Jpn J Radiol (2016) 34:376–382
DOI 10.1007/s11604-016-0523-9

TECHNICAL NOTE

The effect of bladder contrast on dose calculation in volumetric modulated arc therapy planning in patients treated for postoperative prostate cancer

Tülay Ercan[1] · Şefik İğdem[1] · Gül Alço[1]

Received: 8 September 2015 / Accepted: 19 January 2016 / Published online: 2 February 2016

Abstract
Purpose The aim of this study was to evaluate the effect of contrast agent on dose calculation in volumetric modulated arc therapy (VMAT) in the post-prostatectomy setting.
Methods and material Ten patients were studied. Each patient received planning computed tomography (CT) images with contrast agent. All of the plans were done on virtually simulated contrast-free CT scans. The plan approved by the radiation oncologist was replicated to the contrast CT series. In both of the plans the same monitor unit was used. The doses calculated from the two plans were compared in regard to target volumes and organs at risk. A paired sample *t*-test was used to evaluate the differences in cumulative dose volume histogram between the two plans.
Results We showed that the use of contrast agent may cause significant differences in dose distribution. There was a significant decrease in doses received by planning target volume (PTV70), rectum V65 Gy, rectum V40 Gy, bladder V65 Gy, penile bulb V40 Gy in plans with contrast-enhanced CT sets. The decrease in mean, maximum and minimum doses received by PTV70 also contributed to the significant decrease in conformity index.
Conclusions Using a contrast agent at the time of CT simulation may cause significant differences in dose distribution. For this reason, the plan should always be carried out on non-contrast CT data sets to avoid additional errors in the treatment planning process.

Keywords VMAT · Contrast agent · AAA algorithm · Dose calculation · Treatment planning

Introduction

Intensity modulated radiotherapy (IMRT) is a means of safely delivering higher than conventional doses in patients with prostate cancer following surgery. Unlike conventional approaches, IMRT conforms the prescription dose to the shape of the target tissues in three dimensions, thereby sparing the surrounding normal tissues. By allowing conformal treatment of targets and avoidance of normal tissues, IMRT may overcome the limitation of conventional RT. In fact, with the irregular shaped target in the post-prostatectomy setting, IMRT appears to be ideal [1]. In recent years, volumetric modulated arc therapy (VMAT) has gained an advantage over static IMRT as it decreases the required number of monitor units by about 30–40 % compared to conventional IMRT.

Anatomical structures with varying densities are represented on computed tomography (CT) scans by a two-dimensional distribution of Hounsfield units (HU). These units depend on beam attenuation properties and are defined by a relative attenuation coefficient. Treatment planning systems convert the HUs into corresponding electron densities in order to calculate dose, therefore HU values that yield incorrect electron densities may decrease the accuracy of the dose calculation, especially when applying heterogeneity correction. Although bladder opacification improves the reliability of prostate localization, the high electron density of iodinated X-ray contrast material may

✉ Tülay Ercan
tulaye@doruk.net.tr; tulayercan@florence.com.tr

[1] Department of Radiation Oncology, Florence Nightingale Gayrettepe Hospital, Cemil Aslan Güder Sok 8, Floor-1, Gayrettepe, 34349 Istanbul, Turkey

have an artifactual effect on the treatment plan, negatively influencing the final dose distribution [2, 3].

The present study compares the RapidArc IMRT dose distributions in a series of 10 patients with prostate cancer treated in a postoperative setting undergoing CT simulation with bladder opacification.

Materials and methods

Patient selection and simulation

Ten consecutive patients who were treated with post-prostatectomy radiotherapy at our institution were identified. The patients were scanned in the supine position with the arms across the chest and with their knees and feet immobilized. An enema per rectum was given before simulation to empty the rectum as much as possible. The patients were also asked to have a moderately full bladder and advised to avoid uncomfortable bladder overfilling. To define the vesicourethral anastomosis, a retrograde urethrogram was performed with 30–50 ml diluted Urografin intravenous contrast medium (Bayer Plc Newbury, Berkshire, UK). A penile clamp was immediately applied to minimize leakage. The treatment planning CT scan extended from 5 cm above the L5–S1 vertebral body superiorly to 5 cm below the ischial tuberosity with 2.5-mm-thick slices obtained at 2.5-mm intervals. Planning CT scans for the 10 patients were imported into a Varian Eclipse treatment planning station (Eclipse, version 10.0.28; Varian Medical Systems, Palo Alto, CA, USA) for contouring.

Contouring and volume definition

The clinical target volume (CTV70) included the prostate bed and periprostatic tissue, ensuring adequate coverage of the vesicourethral junction. When there was tumor extension into the seminal vesicles in the pathology report, the seminal vesicle bed and any remaining seminal vesicles were included in the CTV70. The planning target volume (PTV70) was defined by adding a 0.8-cm margin in all directions except 0.6 cm posteriorly to the CTV70.

The rectum was contoured as a solid organ from the sigmoid flexure to the ischial tuberosities. The bladder was contoured as a solid organ from the dome to the bladder neck. The penile bulb was contoured as the portion of the bulbous spongiosum of the penis immediately inferior to the GU diaphragm, and the proximal femoral heads from the acetabulum to the minor trochanters, including the major trochanters. Figure 1 shows delineation of target and critical structures outlined on axial, coronal and sagittal CT slices with contrast heterogeneity.

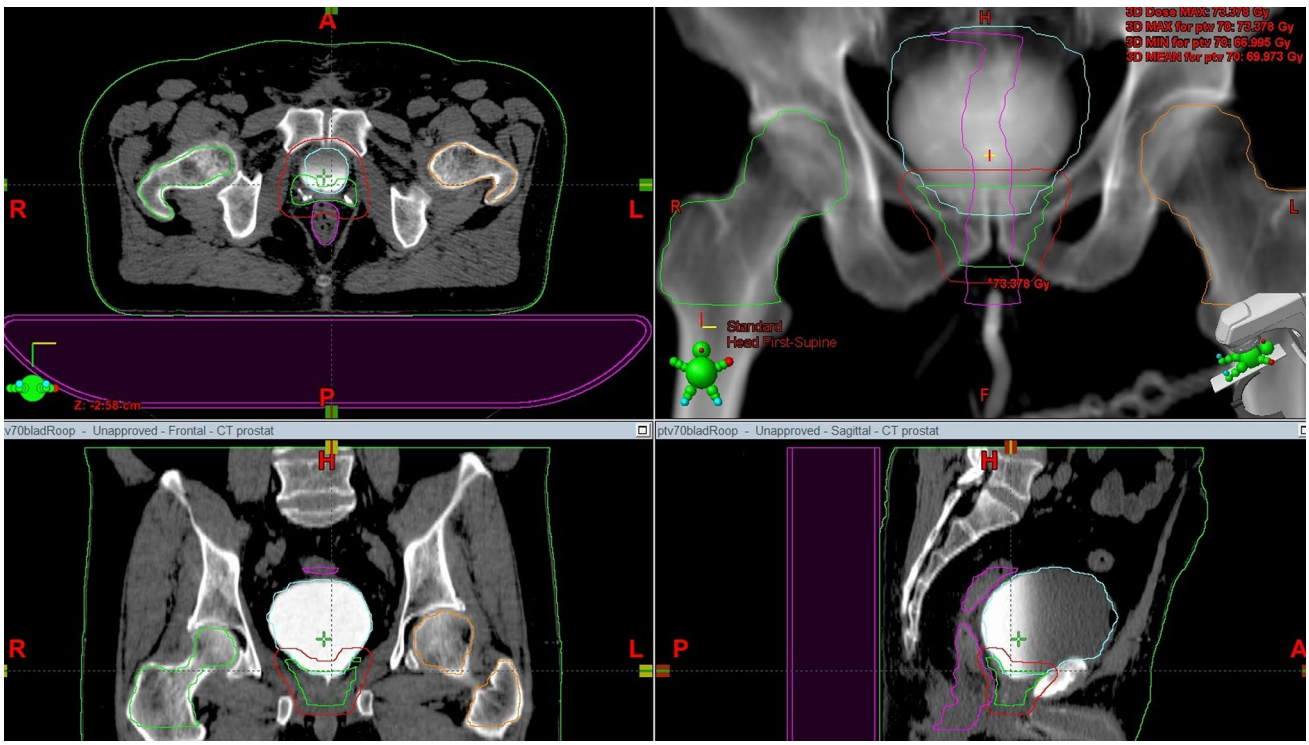

Fig. 1 Delineation of target and critical structures outlined on axial, coronal and sagittal CT slices with contrast heterogeneity

Treatment planning

For the purpose of this study, in order to simulate a contrast-free bladder, the electron matrix density of the contrast-filled bladder was virtually corrected to water density and a base treatment plan was done with the modified electron matrix of the unopacified bladder. We also delineated opacification along the urethra (with an electron density matrix more than 1500 HU) and changed the HU to 0 (water density) as in Fig. 2. And in some patients we also delineated the penile clamp, which was inside the treatment field because of the gantry angle of the arcs (Fig. 3). The HU of the metallic penile clamp was around 3400. Therefore, we corrected the density of the clamp to air density (−1000 HU).

All patients were planned to receive 70 Gy in 2-Gy fractions with two full coplanar arcs. The treatment was planned with Eclipse version 10.0.28 (Varian Medical Systems, Palo Alto, CA, USA) with anisotropic analytical algorithm (AAA). The VMAT optimization algorithm progressive resolution optimizer (PRO), version 10.0.28 was used. We also added the couch top into the calculation area [4, 5].

We made the plan on CT images without contrast and normalized 100 % so that 98 % of the target volume (PTV70) got more than 100 % of the prescription dose. Next, this plan was copied to the contrast-agent CT images and the monitor units were fixed. Then the optimization was done with the same objective template for target volumes and critical organs. The constraints of the target volumes and organs at risk during the optimization are shown in Table 1.

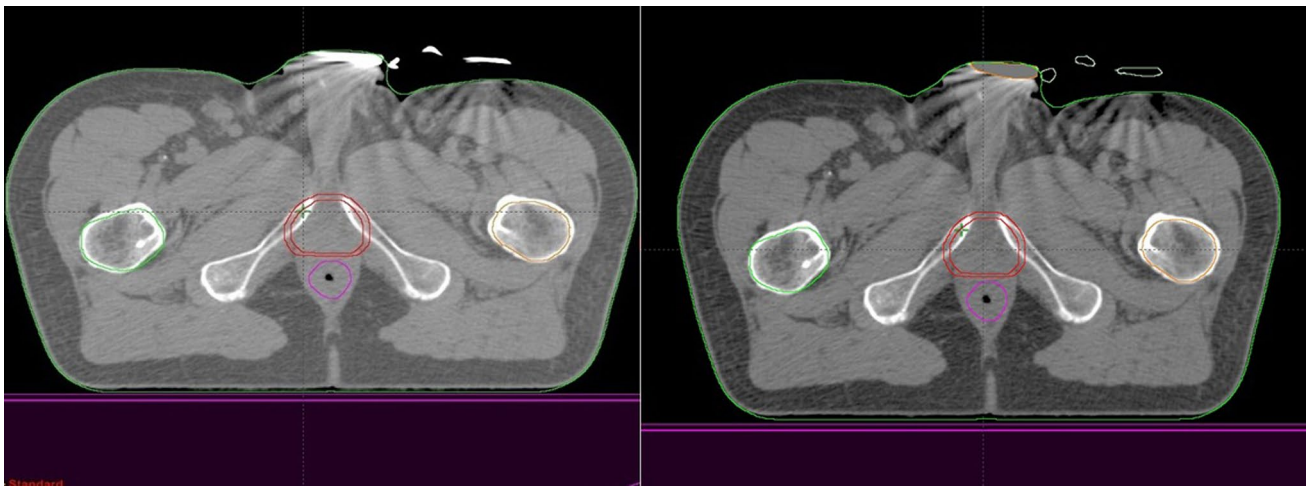

Fig. 2 Clamp and contrast before (*left*) and after (*right*) the assigned contrast heterogeneity

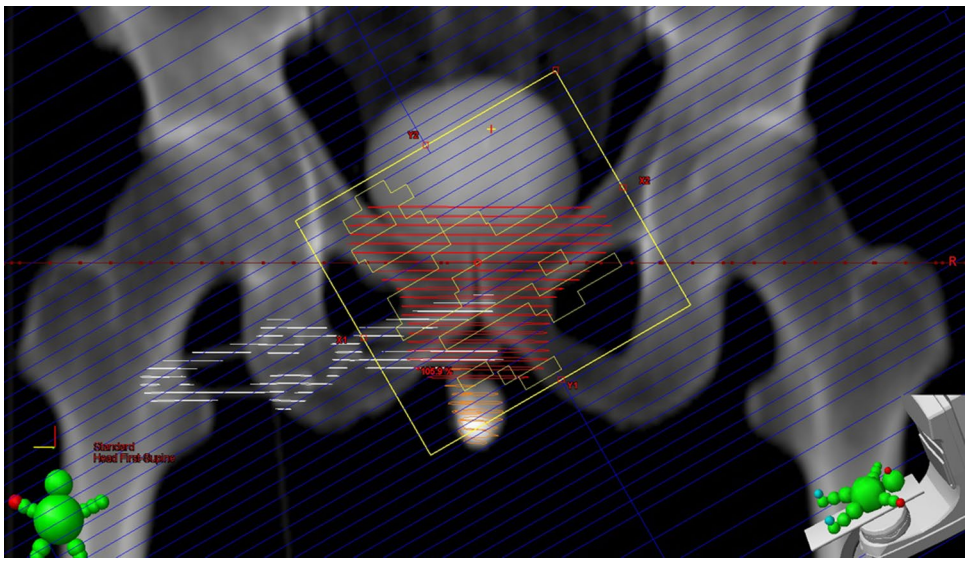

Fig. 3 Beam's eye view showing the clamp inside the treatment volume (*red color* representing the target volume)

Table 1 Dosimetric constraints for the postoperative prostate IMRT plans

Organ	Volume (%)	Dose (Gy)
PTV 70 Gy	≥98	70
PTV 70 Gy	≤1	≤107 %
Rectum	≤35	≤65
	≤55	≤40
Bladder	≤50	≤65
	≤70	≤40
Penile bulb	≤70	≤40
	≤95	≤14
Femoral head	≤10	≤50

Cumulative dose volume histograms were obtained for both plans.

Evaluation

The doses calculated from the two plans were compared with regard to target volumes and organs at risk. A paired sample *t*-test was used to evaluate the differences in cumulative dose volume histogram (cDVH) between the two plans.

This study was approved by our institutional review board.

Results

One of the aims of VMAT was to irradiate 100 % of the PTV70 with the prescribed dose. Therefore, the dose to 98 % of the volume (D98) as displayed on the cumulative DVH, which is considered to be the minimum dose and the dose to 1 % of the target volume (D1), which is considered to be the maximum dose to the target were compared between the plans with enhanced and non-enhanced CTs. The mean D98 and D1 of PTV70 calculated from the enhanced CT were significantly lower than those calculated from the non-enhanced CT (Table 2).

Maximum, mean doses, and the volumes exposed to 40 and 65 Gy (V40 and V65) for the rectum and bladder were also compared between the two plans. Again, there were significant differences at the maximum dose to the rectum, V65 and V40 of the rectum, and V65 of the bladder between the two plans (Table 2).

To determine the quality of irradiation, a conformity index (CI) for both plans was calculated. CI = Vri/TV, where Vri is the reference isodose volume and TV is the target volume. A conformity index equal to 1 corresponds to ideal conformation. A CI greater than 1 indicates that the irradiated volume is greater than the target volume and includes healthy tissue. If the CI is less than 1, the target volume is only partially irradiated [6]. The CI of the RapidArc plans calculated for the enhanced CT

Table 2 c-DVH parameters for prescription volumes in with- and without-contrast-agent CT images

	Mean normalized dose (±SD) without contrast	Mean normalized dose (±SD) with contrast	*p* value[a]
Conformity index	1.19 (0.037)	0.60 (0.477)	**0.004**
Homogeneity index	0.05 (0.012)	0.05 (0.011)	0.30
PTV70 (D98)	71.7 (0.383)	69.8 (1.553)	**0.005**
PTV70 (D1)	73.6 (0.604)	71.9 (1.531)	**0.006**
Rectum V65	14.6 (4.12)	12.9 (3.77)	**0.001**
Rectum V40	33.5 (7.19)	32.3 (7.41)	**0.003**
Rectum max	73.7 (0.91)	72.4 (1.37)	**0.006**
Rectum mean	31.5 (3.82)	31.1 (3.76)	0.09
Bladder V65	18.1 (7.17)	17.2 (6.76)	**0.04**
Bladder V40	30.1 (11.53)	29.5 (11.25)	0.13
Bladder max	75.0 (0.7)	74.2 (1.82)	0.15
Bladder mean	27.1 (8.18)	26.6 (8.16)	0.1
Penile bulb V40	27.5 (32.36)	37.6 (37.08)	**0.04**
Penile bulb V14	83.7 (20.00)	84.8 (23.68)	0.77
Femur right V30	4.44 (5.56)	3.5 (4.08)	0.16
Femur right V20	32.8 (17.04)	30.7 (16.10)	0.87
Femur left V30	6.1 (8.10)	4.9 (6.14)	0.2
Femur left V20	29.8 (14.04)	28.8 (13.73)	0.53

[a] The *p* values were calculated with paired Student's *t*-test. $p < 0.05$ (bold characters) indicates that the difference between the compared parameter sets is statistically significant

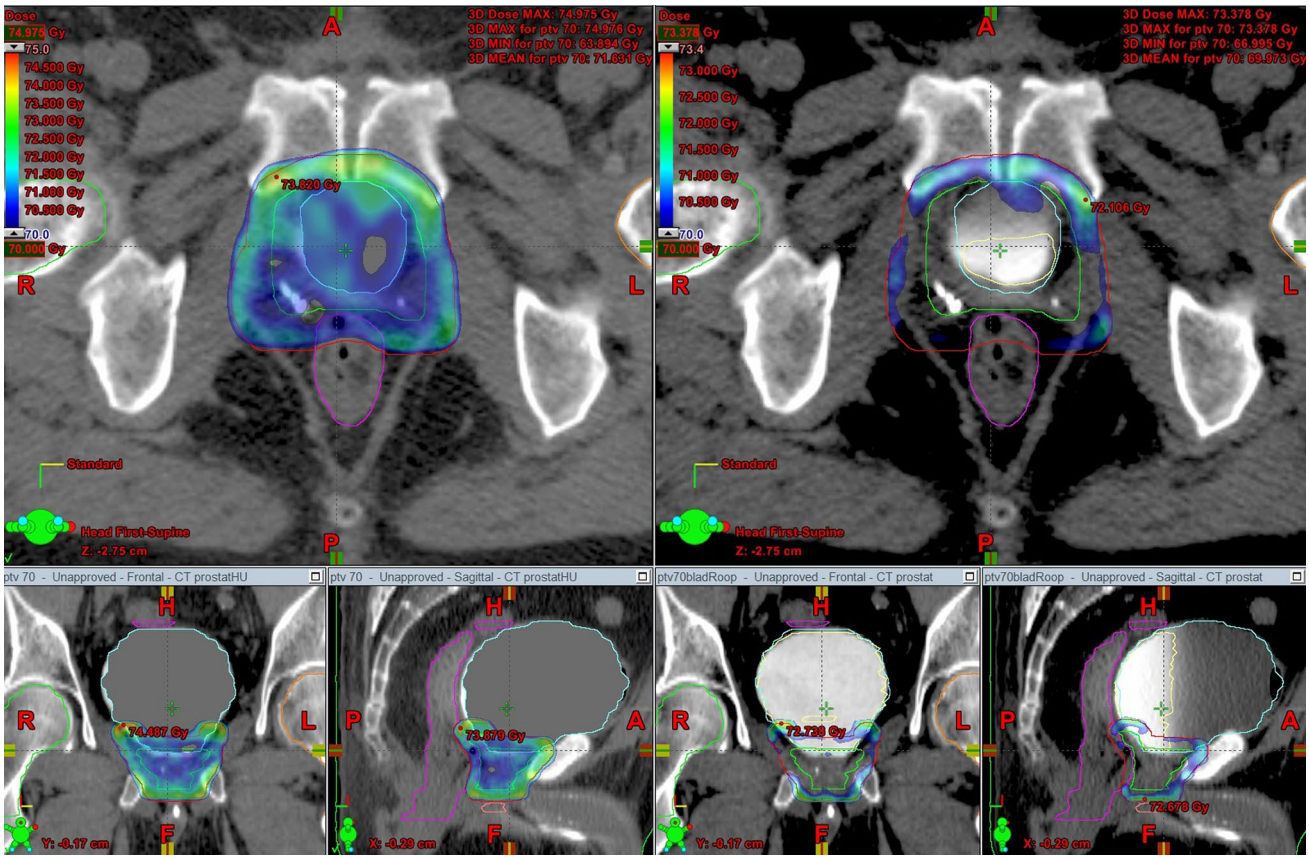

Fig. 4 Dose distribution for one patient at a 70-Gy level. Dose distribution on axial, coronal and sagittal CT slices. **a** Without contrast heterogeneity, **b** with contrast heterogeneity

was significantly lower than that calculated for the non-enhanced CT (1.19 vs 0.6, $p = 0.004$) (Table 2).

We also compared the homogeneity index (HI) for both plans. HI is defined as follows: HI = (D2–D98)/D prescription $\times 100$ %. Lower HI values are indicative of a more homogenous target dose [6]. The HI calculated for plans with enhanced CT and for the non-enhanced CT plans were 0.5. There was no significant difference between the two plans (Table 2).

Figure 4 shows the dose color wash distribution for one patient at a 70-Gy absolute dose level without contrast agent (a) and with contrast agent (b) CT images.

Discussion

Once introduced into clinical practice by Otto [7], VMAT has started to be used in many radiotherapy centers. To our knowledge, this is the first study reporting the effect of contrast agent on dose distribution of VMAT plans for prostate cancer patients in a postoperative setting. The accumulation of large amounts of contrast media in the bladder increases the probability of the presence of contrast within the target volume. This is the main reason why this clinical setting was chosen for this study. The effect of contrast agents on dose calculation for tumors in different anatomical regions has been evaluated [3, 8–13], all with conflicting results. The different concentration rates of the contrast agent within the tissue may be the reason for these discrepancies.

Weber et al. [3] studied prostate cancer patients who received bladder contrast during their planning CT scans to help localize the prostate. In this study the patients received only contrast-enhanced CT for treatment planning. A 3D conformal plan was performed with 6 fields (4 oblique and 2 lateral fields) of 18-MV photon beams. When they compared the plans, where the bladder was either contained contrast or was simply assigned a mass HU of water, the median dose variation was −0.03 % for the prostate volume and −1.13 % for the rectum. They indicated that any contrast-induced prostatic dose decrement would not be relevant for the lateral and posterior oblique beams when six coplanar field arrangements were used.

Although Weber et al. [3] considered that the contrast mass within the treatment volume had not significantly modified the dose distribution, we think that this is the result of the irradiation technique they used. With this

technique, the beams do not see the full bladder, which includes contrast agent. In our study, a part of the rotation (arc) of the beam passed through the target volume, critical organs and radiopaque substance.

In Yabsantia et al.'s [8] study, two CT series were compared, one with intravenous contrast and the other one without. They performed 3D-CRT planning with Pinnacle ver. 7.6 (Philips Radiotherapy planning system Andover, MA, USA). In the treatment plans on different anatomical sides they could not show any statistical dose differences between the two plans. They mentioned reducing the time in process of registration and image fusion between with- and without-contrast-agent CT images, and reducing space to store sets of images in treatment planning as the potential benefits of using with-contrast-agent CT images in dose calculation.

In contrast to Yabsantia et al., Shibamoto et al. [9] showed a difference between with- and without-contrast-agent plans in the upper abdomen. In their study they prospectively investigated the influence of contrast materials on dose calculation in patients undergoing radiotherapy for the brain, head and neck, mediastinum, upper abdomen or pelvis. They used opposing parallel fields in all sites other than upper abdomen, where they used 4 fields and full rotational conformal irradiation. They concluded that the mean increases in monitor units by contrast media administration were less than 1 % and considered this negligible in planning of whole brain, whole neck, mediastinal, and whole pelvic irradiation. However, mean increases over 2 % were seen in planning of upper abdominal radiotherapy.

Rankine et al. [10], Elawadi et al. [11], and Kimlin et al. [12] studied the effect of contrast media on megavoltage photon beam dosimetry in different clinic scenarios with 3D conformal planning. They emphasized that increasing the density of a structure increases the attenuation of photons; therefore, more monitor units (MUs) are required to deliver the same prescribed dose to the specified points. They showed that the errors introduced by carrying out dose calculations on contrast-enhanced CT data sets is typically small and such errors may be considered not clinically significant for target dose. In contrast to their findings, our data suggest that target doses could significantly be affected by the use of contrast media.

Choi et al. [13] studied the influence of intravenous contrast agent on dose calculations of intensity modulated radiation therapy plans for 15 head and neck cancer patients. In their study, each patient underwent two sets of CT scans in the same position before and after intravenous contrast agent. The beam characteristics of the IMRT plan generated from the enhanced CT were copied and applied to the non-enhanced CT, which included radiotherapy fields, leaf sequences, and MUs. Radiation doses were calculated again from the non-enhanced CT by an IMRT plan. They demonstrated that the presence of contrast within planning CT images had a negligible effect on the resultant dose distribution during radiotherapy planning, again in contrast to our findings.

In our study, using the same MUs for both CT sets, we showed that the use of contrast agent may cause significant differences in dose distribution. The decrease in mean, maximum and minimum doses received by PTV70 also contributed to the significant decrease in conformity index. The maximum dose to the rectum, V65 and V40 for the rectum and V65 for the bladder were also significantly decreased in plans with contrast-enhanced CT sets. These dosimetric changes caused by the contrast agent may result in unexpected clinical scenarios, especially in a case where the critical organ receives a dose close to its tolerance.

In conclusion, our results have shown that the use of contrast agents in the postoperative VMAT planning of prostate cancer patients may cause significant changes in dose distribution. We recommend assigning a normal HU value to the bladder before performing the plan. This may also overcome the difficulties of using two sets of CT scans, one with contrast and the other without.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Teh Bin S, Schroeder TM, Mai W-Y, Butler EB. Postoperative prostate cancer: overview. In: Mundt AJ, Roske JC, editors. Intensity modulated radiation therapy. Hamilton, London: BC Decker Inc; 2005. p. 449–58.
2. Valicenti RK, Sweet JW, Hauck WW, Hudes RS, Lee T, Dicker AP, et al. Variation of clinical target volume definition in three-dimensional conformal radiation therapy for prostate cancer. Int J Radiat Oncol Biol Phys. 1999;44:931–5.
3. Weber DC, Rouzaud M, Mirabell R. Bladder opacification does not significantly influence dose distribution in conformal radiotherapy of prostate cancer. Radiother Oncol. 2001;59(1):95–7.
4. Vanetti E, Nicolini G, Clivio A, Fogliata A, Cozzi L. The impact of treatment couch modelling on RapidArc. Phys Med Biol. 2009;54:157–66.
5. Pulliam KB, Howell RM, Followill D, Luo D, White RA, Kry SF. The clinical impact of the couch top and rails on IMRT and arc therapy. Phys Med Biol. 2011;56:7435–47.
6. Feuvret L, Noel G, Mazeron JJ, Bey P. Conformity index: a review. Int J Radiat Oncol Biol Phys. 2006;64(2):333–42.
7. Otto K. Volumetric modulated arc therapy: IMRT in a single gantry arc. Med Phys. 2008;35(1):310–7.
8. Yabsantia S, Tangboonduangjit P, Tannanonta C. The effect of contrast agents on dose calculation in conformal radiotherapy planning using computed tomography for tumors at different anatomical regions. J Thai Soc Therap Radiol Oncol. 2010;16(2):23–7.

9. Shibamoto Y, Naruse A, Fukuma H, Ayakawa S, Sugie C, Tomita N. Influence of contrast materials on dose calculation in radiotherapy planning using computed tomography for tumors at various anatomical regions: a prospective study. Radiother Oncol. 2007;84(1):52–5.
10. Rankine AW, Lanzon PJ, Spry NA. Effects of contrast media on megavoltage photon beam dosimetry. Med Dosimetry. 2008;33(3):169–74.
11. Elawadi AS, Bayoumi Y, Alomran R, El-Moniem RA, Ismail A, Alamro A. Does intravenous contrast agent affect dose calculations of three dimensional treatment planning system? Bull Alex Fac Med. 2009;45:103–8.
12. Kimlin K, Mitchell J, Knight RT. Effects of iodinated contrast media on radiation therapy dosimetry for pathologies within the thorax. The Radiographer. 2006;53(2):30–4.
13. Choi Y, Kim JK, Lee HS, Hur WJ, Hong YS, Park S, et al. Influence of intravenous contrast agent on dose calculations of intensity modulated radiation therapy plans for head and neck cancer. Radiother Oncol. 2006;81(2):158–62.