Original article

2D to 3D Evaluation of Organs at Risk Doses in Intracavitary Brachytherapy for Cervical Cancer

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Abstract

Purpose: To compare International Commission on Radiation Units and Measurements (ICRU) bladder and rectum reference points doses with volumetric doses in 3D intracavitary brachytherapy (ICBT) for cervical cancer. Also to compare bladder, rectum and sigmoid (organs at risk, OARs) volume doses with dose constraints recommended by the (GYN) GEC-ESTRO Working Group.

Material and methods: A retrospective study was carried out on 10 patients with a total of 55 fractions CT-based high dose rate (HDR) ICBT. ICRU bladder (bICRU) and rectum (rICRU) points were defined according to ICRU Report 38 on the CT images and prospectively kept to less than 80% of prescription dose to Point A during real treatment planning. Post-treatment, outer wall of OARs were contoured and minimum dose to 2cc (D2cc) of the most irradiated part of the OARs was obtained from the dose-volume histogram (DVH). Total dose (external beam radiotherapy plus ICBT) were computed with ICRU point dose and D2cc and compared.

Results: The mean ICRU point dose and D2cc volume dose were found to be significantly different for bladder (per fraction: $p = 0.000$; total dose: $p = 0.004$) but no differences were found for rectum (per fraction: $p = 0.055$; total dose: $p = 0.090$). bICRU point dose underestimated D2cc dose with an average ratio of 1.34 ± 0.34. 3 out of 10 patients, 7 out of 10 patients, and 5 out of 10 patients exceeded the recommended dose constraint for bladder, rectum, and sigmoid, respectively.

Conclusions: bICRU was not representative of bladder D2cc and resulted in different total dose. rICRU was found to be similar to D2cc dose and was reliable in total dose computation. Our current institutional practice of point-based planning in ICBT resulted in significant number of patients' OARs doses exceeded the volume constraint, because the total dose concept was not used propectively in planning.

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Key words: brachytherapy, cervical cancer, CT-based, intracavitary.

Purpose

Traditionally, bladder and rectum dose in intracavitary brachytherapy (ICBT) for cervical cancer are estimated using the International Commission on Radiation Units and Measurements (ICRU) reference points [1]. The ICRU points were an acceptable way of estimating dose to bladder and rectum only if 2D orthogonal films were available for ICBT planning. However, the correlation of the ICRU point doses with bladder and rectal complications are debatable [2-5]. With the availability of CT scanner and treatment planning software for 3D brachytherapy in recent years, there is a need to move forward to a 3D assessment of organs at risk (OARs). Instead of using point doses, volumetric assessment of OARs is a better and more complete representation of doses to OARs [6-8].

3D brachytherapy planning became available in National University Cancer Institute Singapore (NCIS) in April 2008. Since then, all treatment plans for cervical cancer brachytherapy patients are designed using CT images for each application. Manchester System Point A prescription is still the standard prescription point and ICRU reference points for bladder and rectum are defined following the ICRU Report 38 [1]. Standard loading pattern is used to achieve the conventional pear-shaped distribution. No contour is drawn at the time of planning and total dose (dose from external beam radiotherapy, EBRT, plus ICBT) is not evaluated prospectively during planning.

As part of the transition from 2D to 3D planning, we hope to evaluate and achieve a better understanding of our current practice of point-based planning using CT images. In addition to the usual planning and treatment, post-treatment dosimetry assessments of OARs were being carried out. By doing so, ICRU bladder and rectum reference point doses can be compared with dose-volume histogram (DVH) doses. This study also aims to compare bladder, rectum and sigmoid doses with dose constraints recommended by the (GYN) GEC-ESTRO Working Group [9] to evaluate our current institutional protocol for ICBT.

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Material and methods

Patient selection

Ten patients with a total of 55 fractions of CT-based high dose-rate (HDR) ICBT for cervical cancer were selected for this retrospective study. Selected patients were treated in NCIS between June 2008 and July 2009.

Treatment scheme

The standard treatment for cervical cancer consists of external beam radiotherapy (EBRT) using four-field box technique, with or without concomitant chemotherapy, and ICBT. In this study, EBRT dose was 45 Gy (2 patients) and 50.4 Gy (8 patients) delivered at 1.8 Gy per fraction. As for ICBT, prescription dose was 5.3 Gy to Point A in 5 fractions (5 patients) or 6 fractions (5 patients). ICBT was carried out on alternate days amounting to 2 to 3 treatments a week. We aim to complete the whole course of treatment within 50 days.

Brachytherapy insertion and scanning

Fletcher Williamson "Asia Pacific" metal ovoid applicators were used (ovoid sizes: half ovoid, 20 mm, and 25 mm; tandem angles: 15°, 30° and 45°). Combination of ovoid size and tandem angle were chosen according to patient's anatomy. Packing was done to set the applicators in place and also to displace the bladder and rectum. Foley balloon was inserted and filled with 7 cc air and pulled to sit on the bladder trigone. All procedures were done under conscious sedation without general or spinal anesthetics. After that, patients were CT-scanned with applicators in place. Scanning was done with Philips Brilliance Big Bore CT scanner using 120 kV, 325 mAs, and a combination of 3 mm and 5 mm slices. No contrast was used.

Brachytherapy planning

Planning were done using Oncentra Treatment Planning System (Nucletron). 5.3 Gy was prescribed to Point A of the Manchester System using standard loading pattern without optimization. Limited optimization was done in some patients whenever necessary. Mean TRAK value was 0.34 ± 0.03 cGy at 1 m. Bladder and rectum points were defined according to ICRU Report 38 [1]. As a standard institutional practice, bladder and rectum point doses were kept to less than 80% of dose to Point A for each fraction, except in 3 applications where ICRU bladder point dose was exceeded. No contouring was done during the actual treatment planning.

Post-treatment OARs delineation and treatment planning

Post-treatment, radiation oncologists delineated the outer wall of OARs (bladder, rectum, sigmoid) on all the 55 sets of CT images. Rectum was contoured from above the anal sphincter to the level of transition to sigmoid and sigmoid was contoured from the recto-sigmoid flexure. Original treatment plans were assessed for the respective applications with the contours now drawn. DVH parameters for minimum dose to the most irradiated contiguous volume of 0.1 cc, 1 cc and 2 cc (D0.1, D1cc, and D2cc respectively) were produced for each OARs with 100 000 sample points. ICRU point doses for bladder (bICRU) and rectum (rICRU) were recorded. Total dose was computed separately for OARs using ICRU point dose and D2cc. Total dose represents absorbed dose contributed by both EBRT and ICBT with the assumption that the OARs received full dose from EBRT and the same area of OARs were irradiated for all ICBT fractions. The difference in total dose when calculated using the ICRU point dose versus D2cc was analyzed. Physical doses were converted to a biologically equivalent dose and normalized to conventional 2 Gy fractions ($\alpha/\beta = 3$), EQD2.

Data analysis

All parameters were tested for normal distribution. Paired T-test was used as a parametric test to compare means of ICRU point doses and D2cc volume doses as well as the total dose computed, using these two parameters. Mean ratio was also calculated as an average of each application.

Results

Table 1 shows the comparison of means between ICRU point doses and D2cc volume doses. Mean ICRU and D2cc doses calculated as an average of each fraction presented a statistically significant difference for bladder ($p = 0.000$) but no difference was found for rectum ($p = 0.055$). Similarly, comparison of mean total dose (ICRU point Vs D2cc) for each patient was found to be significantly different for bladder ($p = 0.004$) but not for rectum ($p = 0.090$). For bladder, bICRU underestimated D2cc dose with an average ratio of 1.34 ± 0.34 and total dose computed using bICRU underestimated total dose computed using D2cc with an average ratio of 1.16 ± 0.12.

Comparison of values from this study with other published values [10, 11] can be found in Table 2. In general, various dose parameters for bladder from this study were lower than in two others published data, while rectum and sigmoid doses were higher in this study.

3 out of 10 patients, 7 out of 10 patients, and 5 out of 10 patients exceeded the (GYN) GEC-ESTRO Working Group [9] recommended dose constraint for bladder, rectum, and sigmoid, respectively (Table 3).

Discussion

The whole volume (outer wall) of OARs was contoured in this study. Organ and organ wall contouring yield comparable results when volumes up to 3 cc are considered [12, 13]. 0.1 cc, 1 cc, and 2 cc volumes were being analyzed, focusing on the 2cc parameter. Currently, NCIS uses only CT-based planning for all ICBT applications. CT images were found to be comparable to MRI images for delineation of outer wall of OARs [14]. Interobserver variation was not addressed in this study.

Bladder

Results from this study showed that bICRU underestimated bladder D2cc dose by a ratio of 1.34. Similar trend

Table 1. Comparison of means for ICRU point doses and D2cc volume doses in bladder and rectum

BT[1]	Bladder	Rectum
Mean ICRU[2] (Gy)	2.9 (range: 1.2-4.5)	3.4 (range: 2.4-4.2)
Mean D2cc[3] (Gy)	3.9 (range: 1.3-6.3)	3.6 (range: 1.8-5.9)
Paired T-Test	P = 0.000, 95% CI (–1.18, –0.71)	P = 0.055, 95% CI (–0.41, 0.01)
Average Ratio (D2cc/ICRU)	1.34 ± 0.34	1.07 ± 0.25
EBRT[4] + BT	**Bladder**	**Rectum**
Mean Total Dose using ICRU (Gy_{EQD2})	67.3 (range: 58.5-78.1)	71.7 (range: 62.4-81.5)
Mean Total Dose using D2cc (Gy_{EQD2})	78.5 (range: 61.6-106.6)	74.3 (range: 63.9-80.2)
Paired T-Test	P = 0.004, 95% CI (–17.89, –4.52)	P = 0.090, 95% CI (–5.74, 0.50)
Average Ratio (D2cc/ICRU)	1.16 ± 0.12	1.04 ± 0.06

[1] *BT – Brachytherapy*
[2] *ICRU – International Commission on Radiation Units and Measurements (ICRU defined point doses)*
[3] *D2cc – Minimum dose to the most irradiated contiguous volume of 2cc*
[4] *EBRT – External beam radiotherapy*

Table 2. Comparison of total dose for OARs with other findings

	Mean ± StDev[5] (Gy α/β = 3)		
	NCIS[6]	Koom *et al.* [10]	Kirisits *et al.* [11]
Bladder			
ICRU Point	67 ± 7	75 ± 19	75 ± 16
ICRU 1.5[7]	84 ± 19	–	100 ± 25
ICRU 2.0	94 ± 29	–	112 ± 34
D0.1cc[8]	104 ± 29	107 ± 30	121 ± 25
D1cc	85 ± 18	90 ± 18	92 ± 11
D2cc	79 ± 15	84 ± 15	83 ± 9
Rectum			
ICRU Point	72 ± 6	69 ± 10	69 ± 13
D0.1cc	95 ± 0	80 ± 14	77 ± 10
D1cc	80 ± 7	71 ± 10	66 ± 7
D2cc	74 ± 6	67 ± 9	64 ± 6
Sigmoid			
D0.1cc	102 ± 22	82 ± 20	79 ± 12
D1cc	82 ± 12	71 ± 13	67 ± 8
D2cc	76 ± 10	67 ± 11	63 ± 7

[5] *StDev – Standard deviation*
[6] *NCIS – National University Cancer Institute, Singapore*
[7] *ICRU 1.5, ICRU 2.0 – Points defined 1.5cm and 2.0cm respectively, cranially from the ICRU point*
[8] *D0.1cc, D1cc - Minimum dose to the most irradiated contiguous volume of 0.1cc and 1cc respectively*

Table 3. Number of patients with OARs D2cc total dose exceeding the recommended tolerance

	Bladder	Rectum	Sigmoid
†Number of patients (n = 10)	3/10	7/10	5/10

† *Data presented as number of patients with OARs D2cc total dose exceeding the (GYN) GEC-ESTRO Working Group [9] recommended tolerance (Bladder > 90Gy_{EQD2}, Rectum and Sigmoid > 70-75Gy_{EQD2})*

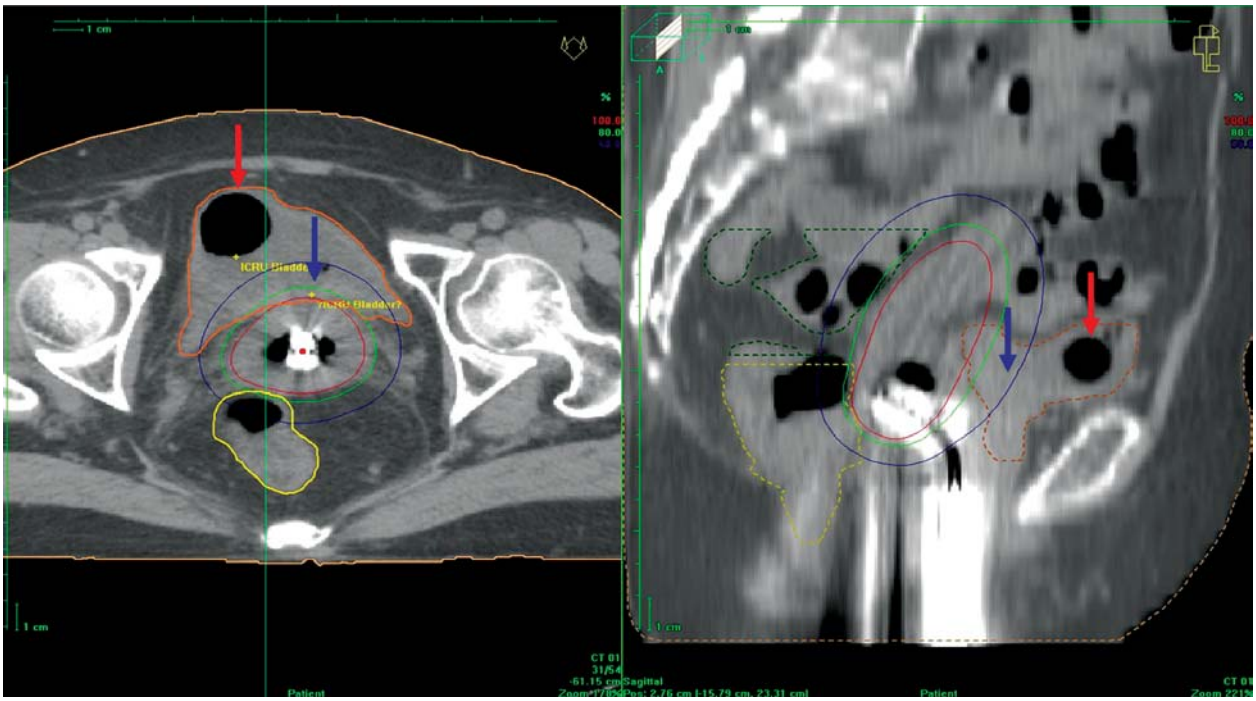
was reported by other studies [6, 11, 15-17]. There was also a statistically significant difference in total dose to bladder when using bICRU versus D2cc (p = 0.004). bICRU did not accurately reflect correct dose to bladder and it was not a reliable parameter to use as a criteria in planning. Retrospective evaluation of correlation by Kirisits *et al*. [11] found that D2cc overdose were not reflected in the ICRU reference point and patients subsequently develop Grade 4 late side effects.

Overall comparison of bladder dose parameters with Koom *et al*. [10] and Kirisits *et al*. [11] presented that both point dose and volume dose parameters were lower in this study. A review of images used in this study showed that inappropriate location of Foley balloon may have caused the bICRU to move out of the high dose region. The Foley balloon was seen to be 'floating' cranially from the bladder trigone in some cases (Fig. 1). Fluid-filled balloon is recommended to fix Foley balloon in an appropriate location [1]. Besides that, it was also noted that Foley balloon was not properly inflated to the 7 cc volume in a few applications (Fig. 2). These may be the reasons for the low bladder point dose observed in this study. As Koom *et al*. [10] uses the same applicator model as in this study, the lower bladder volume doses can only be attributed to differences in applicator position and planning (difference in dwell position and dwell time activation).

3 out of 10 patients received a calculated bladder dose (using D2cc definition) exceeding the (GYN) GEC-ESTRO Working Group recommendation [9]. However, no bladder overdose was detected when computed using bICRU (Table 4). Therefore, bICRU may not be a reliable parameter for estimating total dose to the bladder.

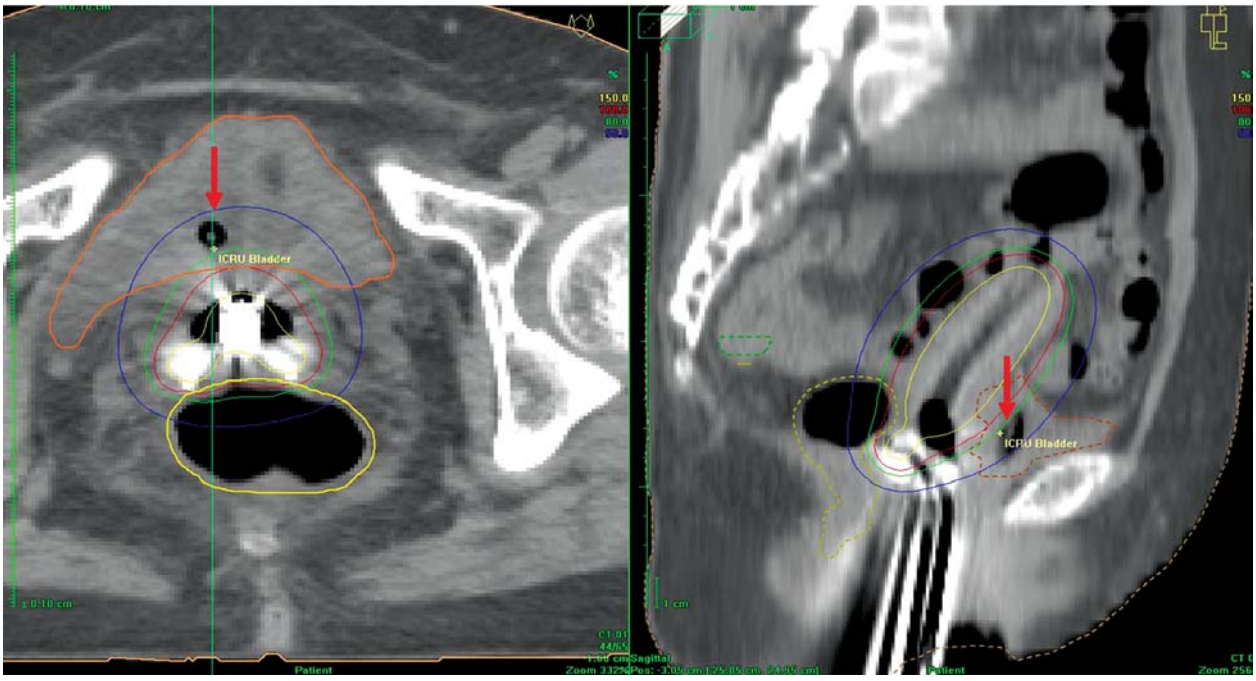
Rectum

There was no difference found between rICRU and D2cc doses (p = 0.055) in this study. A few other studies also



Red Arrow indicates the inappropriate location of Foley balloon during treatment, resulting in inaccurate definition of ICRU bladder point dose. Blue Arrow indicates the appropriate location where the Foley balloon should be.

Fig. 1. Inappropriate placement of Foley balloon



Red Arrow indicates the Foley balloon that was not properly inflated during treatment, resulting in inaccurate definition of ICRU bladder point dose.

Fig. 2. Example of Foley balloon not properly inflated

reported similar finding [6, 11, 15, 16]. The average ratio (D2cc/rICRU) in this study was 1.07, similar to the ratio reported by Pelloski *et al*. [17]. rICRU underestimate D2cc although the difference was not significant (p = 0.055). When total dose to rectum was computed for each individual patient in this study, the difference between rICRU and D2cc was also insignificant (p = 0.090). So, it is possible to use rICRU to calculate the total dose to rectum for comparison against the recommended constraint during planning. However, care has to be taken to visually check

the 3D images (if available) for high dose region especially in the superior part of the rectum. Although ICRU point can represent D2cc in the analysis of total dose to rectum, 7 out of 10 patients exceeded the (GYN) GEC-ESTRO Working Group recommended value [9] because the concept of total dose evaluation was not used prospectively during planning in these cases. It was also found that the lower end of the recommended constraint (70 Gy_{EQD2}) should be used if total dose was computed using rICRU dose (Table 5). Bowel preparation is also crucial to avoid

Table 4. Comparison of bladder total doses computed using bICRU and D2cc for each individual patient

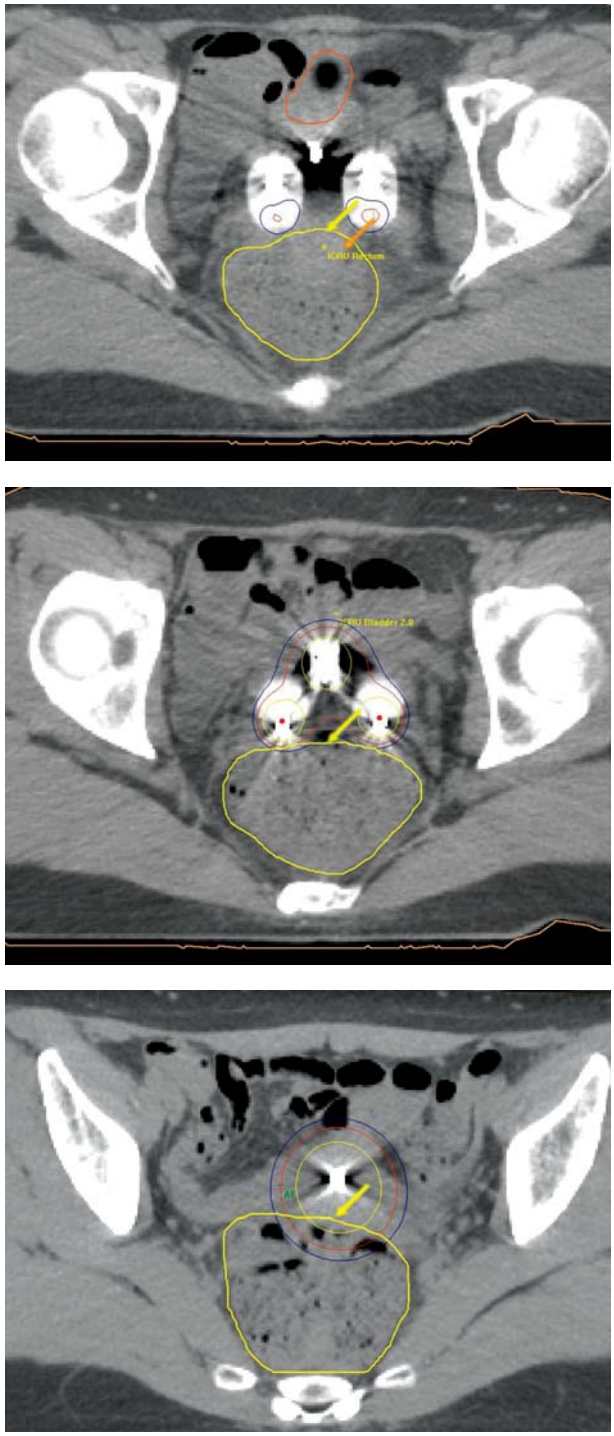
	Total Dose (Gy_{EQD2})	
	bICRU[9]	Bladder D2cc
Pt1	59.5	66.4
Pt2	64.7	78.5
Pt3	74.0	**94.8**
Pt4	78.1	**92.8**
Pt5	66.7	66.7
Pt6	67.5	74.7
Pt7	64.0	75.7
Pt8	58.5	61.6
Pt9	75.9	**106.6**
Pt10	64.6	67.6
Average	67.3	78.5
StDev	6.7	14.8
Min	58.5	61.6
Max	78.1	106.6

[9] bICRU - ICRU defined point dose for bladder
Bold font: *> 90 Gy_{EQD2}*

Table 5. Comparison of rectum total doses computed using rICRU and D2cc for each individual patient

	Total Dose (Gy_{EQD2})	
	rICRU[10]	Rectum D2cc
Pt1	66.8	**76.9**
Pt2	70.9*	**76.4**
Pt3	72.0*	**76.6**
Pt4	**79.7***	**77.8**
Pt5	72.2*	**78.0**
Pt6	67.4	67.6
Pt7	68.9	65.2
Pt8	62.4	63.9
Pt9	74.6*	**80.2**
Pt10	**81.5***	**80.2**
Average	71.7	74.3
StDev	5.8	6.2
Min	62.4	63.9
Max	81.5	80.2

[10] rICRU - ICRU defined point dose for rectum
Bold font: *> 75 Gy_{EQD2}*
** Total dose computed using rICRU point dose can detect overdose if lower end of the recommended constraint (70 Gy_{EQD2}) is used.*



Top to bottom: Consecutive CT images of a patient with full bowel. Yellow Arrow indicates the location of anterior rectal wall. Orange Arrow indicates the rectum point dose defined according to ICRU Report 38.

Fig. 3. Large discrepancies between rICRU dose and D2cc rectum dose in patient with full bowel

large difference between rICRU dose and D2cc dose that will affect the total dose computation (Fig. 3). Comparison of rectum values with Koom *et al*. [10] and Kirisits *et al*. [11] showed that dose to rectum is higher in this study. Review of images used in this work found that poor bowel preparation and inadequate packing may have caused higher volume dose while differences in applicator position and planning may be the reason for the higher ICRU point dose observed. As all procedures were performed under conscious sedation, sufficient packing was difficult. The use of radio-opaque packing in the vagina for better visualization of vaginal and rectal wall as well as careful assessment of ovoid position with respect to the axis of the tandem may help to reduce dose to rectum [6].

Sigmoid

Dose to sigmoid is traditionally not reported for ICBT. Therefore, no comparison was made to the sigmoid D2cc dose. Although sigmoid dose was not reported in the past because of its mobility, it was noted that sigmoid actually received a substantial amount of dose. Half of the patients evaluated in this study exceeded the dose constraint.

A higher percentage of patient's total dose to rectum (7 out of 10 patients) exceeded the recommended value compared to bladder (3 out of 10 patients). This is due to higher tolerance value recommended by (GYN) GEC-ESTRO Working Group [9] for the bladder (80-90 Gy_{EQD2}) compared to rectum (70-75 Gy_{EQD2}) while the ICRU point-based planning criteria used in our institution is the same for both OARs (< 80% of dose to Point A). As a result, more patients received dose exceeding the recommended tolerance value for rectum compared to bladder. The '< 80% of dose to Point A' should not be used as generic planning criteria. The percentage should be calculated individually according to the different prescription dose and fractionation using the total dose concept.

Conclusions

ICRU reference point doses underestimated D2cc volume doses for bladder but no difference were found for rectum. Therefore, rICRU can be used to calculate total dose to rectum but the total dose to bladder should only be computed using the bladder D2cc value. A single generic point dose criterion for both bladder and rectum is not appropriate. Our current institutional practice of point-based planning using the '< 80% prescription dose' rule alone resulted in a significant number of patients' OARs doses exceeding the volume tolerance recommended by (GYN) GEC-ESTRO Working Group especially for rectum due to lower dose tolerance. Total dose assessment, even for point-based planning, can reduce the number of overdose incident. ICRU reference point dose should be used with caution for the dose estimation to OARs in ICBT. Volume-based planning should be applied whenever feasible and if not, the total dose concept must be incorporated for all ICBT planning including point-based planning.

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