

## Original Article

# Influence of the intravenous contrast media on treatment planning dose calculations of lower esophageal and rectal cancers

### ABSTRACT

**Background:** The impact of intravenous (IV) contrast media (CM) on radiation dose calculations must be taken into account in treatment planning.

**Purpose:** The aim of this study is to evaluate the effect of an intravenous contrast media on dose calculations in three-dimensional conformal radiation therapy (3D-CRT) for lower esophageal and rectal cancers.

**Materials and Methods:** Seventeen patients with lower esophageal tumors and 12 patients with rectal cancers were analyzed. At the outset, all patients were planned for 3D-CRT based on the computed tomography (CT) scans with IV contrast media. Subsequently, all the plans were copied and replaced on the scans without intravenous CM. The radiation doses calculated from the two sets of CTs were compared.

**Results:** The dose differences between the planning image set using intravenous contrast and the image set without contrast showed an average increase in Monitor Units (MUs) in the lower esophageal region that was 1.28 and 0.75% for 6 and 15 MV photon beams, respectively.

**Conclusion:** There was no statistical significant difference in the rectal region between the two sets of scans in the 3D-CRT plans. The results showed that the dose differences between the plans for the CT scans with and without CM were small and clinically tolerable. However, the differences in the lower esophageal region were significant in the statistical analysis.

**KEY WORDS:** Contrast media, esophageal and rectal cancers, treatment planning

### INTRODUCTION

Nowadays, computerized tomography (CT) plays an important role in many Radiation Therapy Departments. CT-based radiation therapy treatment planning has many advantages and it provides a lot of information.<sup>[1]</sup>

To obtain accurate delivery of radiotherapy, an accurate delineation of the treatment target is essential. Intravenous (IV) contrast-enhanced computed tomography could be utilized in radiotherapy treatment planning to improve the delineation of the tumor volume and organ at risk (OAR).<sup>[2]</sup>

However, the use of contrast-enhanced CT scans for treatment planning where heterogeneities are accounted could adversely influence the dose distribution, as the contrast media (CM) will not be present at the time of treatment. This may be the reason why some treatment centers have not used the contrast agents CT for treatment planning.<sup>[3]</sup> As intravenous CM is helpful in improving the

recognition and delineation of tumors from CT images, conducting a comprehensive study on the impact of intravenous CM on the radiation dose distribution in CT-based treatment planning is necessary.

To date, two kinds of studies have been carried out on the effect of contrast-enhanced CT scans on dose computations. Investigations carried out on phantoms or mathematical calculations belong to the first group.<sup>[4,5]</sup> Their results have shown that the contrast agent does influence the dose calculation and depends on the concentrations of the CMs and photon beam energies. It must be noted that the concentrations of the contrast media in the tissues are not so high in clinical applications. The intravascular concentration of the contrast media is affected by the concentration of the injected contrast media, the rate of contrast delivery, and the rate of blood flow.<sup>[6]</sup>

The effects of iodinated contrast media on the dose calculation for tumors at various anatomical regions in patients have been investigated by the second

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group. Their results have shown that the influence of contrast agents on dose calculation in treatment planning is negligible for regions where the CM concentration and its expansion are relatively low.<sup>[7-11]</sup> One of the recent studies in this group has demonstrated that the mean increases in the monitor units if the contrast media administration is less and is considered negligible in the planning of whole-brain, whole-neck, mediastinal, and whole-pelvic irradiation. Their results also indicate that the use of contrast media does have an influence on treatment planning of the upper-abdominal irradiation.<sup>[10]</sup>

The study's results on lung cancers indicate that the dose differences between the plans from CT scans, with and without CM, are small and clinically tolerable, although IV contrast is unlikely to cause important errors in the radiation dose calculations in most patients with lung cancer.<sup>[3,11]</sup> It is clear that IV contrast is useful in the delineation of the surrounding structures, for example, aorta, liver, and the like, in the treatment planning of abdominal and lower esophageal cancers. CT is still considered to be at least equal to magnetic resonance (MR) in staging cancer of the esophagus and rectum, while superior in the rest of the gut.<sup>[12]</sup> CT with IV contrast media is recommended for staging esophagus cancers. In addition, CT with IV contrast media is recommended for staging, to identify lung metastases and the region from the liver to the rectum.<sup>[13]</sup> Therefore, the impact of IV contrast media on radiation dose calculations must be taken into account in these regions. We have undertaken the present study to examine the effect of IV contrast media on dose calculations in three-dimensional conformal radiation therapy (3D-CRT) for lower esophageal and rectal cancers.

## MATERIALS AND METHODS

### Patient selection

A total of 29 patients (12 females and 17 males), with a mean age of  $60.65 \pm 10.37$  years were included in this study. Seventeen patients undergoing radiotherapy for lower esophageal cancers at the diaphragm level and twelve patients undergoing rectal irradiation were chosen for this study. The patient characteristics are listed in Table 1. All the patients were also examined with a six-row spiral CT-scanner. The tumors were staged according to the 2003 American Joint Committee on Cancer (AJCC) staging system. All patients with a stage II – IV were prospectively enrolled between April 2012 and December 2012.

### Acquisition of computed tomography

Treatment planning CTs were performed using a six-detector, multislice CT scanner (SOMATOM Emotion 6; Siemens Healthcare, Germany). Table 2 shows the scanning parameters used in this study.

For every patient two sets of planning CTs were performed. These were initially taken without intravenous CM and then with CM, in the same position and with the same coordinates. Helical studies were started in a craniocaudal direction. The

patients were instructed to hold their breath at the tidal inspiration level during scanning. The contrast agent contained 300 mg/ml of nonionic contrast media (Omnipaque). The total dose of the contrast media was 1.2 ml/kg body weight or about 90 ml for patients with a body weight of over 60 kg. The enhanced abdomen and thorax scans were started about 60 and 35 seconds after a bolus injection, respectively. For the contrast injection, we used a power injector (MEDRAD Vistron CT, USA).

### Treatment planning and dose evaluation

After the acquisition of the CT, the two sets of CTs were transferred to a radiotherapy planning system using a DICOM RT format. An example of the difference between the two scans is shown in Figure 1. Note the presence of intravenous CM within the aorta and other soft tissues on the left image.

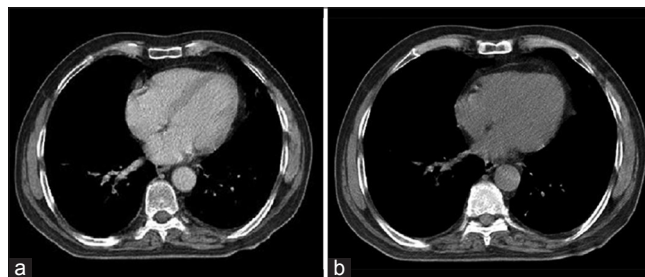
All plans were generated in the CorePLAN version 3.5.0.5 planning system (Seoul, Korea), which adjusted to the Siemens primus linear accelerator with 6 and 15 MV photon beams. CorePLAN is a representative product of Seoul C and J, Inc. for radiotherapy treatment planning, which is proven by the KFD (Korea Food and Drug Administration). This product is a convenient and comprehensive radiation therapy planning system that supports 3D-CRT, multi-plan, Intensity Modulated Radiation Therapy (IMRT), with useful intelligent functions and an automatic registration suite. CorePLAN

**Table 1: Patient characteristics (n=29)**

Site	Sex	Number of patients	Patients age distribution (year)			
			Min. range	Max. range	Median	Average±SD
Esophagus	Male	10	55	86	57	60.40±9.19
	Female	7	45	80	59	61.14±12.87
Rectum	Male	7	53	60	57	56.20±2.77
	Female	5	51	82	59	63.71±13.31

**Table 2: The scanning parameters used in the abdomen and thorax scanning**

Parameters	Abdomen	Thorax
KV	130	130
Effective mAs	95	70
Rotation time	0.6 second	0.6 second
Slice collimation	3 mm	4 mm
Pitch factor	1.5	1.5
Intersection gap	3 mm	4 mm



**Figure 1: (a) Contrast-enhanced CT scan; (b) No contrast CT scan as an example**

provides accurate dose calculations based on the collapsed cone convolution (CCC) and equivalent tissue air ratio (ETAR) algorithms for photon beams, and the Hogstrom algorithm for electron beam dose calculations. The accuracy of its algorithms was confirmed through numerous clinical tests.<sup>[14-18]</sup> In this study the CCC algorithm was used for dose calculations.

To compare the density difference between the two sets of CT scans, changes in the CT number (Hounsfield Units, HU) between the enhanced and non-enhanced CT sets were evaluated in tissues and vessels on the CorePLAN. The mean and standard deviation of the Hounsfield units (HU) for each tissue and vessel was obtained from five points in each tissue and vessel site. These sites for the lower esophageal region included the diaphragm muscle, thoracic aorta, and the superior vena cava vein, and for the rectal region included the rectum wall and bladder.

The enhanced CT set was fused with the non-enhanced CT set using the CoreFusion software. The fused images were imported to the CorePLAN 3D treatment planning software. The gross target volumes (GTV), clinical target volumes (CTV), planning target volumes (PTV), and organs at risk (OARs) were delineated. First, every plan was accomplished in the enhanced CT set. These plans included the contours of the targets and the OARs were copied and replaced from the enhanced CT set to the non-enhanced CT scans. The beam characteristics of the plan generated in the enhanced CT set were also copied and applied to the non-enhanced CT set, which included the radiotherapy fields, energy beams, and dose per fraction for each field. Radiation doses and their distributions in the non-enhanced CT set could be obtained by recalculation of each plan using the same parameters of the enhanced plans.<sup>[3]</sup> Dose calculations were performed for 6 and 15 MV photon beams of the linac.

After image fusion, the source-to-surface distances (SSDs) of the corresponding beams were compared with the corresponding plans, for evaluating the equivalence of the patient's positions and coordinates between the two sets of CTs, with and without CM.

In this study the lower esophageal irradiation was planned by using three fields, which included anteroposterior (AP), right posterior oblique (RPO) and left posterior oblique (LPO) beams. The rectal irradiation was also planned by using four fields, which included AP, posteroanterior (PA), right lateral (RL), and left lateral (LL) beams, as a box. All the radiation beams were oriented freely in three dimensions for the planning and delivery process, and the structures that traversed by the beam were visualized with the beams' eye views.

The prescription dose was 200 cGy per fraction for PTV. Thus, the required monitor units to deliver 200 cGy doses for each plan were calculated and dose of targets and OARs between the plans, with and without CM, in each patient were compared. The monitor units and dose distributions in the enhanced and non-enhanced CT sets were evaluated

separately for each field of conformal plans. The objective of planning was to deliver the prescribed dose to at least 95% of the PTV, with the maximum dose being less than 110% of the prescription. The analysis of OARs included the average dose received by the delineated critical organs, for each patient. The differences were analyzed by the Wilcoxon's signed rank test (SPSS, Release 16.0). A  $P < 0.05$  was considered to be of statistical significance.

## RESULTS

The difference of SSDs between the corresponding beams in each patient validates the accordance of fusion between the enhanced and non-enhanced CT images. The difference of SSDs between the corresponding beams on the two sets of CT images is shown in Table 3. These results show that the two sets of CT images are considered to be taken nearly in identical positions. Thus, the influence of the position difference between the two sets of CT images in each patient can be considered negligible.

Table 4 shows the changes in Hounsfield Units (HUs) by contrast agent administration. The mean increase in HU was 33.70 in the diaphragm muscle and 42.82 in the superior vena cava vein, whereas, it was 141.23 in the thoracic aorta. It was 17.12 for the rectum wall and 9.56 for the bladder.

Table 5 summarizes the changes in monitor units (MUs) by contrast agent administration. In the lower esophageal region

**Table 3: Difference of SSDs between the corresponding beams on the two sets of CT images**

Region	Beam direction	SSD difference (mm)			
		Min. range	Max. range	Median	Average±SD
Esophagus	AP	-7.60	6.80	1.00	0.72±3.56
	LPO	-7.30	5.10	0.00	0.47±2.78
	RPO	-5.40	4.30	0.00	0.12±2.26
	Conformal	-2.64	2.31	0.47	0.33±2.61
Rectum	AP	-6.2	5.70	0.00	0.29±2.86
	PA	-7.70	5.30	0.00	0.16±3.01
	RL	-7.10	5.20	0.00	0.20±3.56
	LL	-7.80	4.40	0.00	0.80±3.51
	Conformal	-2.87	2.20	0.10	0.22±2.28

SDs=Source-to-surface distances, AP=Anteroposterior, LPO=Left posterior oblique, RPO=Right posterior oblique, PA=Posteroanterior, RL=Right lateral, LL=Left lateral

**Table 4: The changes in Hounsfield Units by contrast agent administration**

Region	Site	Increase in Hounsfield Units			
		Min. range	Max. range	Median	Average±SD
Esophagus	Diaphragm muscle	12	79	30	33.70±17.23
	Thoracic aorta	65	193	155	141.23±35.32
	Superior vena cava	10	89	45	42.82±21.68
Rectum	Rectum wall	5	35	19.7	17.12±9.47
	Bladder	4	17	9.6	9.56±4.52

**Table 5: Changes in monitor unit numbers by contrast media administration**

Region	Beam direction	Increase in MU (%) for 6 MV		Increase in MU (%) for 15 MV	
		Range	Average±SD	Range	Average±SD
Esophagus	AP	-1.12, 5.87	2.42±1.67	-0.60, 4.40	1.74±1.35
	LPO	-2.73, 4.04	1.01±2.15	-2.51, 2.90	0.62±1.67
	RPO	-1.5, 4.28	1.35±1.79	-1.27, 2.81	0.67±1.23
	Conformal	-1.4, 3.23	1.28±1.39	-1.23, 4.33	0.75±1.36
Rectum	AP	-2.65, 1.70	-0.003±1.10	-1.87±0.99	-0.12±0.74
	PA	-2.80, 1.25	-0.14±1.02	-2.33, 0.77	-0.24±0.79
	RL	-3.63, 3.45	0.12±2.05	-1.43, 2.58	0.23±1.20
	LL	-2.93, 1.69	-0.48±1.27	-2.08, 0.92	-0.29±0.90
	Conformal	-2.57, 3.36	-0.38±1.52	-1.94, 3.63	0.05±1.39

AP=Anteroposterior, LPO=Left posterior oblique, RPO=Right posterior oblique, PA=Posteroanterior, RL=Right lateral, LL=Left lateral

an average increase in MU for 3D conformal irradiation was 1.28 and 0.75% for 6 and 15 MV photon beams, respectively. In 3D conformal irradiation of the rectal region, the change in MU was -0.38 and 0.05% for 6 and 15 MV photon beams.

For tumors in the lower esophageal region the 3D-CRT was considered as three-field irradiation. As each of the three beams passed through different tissues and organs, the MU changes were analyzed for each beam. The mean increase in MU for 6 MV was 2.42% for AP beams, 1.01% for LPO beams, 1.35% for RPO beams, and 1.28% for conformal irradiation; even as the mean increase in MU for 15 MV was 1.74% for AP beams, 0.62% for LPO beams, 0.67% for RPO beams, and 0.75% for conformal irradiation. This decrease in MU difference between the two plans of the enhanced and non-enhanced CT sets indicated that the difference between the tissues reduced with increasing photon beam energies. In the rectal region, the average changes in MU for all single beams (AP, PA, RL, and LL) and conformal irradiation for two photon beam energies were less than 1%.

The effect of the IV contrast agent on the radiation dose calculation of normal-tissue structures was also evaluated [Table 6]. For the conformal irradiation, the mean calculated dose of critical organs from the enhanced CT was lower than that calculated from the non-enhanced CT, except the dose to the bladder, for 6 MV. However, they were not significant in statistic analysis ( $P > 0.05$ ).

**DISCUSSION**

In this study, the effect of the IV contrast agent on dose calculations in radiation treatment planning was evaluated. Application of enhanced CT images for treatment planning might introduce errors in dose calculation, as the CM would not be present at the time of treatment. Previous studies on the phantoms or mathematical calculations had shown that high concentration contrast media could influence dose calculations.<sup>[4,5]</sup>

However, because the concentration of the contrast media used for tumor staging was lower in the CT scan than in the theoretical settings, its evaluation was necessary. For determining this concern the two sets of CTs (enhanced and

**Table 6: Comparison of critical normal structures dose calculated from the computed tomographies with and without CM enhancement in 3D-plans for 6 and 15 MV photon beams**

Critical normal structures in the lower esophageal region	Dose (cGy) per fraction (Mean±SD)			P value
	D <sub>nonCM</sub> <sup>†</sup>	D <sub>CM</sub> <sup>**</sup>	(D <sub>nonCM</sub> -D <sub>CM</sub> )/D <sub>CM</sub> (%)	
Lung (6 MV)	48.93±6.76	48.81±6.72	0.25±0.64	0.231
Lung (15 MV)	47.29±6.57	47.07±6.38	0.44±1.21	0.302
Spinal cord (6 MV)	70.42±7.26	70.25±7.23	0.17±0.97	0.471
Spinal cord (15 MV)	70.01±7.17	69.24±7.11	1.50±4.14	0.130
Critical normal structures in the rectal region	Dose (cGy) per fraction (Mean±SD)			P value
	D <sub>nonCM</sub>	D <sub>CM</sub>	(D <sub>nonCM</sub> -D <sub>CM</sub> )/D <sub>CM</sub> (%)	
Bladder (6 MV)	118.94±17.44	119.24±17.36	-0.17±1.84	0.460
Bladder (15 MV)	116.75±16.68	115.69±16.63	1.28±2.13	0.105
Femur (6 MV)	64.45±6.78	64.21±6.69	0.41±1.12	0.621
Femur (15 MV)	63.35±6.18	63.22±6.11	0.06±0.93	0.416

<sup>†</sup>Dose calculated for the CTs without intravenous, <sup>\*\*</sup>Dose calculated for the CTs with intravenous

non-enhanced) were taken nearly in an identical position. By evaluating the SSD difference between the enhanced and non-enhanced CTs, the accordance of fusion between the two sets of CTs was validated. In the 3D radiation treatment plans for the lower esophageal and rectal regions the range of SSD difference in each beam was less than that for the lung, head, and neck plans.<sup>[3,8]</sup> In the treatment planning systems based on CT scans, dose calculation is based on the conversion of HUs into electron density. The use of CM, during treatment planning CT scan, influences the HUs of the tissues. In the lower esophageal region the highest increase in HU (141.23 ± 35.32) was found in the thoracic aorta. This was lower than the reported value of Yuta Shibamoto *et al.*'s study.<sup>[10]</sup> In fact, the reason for this difference might lie in the fact that the total contrast media dosage for patients in their study was higher than in our study. Previous studies on lung scans demonstrated that the use of IV contrast agents could significantly change the CT number of vessels, although this had little impact on the radiation dose calculation.<sup>[3,11]</sup>

In the case of lower esophageal irradiation the average changes in the MUs were 2.42% ± 1.67% and 1.74% ± 1.35% for AP beams of 6 and 15 MV photon beams, respectively. Also the average changes in MUs for 3D conformal irradiation of the lower esophageal region were 1.28% ± 1.39% and

0.75%  $\pm$  1.36% for 6 and 15 MV photon beams, respectively. These findings were in agreement with a recent prospective study, which found that contrast agents did have an influence on the planning of upper-abdominal radiation.<sup>[10]</sup> Another study by Burrige *et al.*, demonstrated that a mean increase of the overall monitor units (MUs) of 1.0%  $\pm$  0.8% (maximum increase, 3.3%) occurred when the contrast media was used during dose computations in the lung.<sup>[9]</sup> In addition, our findings also indicated that the influence of the IV contrast agent on dose calculations decreased with an increase in the photon beam energy.

We also found that although the use of IV contrast agent significantly changes the HU of vessels, this has little impact on dose calculations, especially in 3D conformal irradiation. Our results are in good agreement with Ramm *et al.*'s study.<sup>[4]</sup> The aim of their study had been to evaluate the effect of CT contrast media on dose calculations in a 3D treatment planning system, by irradiating a 3 cm diameter cylinder of barium sulfate in a water phantom, using either 6 or 25 MV photons. They concluded that the effect of the contrast media was extremely low when the number of beam angles increased above one.

In the rectal area the highest increase in HU (17.12  $\pm$  9.47) was observed in the wall of the rectum. On account of the low increase in CT numbers, the average changes in MU as a result of contrast media administration was less than 1% for 6 and 15 MV photon beams. This indicates that the changes in MU by the use of contrast media are not significant and may be considered negligible at the pelvic anatomical region. These results are in agreement with the previous investigations.<sup>[7,19,20]</sup> The exact identification of the OARs and the sparing of them in radiation therapy is critical. Therefore, a 3D treatment planning CT, performed with a contrast agent, is usually recommended.

We evaluated the mean dose parameter of critical normal structures. With the use of an IV contrast agent, critical normal structure doses were underestimated, except dose to bladder, for 6 MV. For all OARs the dose differences between the plans of CT scans with and without CM were not significant ( $P > 0.05$ ). Our findings on the critical organs in the thorax area were similar to the study of Jianghong Xiao and Wenyin Shi.<sup>[3,11]</sup> They stated that the lung and spinal cord tolerance doses from the treatment plans of CT scans with and without CM could be considered clinically acceptable. Compared with other pelvic organs, the bladder is more radiation-resistant. Based on the Emami *et al.* recommendations, the tolerance dose for whole bladder irradiation is approximately 45 Gy.<sup>[21]</sup> Although, there is no clear tolerance dose for the head and neck of the femur, most radiation oncologists consider it to be 45–50 Gy.<sup>[22]</sup> In the rectal plans of this study, we found that the doses to the rectum, bladder, and femur were less than their tolerance dose. One potential problem in this study was the patients' motion both voluntary and involuntary during image acquisition. Therefore, cross-section images could be changed during inspiration and expiration CT scans, which

might have an influence on the enhanced and unenhanced image comparisons.

## CONCLUSION

The present investigation on the effect of the IV contrast media on dose calculation in the rectal region for 3D-CRT plans showed that the dose differences between the plans from CT scans with and without CM were small and clinically tolerable. However, the differences in the lower esophageal region were significant in the statistical analysis. Therefore, in order to improve the accuracy of target and normal structure delineation, we recommended that radiation oncologists perform planning scans with IV contrast media in most cases.

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