; 2: 145 HU; 3: 245 HU; 4: 345 HU; 5: 445 HU; 6: 1000 HU; 7: -1000 HU. Group 1: patients (n=4) whose PTV covered the cervical and upper thoracic region; Group 2: patients (n=13) whose PTV covered the upper and middle thoracic region (± cervix); Group 3: patients (n=5) whose PTV covered the whole thorax (± upper abdomen)

*MU differences*

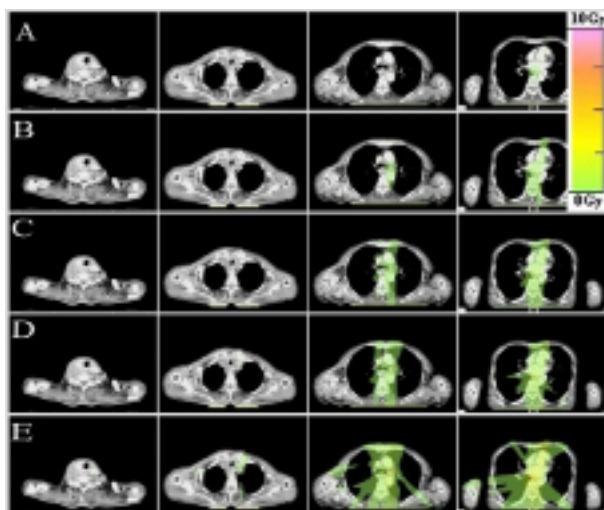
After changing the HU value of the enhanced blood stream and performing the dose calculation, the numbers of MU were calculated. The mean increases in the numbers of MU in the simulated contrast enhancement (145 HU–445 HU) compared to the primary contrast dataset were less than 1.0 %. In the extreme scenarios of 1000 HU and -1000 HU, the mean changes in MU number were less than 2.0 %, though the maximum was greater than 3.0%.

*Dose variation for PTV*

A DVH was applied to determine the minimum dose received by 99% (D99), 95% (D95), 90% (D90), 80% (D80), and 50% (D50) of the PTV after the dose calculation for a certain HU value. Table 2 lists the variations of PTV in the dose calculations between the simulated non-contrast scenario and the contrast-enhanced scenarios. The differences in dose distribution increased linearly with the HU value of the blood stream. However, even in the non-physiologic extreme scenarios, the variations of PTV in the dose calculations were less than 1%. For the simulated contrast-enhanced scenarios (145 HU–445 HU), the dose differences to the PTV ranged from -0.70% to 0.85%, corresponding to a maximal dose decrease of 43 cGy and a maximal dose increase of 51 cGy (prescription dose, 60 Gy). For the primary contrast administration, slightly smaller variations were observed. Therefore, the influence of intravenous contrast medium on the PTV was not strong enough to have clinical significance on the dose distribution calculation.

*Dose variation for OAR*

The dose variations for OARs from the comparison of different contrast scenarios with the simulated non-contrast scenario are summarised in Table 3. In terms of the simulated contrast-enhanced scenarios (145 HU–445 HU), the differences in dose distribution increased linearly with the HU value of the blood stream. A slightly smaller effect was observed with the primary contrast scenario. The mean variation was less than 0.5% for the total lung V20, V30, and spinal cord D0.1. Of the 22 patients, 9 had a heart V40 of 0%, so the analysis of the heart V40 was limited to the other 13 patients. In the primary contrast scenario, the percent variations of heart V40 ranged from -1.27% to 0.82%, corresponding to an absolute variations of -0.25% to 0.14%. By comparison, for the simulated contrast-enhanced scenarios (145 HU–445 HU), the average variation exceeded 1% and reached 2% when the HU value of the blood stream exceeded 245.



**Figure 4. The Comparative Dose Distribution of Various HU Levels and 45 HU.** Row A: 145 HU scenario; row B: 245 HU scenario; row C: 345 HU scenario; row D: 445 HU scenario; row E: 1000 HU scenario. Columns 1 to 4 (left to right) display the different slices from the same patient: annular cartilage, jugular notch, trachea, and left atrium, respectively

The maximal variation existed in the 445 HU scenario, which underestimated the heart V40 by 5.86%, which corresponded to an absolute difference of 1.14% (18.25% for 445 HU vs. 19.39% for 45 HU). In the extreme scenarios of 1000 HU and -1000 HU, the mean variations were large, especially for -1000 HU, in which the mean variation was as great as 3.45% for the total lung V20, -4.02% for the total lung V30, 1.96% for the MLD, 2.85% for the spinal cord D0.1, and -7.79% for heart V40. Thus, in the extreme scenarios, the contrast agents strongly affected the variations of OARs.

## Discussion

In the present study, the HU value of blood stream on the contrast-enhanced CT images of oesophageal cancer was overridden with a 45 HU scenario (serving as the simulated unenhanced image), which was used to formulate the primary treatment plans for oesophageal cancer patients. Then, the HU value of the enhanced blood stream was overridden with several HU levels to model different contrast-enhanced scenarios, and the dose calculations were performed. The influence of intravenous contrast medium on dose calculations was investigated by comparing the dose results between the simulated non-contrast scenario and the other contrast-enhanced scenarios in the same 3D treatment plans. The study results show that the differences in dose distribution increased linearly with the HU value of the blood stream for both target and OARs. In the simulated contrast-enhanced scenarios, the mean variations of the MU number and PTV were less than 1.0%. In the non-physiologic extreme scenarios of 1000 HU and -1000 HU, the variations of PTV in the dose calculations were less than 1.0%, while the changes in the MU numbers and dose calculations of the OARs were greater than 2.0%. However, this was merely a hypothetical situation; thus, the influence of intravenous contrast medium was not sufficient to reach

clinical significance, according to the upper limit of errors of 2.0% (Shibamoto et al., 2007). Generally, the effect of the -1000 HU scenario was greater than the 1000 HU scenario, especially for OARs, possibly because of the larger gap in the relative electron density for -1000 HU (0 for -1000 HU vs. 1.068 for 45 HU) than 1000 HU (1.668 for 1000 HU vs. 1.068 for 45 HU). For the total lung V20, V30, and spinal cord D0.1, the mean variations were less than 0.5% in the simulated contrast-enhanced scenarios. However, for heart V40, when the HU value of the blood stream exceeded 245, the average variation exceeded 1.0%, and the variation of a few patients even reached 2.0%.

There are multiple reasons why the contrast medium had a greater effect on heart V40 than on the lung and spinal cord. First, the volume of the enhanced blood stream in the heart is large, and the difference in the calculated doses increased proportionally to the volume of contrast medium (Shibamoto et al., 2007). Second, the containment relationship of the heart to the blood stream magnified the influence of contrast agent on the dose calculation. Finally, the PTVs of the 13 patients included in the statistical analysis for heart V40 were all located in the thoracic segment, and the influence of contrast material in the enhanced vessel of the cervical segment might have no clinical significance because contrast medium slightly influences the treatment planning in head-and-neck region (Choi et al., 2006; Létourneau et al., 2008).

The relationship between PTV segments and the blood stream (Figure 2) showed that the target in the thoracic region is closely encompassed by the great vessels and heart, while the volume of the blood stream is small around the cervical and upper abdominal target. Therefore, a PTV scope in the superior-inferior direction does influence the variation of both the target and the critical normal structures. Shibamoto et al. reported that contrast agent is unlikely to cause important errors in radiation dose calculations on mediastinum tumours (Shibamoto et al., 2007). This could be because the target of the patients recruited in that study focused on the upper thorax; thus, the volume of enhanced blood surrounding the target was relatively small. As a result, further analysis is necessary to evaluate the influence of intravenous contrast medium on dose calculations according to the target position.

Figure 3 shows the distribution of variation of the contrast-enhanced scenarios for the different PTV scopes. This figure confirms the statistical results that the differences in dose distribution increased linearly with the HU value of the blood stream for both target and OARs. The variations in the dose calculation of group 1 (patients whose PTV covered the cervical and upper thoracic region) were smaller than those of group 2 (patients whose PTV covered the upper and middle thoracic region  $\pm$  cervix) and group 3 (patients whose PTV covered the whole thorax  $\pm$  the upper abdomen). For a certain HU scenario, the maximal variation usually appeared in group 2 and group 3 (Figure 2). For example, the primary values of heart V40 were 0% for all of the patients in group 1; thus, the variations of heart V40 in group were all 0, while the variations of group 2 and group 3 were relatively large. This result indicates that the thoracic segment is more

subject to the influence of intravenous contrast medium than the cervical segment. The dose differences of several HU scenarios and the simulated non-contrast scenario for the same plan were assessed with the comparative dose distribution, which were obtained by subtracting the absolute dose of the simulated unenhanced scenario from different HU scenarios (Figure 4). The use of contrast had a negligible effect on the dose distribution for the cervical and upper thoracic segments, while contrast had a significant influence on the middle thoracic and lower thoracic segments. In addition, according to columns 3 and 4 of Figure 4, the difference in the calculated doses increased with the HU value. All of these results support the findings of Ramm et al. (2001) that the difference in calculated doses increased proportionally to the concentration (HU value) and to the volume of contrast medium in their phantom-based study of the influence of CT contrast agents on dose calculation in a 3D treatment planning system.

In summary, the current study indicates that the use of contrast agent does not significantly influence dose calculation of PTV, lung and spinal cord in the treatment planning for oesophageal cancer, either with IMRT or 3D CRT. It seems to be secure and reliable to use a contrast medium of <445 HU for oesophageal cancer, in accord with Ramm et al. (2001). However, to evaluate accurately the dose distribution of the heart, we still recommend modifying the HU value of the blood stream in the heart to 45 HU.

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