RESEARCH ARTICLE

# CT Based 3-Dimensional Treatment Planning of Intracavitary Brachytherapy for Cancer of the Cervix : Comparison between Dose-Volume Histograms and ICRU Point Doses to the Rectum and Bladder

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## Abstract

**Background: CT based brachytherapy allows 3-dimensional (3D) assessment of organs at risk (OAR) doses with dose volume histograms (DVHs). The purpose of this study was to compare computed tomography (CT) based volumetric calculations and International Commission on Radiation Units and Measurements (ICRU) reference-point estimates of radiation doses to the bladder and rectum in patients with carcinoma of the cervix treated with high-dose-rate (HDR) intracavitary brachytherapy (ICBT). Materials and Methods: Between March 2011 and May 2012, 20 patients were treated with 55 fractions of brachytherapy using tandem and ovoids and underwent post-implant CT scans. The external beam radiotherapy (EBRT) dose was 48.6Gy in 27 fractions. HDR brachytherapy was delivered to a dose of 21 Gy in three fractions. The ICRU bladder and rectum point doses along with 4 additional rectal points were recorded. The maximum dose ($D_{Max}$) to rectum was the highest recorded dose at one of these five points. Using the HDRplus 2.6 brachyhtherapy treatment planning system, the bladder and rectum were retrospectively contoured on the 55 CT datasets. The DVHs for rectum and bladder were calculated and the minimum doses to the highest irradiated 2cc area of rectum and bladder were recorded ($D_{2cc}$) for all individual fractions. The mean $D_{2cc}$ of rectum was compared to the means of ICRU rectal point and rectal $D_{Max}$ using the Student's t-test. The mean $D_{2cc}$ of bladder was compared with the mean ICRU bladder point using the same statistical test .The total dose, combining EBRT and HDR brachytherapy, were biologically normalized to the conventional 2 Gy/fraction using the linear-quadratic model. (α/β value of 10 Gy for target, 3 Gy for organs at risk). Results: The total prescribed dose was 77.5 Gyα/β10. The mean dose to the rectum was 4.58±1.22 Gy for $D_{2cc}$, 3.76±0.65 Gy at $D_{ICRU}$ and 4.75±1.01 Gy at $D_{Max}$. The mean rectal $D_{2cc}$ dose differed significantly from the mean dose calculated at the ICRU reference point (p<0.005); the mean difference was 0.82 Gy (0.48 -1.19Gy). The mean EQD2 was 68.52±7.24 $Gy_{α/β3}$ for $D_{2cc}$, 61.71±2.77 $Gy_{α/β3}$ at $D_{ICRU}$ and 69.24±6.02 $Gy_{α/β3}$ at $D_{Max}$. The mean ratio of $D_{2cc}$ rectum to $D_{ICRU}$ rectum was 1.25 and the mean ratio of $D_{2cc}$ rectum to $D_{Max}$ rectum was 0.98 for all individual fractions. The mean dose to the bladder was 6.00±1.90 Gy for $D_{2cc}$ and 5.10±2.03 Gy at $D_{ICRU}$. However, the mean $D_{2cc}$ dose did not differ significantly from the mean dose calculated at the ICRU reference point (p=0.307); the mean difference was 0.90 Gy (0.49-1.25Gy). The mean EQD2 was 81.85±13.03 $Gy_{α/β3}$ for $D_{2cc}$ and 74.11±19.39 $Gy_{α/β3}$ at $D_{ICRU}$. The mean ratio of $D_{2cc}$ bladder to $D_{ICRU}$ bladder was 1.24. In the majority of applications, the maximum dose point was not the ICRU point. On average, the rectum received 77% and bladder received 92% of the prescribed dose. Conclusions: OARs doses assessed by DVH criteria were higher than ICRU point doses. Our data suggest that the estimated dose to the ICRU bladder point may be a reasonable surrogate for the $D_{2cc}$ and rectal $D_{Max}$ for $D_{2cc}$. However, the dose to the ICRU rectal point does not appear to be a reasonable surrogate for the $D_{2cc}$.**

**Keywords:** Cancer of cervix - brachytherapy - D2cc rectum - D2cc bladder - rectal Dmax

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## Introduction

CT based 3D brachytherapy is fast becoming the standard mode of treatment for patients with cervical carcinoma treated radically by radiation therapy. It is now possible to perform full- fledged anatomy-based dose specification using 3D CT studies acquired with the applicator system in place. 3D images provide more

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anatomic information regarding the target, its relation to the surrounding anatomy and the organs at risk (OARs) and the position of the brachytherapy applicator or catheters relative to the anatomy. Sophisticated software has been developed that allows slice-by-slice delineation of targets, applicators and organs at risk. 3D reconstruction of the structures permits display in any plane with the overlaid isodose curves. Treatment plans can be assessed and appraised by viewing isodose curves, isodose surfaces, or dose volume histograms. 3D anatomy-based, dose-optimization planning approach provides a truly personalized treatment. Multiple studies have proven that anatomy-based dose specification using 3D CT or MRI is better in terms of target coverage as well as estimation of dose to organs at risks.

The GEC-ESTRO group has recently published recommendations for three-dimensional image-based brachytherapy (Potter et al., 2006). This recommendation aims at an individualised adaptation of the dose distribution to a target at high and/or intermediate risk for recurrence; high risk clinical target volume (HR CTV)/ intermediate risk clinical target volume (IR CTV) and to find a balance with dose volume constraints to be taken into consideration for the adjacent OARs. The total dose, including EBRT dose, should be isoequivalent to 80-90 Gy in 2 Gy fractions for the HR CTV, and 60 Gy for the IR CTV. Doses for 2 mL of tissue volume ($D_{2cc}$) for the OAR are calculated at 2 Gy per fraction. Isoequivalent doses of 80-90 Gy for the bladder and 70-75 Gy for the rectum and sigmoid colon are generally accepted. The minimum dose in the most irradiated tissue volume adjacent to the applicator (0.1, 1, 2 and 5 cm3) is recommended for recording and reporting. The American Brachytherapy Society (ABS) also recommends a total tumour dose of 80-90 Gy, depending on tumor size at the time of brachytherapy (Viswanathan and Thomadsen, 2012; Viswanathan et al., 2012). The dose delivered to point A should be reported for all brachytherapy applications regardless of treatment-planning technique. The ABS also recommends adoption of the Groupe Européen Curiethérapie-European Society of Therapeutic Radiation Oncology (GEC-ESTRO) guidelines for contouring, image-based treatment planning, and dose reporting.

The curative potential of radiation with integration of brachytherapy for the treatment of non-metastatic cervical carcinoma is undeniable. However, there is a major concern regarding late toxicities to the OARs using brachytherapy. Many studies had found correlation between total dose to the rectum and bladder with late radiation toxicities. Others have tried to compare the late radiation toxicities with volumetric doses. While many studies could be found correlating dose with toxicities to the rectum, there were very few studies looking at the urinary bladder toxicities. Perez and colleaugues (1999) had analyzed records of 1456 patients (Stages IB-IVA) treated with external-beam irradiation plus two LDR intracavitary insertions to deliver 70 to 90 Gy to point A. Doses below 80 Gy in the bladder, correlated with less than 3% incidence of morbidity and 5% with higher doses (p=0.31). The incidence of significant morbidity in the rectosigmoid was less than 4% with doses below 75 Gy and increased to 9% with higher doses. When the ratio of dose to the bladder or rectum in relation to point A was 0.8 or less, the incidence of rectal morbidity was 2.5% (8 of 320) *vs* 7.3% (80 of 1095) with higher ratios ($p<0.01$); bladder morbidity was 2.3% (7 of 305) and 5.8% (64 of 1110), respectively (p=0.02). In another review of 1784 patients with Stage IB cervical carcinoma treated with radical EBRT and LDR brachytherapy, a 9.3% incidence of major complications at 5 years was reported (Eifel et al., 1995). Minor Grade 1 or 2 urinary tract complications occurred most often during the first 3 years after treatment. Approximately two-thirds of these were Grade 1 (a single brief episode of mild hematuria or sterile dysuria). The time course for developing rectal complications contrasted markedly with that for developing urinary tract complications. The greatest risk for developing major rectal complications was during the first 2 years of follow-up (1% per year) with a subsequent continuous risk of only ~0.06% per year.

A retrospective review of 141 uterine cervical cancer patients (1b-IVb), treated with teletherapy combined with HDR cobalt-60 brachytherapy reported the mean onset time to develop radiation proctitis and radiation cystitis were 15 and 30 months respectively (Pesee et al., 2010) While many studies were looking at the relationship between dose and organs at risk toxicities, Lin Yang and Yin LV (2012) analysed the possible risk factors associated with the development of radiation proctitis or radiation cystitis in 1518 cervical cancer patients following radiation therapy. The prevalence of Grade 1 and 2 radiation proctitis and radiation cystitis was lower than Grade 3 and was significantly higher in patients with late stage tumour (IIIb). No correlation between incidence of radiation proctitis/cystitis with age and time period following radiation.

Kang and colleagues (2010) have reported on the impact of 3D CT-based HDR ICBT on late rectal bleeding and local control in patients with cervical cancer. The overall rectal bleeding rate was similar between the groups (42% for 3D-ICBT *vs* 44% for 2D-ICBT). Even so, the incidence of severe late rectal bleeding was higher in the 2D-ICBT group than in the 3D-ICBT group (13% *vs* 2%, respectively; p=0.02). The factors associated with severe late rectal bleeding were tumour >4 cm (12% *vs* 3%) and 2D-ICBT (10% *vs* 2%).

The $D_{2cc}$ is now the most commonly used parameter for evaluation of rectal and bladder doses with 3D CT-based ICBT ((Potter et al., 2006). However, there is still uncertainty regarding the older ICRU rectal and bladder points on whether these points can continue to be used as surrogates for the $D_{2cc}$. There have been reports that suggest a good correlation of the $D_{2cc}$ for the rectum and the ICRU rectal point (Wachter-Gerstner et al., 2003; Kristis et al., 2005; Pelloski et al., 2005).

In addition, there are centres that use the maximal rectal point dose other than the ICRU reference point. Our centre has started using 3D CT-based ICBT in 2011 but still optimises the dosimetry using the older ICRU rectal and bladder point doses and the maximal rectal point dose. This study aims to compare the $D_{2cc}$ of the rectum and the ICRU rectal point dose and maximal rectal point dose. The

$D_{2cc}$ of the bladder will be compared to the ICRU bladder point dose.

## Materials and Methods

This is a retrospective study of 22 patients who underwent radical radiotherapy with or without concurrent cisplatin chemotherapy for cervical cancer at Clinical Oncology Unit, University of Malaya Medical Centre (UMMC). All patients underwent external beam radiotherapy followed by CT based HDR intracavitary brachytherapy. Each insertion was evaluated individually in their respective physical dose. Statistical analysis was performed using SPSS statistical computer package version 18 (IBM Corporation, NY, USA). Comparisons of means between $D_{2cc}$ rectum and bladder and dose to rectal and bladder ICRU points were calculated using paired t-test. According to Clinical Oncology Unit UMMC radiation therapy protocol for cervical cancer, the external beam radiotherapy (EBRT) was given to the pelvis with a standard EBRT dose of 48.6 Gy in 27 fractions for 6.5 weeks. The EBRT was 3D-planned with conformal four- field box technique using 10 MV photons. In the case of bulky tumours with posterior and anterior extent of disease towards rectum and/or bladder, an APPA two fields technique prescribed to mid-plane dose was used. The superior border of the pelvic portal is set at the L5-S1 interspace and the inferior border is set below the obturator foramen or 3 cm inferior to distal disease, whichever is lower. The lateral borders were located 1.5 cm outside the bony pelvic sidewalls. The lateral ports anterior margin is placed at the mid-pubic symphysis and posterior border for the lateral field is placed at S2 and S3 junction. Few patients had parametrial boost up to 54 Gy with central shield introduced for the last 3 fractions. Patients who had paraortic lymph node involvement had radiotherapy field extended to include the para-aortic strip. The full insertion HDR brachytherapy was given for 3 fractions, 7 Gy each and delivered at week 4, 5 and 6 of EBRT.

*Brachytherapy*

Each application was performed under regional (spinal) anaesthesia in the lithotomy position. The procedure was performed under general anaesthesia when there was failure or contraindication to spinal anaesthesia. A Foley catheter was inserted into the bladder, and 7cc of radio-opaque contrast was injected into the balloon to aid in the identification of the ICRU bladder reference point. A thorough gynaecological examination was performed and tumour factors assessed. The length of the uterine cavity was determined using a uterine sound. The applicators used were IBT Bebig Fletcher set CT/MR compatible tandem and ovoids. Radiopaque 2 inch gauze soaked with acriflavine 0.1% emulsion was used to pack the vagina to fix the applicators in placed and to push the bladder and rectum away. The applicators were further stabilized with a gamgee which was taped on the patient's skin. The patient was transferred to the CT simulator suite. A CT scan (Philips Brilliance Big Bore Simulation CT System) of the pelvis was performed with the patient in a supine position using 3- mm slices and exported digitally to the HDR plus 2.6 brachyhtherapy treatment planning system. A dose of 7 Gy (±1 Gy) was prescribed to point A. Point A was specified at 2 cm above and 2 cm lateral to the flange of the intrauterine tube at the external os. Reference bladder and rectal points were inserted in treatment plans to calculate the ICRU bladder and rectal reference doses as recommended by the ICRU-38 guidelines. The ICRU rectal point was identified at the level of the flange on the tandem, on an antero-posterior line drawn through the tandem, 5 mm behind the posterior vaginal wall. Four additional rectal points were also inserted at 3 and 6 mm above and below the ICRU point. The maximum dose ($D_{Max}$) to rectum was the highest recorded dose at one of these five points. The ICRU bladder point was identified at the most posterior part of the Foley catheter balloon. Manual optimization of the plan was done starting with standard loading pattern and dwell times; adjustments were made until an optimal plan result was reached. As much as possible, the bladder dose was kept less than 80% and the rectal dose kept less than 60%. The outer wall of the rectum was contoured inferiorly from the lowest level of the ischial tuberosities (right or left) and ends superiorly before it connects anteriorly with the sigmoid. The outer wall of the bladder was contoured from the base of the contrast-filled Foley catheter balloon to the superior most aspect of the bladder (dome of bladder). Careful analyses of the coronal and sagittal views were also done to properly delineate these structures. The contouring was performed by a clinical oncology trainee and checked by at least a clinical oncologist.

The DVHs were calculated using HDRplus 2.6 (sonoTech GmbH, Germany) brachytherapy planning system. The dose per fraction from brachytherapy is given in terms of the physical dose. The minimum dose to the highest irradiated 2 cc area of rectum and bladder were recorded ($D_{2cc}$) for all individual fraction. Comparisons were then made between the volumetric 2cc doses of the bladder and rectum with the doses at the bladder and rectum ICRU points. Four additional rectum points were determined at 9 and 18 mm above and below the ICRU rectum point. The maximum dose to rectum ($D_{Max}$) was the highest recorded dose at one of these five rectum points. The total isoeffective dose was computed for 17 patients who completed EBRT and 3 fractions of brachytherapy per protocol. The total dose, combining EBRT and HDR brachytherapy, was normalized to the conventional 2 Gy/fraction using the linear-quadratic (LQ) model for incomplete sublethal damage repair and called the "isoeffective dose" in this thesis. $\alpha/\beta$ value of 10 Gy was used for tumour and $\alpha/\beta$ value of 3 Gy for OARs. The equivalent dose in 2 Gy/fraction was obtained by using the following formula: total dose [ dose/fraction+$\alpha/\beta$ / 2+$\alpha/\beta$].

## Results

A total of 55 full intrauterine insertions with a tandem and two vaginal ovoids of 20 patients were treated during the study time period from March 2011 to May 2012. Patient characteristics are shown in Table 1. The mean age was 60 years old (range 32-82 years old). FIGO IIB

has the highest number of cases (6 cases) followed by IIIB, IVA and IIA2. FIGO IB2 and IIIA had 1 case each. The most common histological subtype was squamous cell carcinoma which constituted 85% of the cases. One patient had neuroendocrine tumour. All patients received EBRT dose following the UMMC protocol (48.6 Gy in 27 fractions in 6 weeks). Four-field technique was used for 14 patients and 6 patients had anterior posterior opposing fields for pelvic EBRT. Three (3) patients had parametrial boost up to 54 Gy. One patient received an extended field EBRT to cover for para-aortic nodes seen on staging CT scan. Eighteen (18) patients had concurrent chemotherapy with radiation therapy. Twelve (12) patients had concurrent chemo therapy with weekly cisplatin, one patient had weekly carboplatin and five patients received weekly gemcitabine and cisplatin. Two patients did not receive concurrent chemoradiation due to old age and impaired renal profile. Out of 55 full insertions analysed, 51 full insertions were prescribed 7 Gy to Point A. The remaining 4 full insertions had prescription dose of 6 Gy to Point A. High ICRU doses received by the rectum necessitate dose reduction in these 4 cases. Only 18 patients completed EBRT and three fractions of HDR brachytherapy at the time of analysis. The mean dose to point A was 7.0±0.03 Gy for all individual fractions. The mean $EQD_2$ was 77.51±0.10 Gyα/β10 for tumour for 18 patients who completed EBRT and 3 fractions of HDR brachytherapy according to UMMC protocol.

The results of this study is presented in Table 1. The mean dose to rectum at $D_{Max}$ 4.75±1.01 Gy and the mean $EQD_2$ was 69.24±6.02 $Gy_{\alpha/\beta 3}$. As shown in Table 2, the mean dose to the rectum and the mean $EQD_2$ were higher for $D_{2cc}$ compared to DICRU. The mean ratio of $D_{2cc}$ rectum to DICRU rectum was 1.25 and the mean ratio of $D_{2cc}$ rectum to $D_{Max}$ rectum was 0.98 for all individual fractions. The mean $D_{2cc}$ doses differ significantly from the doses calculated at the ICRU reference point ($p<0.005$); the mean difference was 0.84 Gy (0.48 -1.19Gy). Analysis was also done to examine the difference between $D_{2cc}$ rectum and maximum rectal point dose. The $D_{2cc}$ doses did not differ significantly from the doses calculated at the maximum rectal point dose ($p= 0.30$); the mean difference was 0.17 Gy (±1.21Gy). The mean dose to the bladder and the mean $EQD_2$ at $D_{2cc}$ were also higher than DICRU. The mean ratio of $D_{2cc}$ bladder to DICRU bladder was 1.24. The $D_{2cc}$ doses did not differ significantly from the doses calculated at the ICRU reference point ($p=0.307$); the mean difference was 0.89 Gy (0.49-1.25Gy).

**Table 1. Results for 55 Fractions ofFull Insertion HDR Brachytherapy**

| Dose parameters | | Mean dose for individual fractions (Gy) | Mean total isoeffective) dose in 2-Gy fractions (Gy) |
|---|---|---|---|
| Rectum | $D_{ICRU}$ | 3.75± 0.65 | 61.71±2.77 |
| | $D_{Max}$ | 4.75±1.01 | 69.24±6.02 |
| | $D_{2cc}$ | 4.58±1.22 | 68.52±7.24 |
| Bladder | $D_{ICRU}$ | 5.10±2.03 | 74.11±19.39 |
| | $D_{2cc}$ | 6.00±1.90 | 81.85±13.03 |

*DICRU: Dose to ICRU point, DMax : Dose to maximum rectal point, D2cc : Dose to 2cc volume

## Discussion

Brachytherapy for cervical cancer has impressively progressed in the last decade through the introduction of image-guided brachytherapy. For some developed country, image-guided brachytherapy is the new gold standard for cervix cancer brachytherapy. In the UK, the number of centres offering computed tomography or magnetic resonance imaging-based ICBT for cervix cancer has increased to 32 (71%) in 2011 compared with 12 (26%) in 2008 (Tan LT, 2011). In Malaysia, UMMC has started to use CT-based ICBT for cervical cancer since March 2011. Traditionally, our intracavitary brachytherapy treatment planning and technique has been based on 2D orthogonal film-based approach. The dose was prescribed to point A, a position defined with respect to the applicators. A standardized system of dose reporting has been established by the ICRU report 38. The reporting is based on points representative of the parametria, pelvic side walls and organs at risk - the rectum and bladder. We have been using these points to evaluate and guide us in the brachytherapy planning. However, these points are not the best surrogates. Many studies have reported inconsistencies between these points compared with volumetric image-based 3D dose calculation and they cannot be the best estimate to predict late complication to organs at risk (Ling et al., 1987; Schoeppel et al., 1993; Barillot et al., 1994; van der Bergh et al., 1998; Fellner et al., 2001; Jason et al., 2003; Kirisits et al., 2005; Pelloski et al., 2005; Tan et al., 2009; Vinod et al., 2011). Image-based brachytherapy allows more conformal treatment, integrating the concepts of anatomy, tumour features, and tumour response with time. It enables reconstruction of cross-sectional images of the applicators, tumour and the neighbouring normal structures in chosen image plane and creates spatial 3D representations of them. This provides accurate and reproducible delineation of the tumour, as well as critical organs at risk and allows a clinically meaningful dose escalation in the target, while respecting normal tissue tolerance. Point A prescription may overtreat small tumours but may result in suboptimal dose distribution for larger tumours (Takenada T et al. 2012). With these superior imaging modalities, the

**Table 2. Expected Total Isoeffective dose to Organs at Risk ( α/β 3 ) for the HDR Brachytherapy Schedules**

| Schedule | Total isoeffective dose to tumour (Gy) | | Expected total isoeffective dose to organs at risk (α/β 3 ) (Gy) | |
|---|---|---|---|---|
| | α/β 10 | α/β 3 | Rectum (77% from total isoeffective dose α/β 3) | Bladder (92% from total ) isoeffective dose α/β 3 |
| Schedule 1 (7.5 Gy x 3) | 80.6 | 93.6 | 72.1 | 86.1 |
| Schedule 2 (6.5 Gy x 4) | 83.5 | 96.1 | 74 | 88.4 |

quality of brachytherapy could be improved and this will indefinitely lead to a better clinical outcome and reduced late radiation toxicities. Tan LT and colleagues from Addenbrooke has reported their 3 years experience of chemoradiotherapy for cervical cancer with CT-based image-guided HDR brachytherapy using the tandem-ring applicator (Tan et al., 2009). They gave an account of 96% pelvic control rate and 3- year cancer-specific survival of 81%. They have concluded that implementation of a CT-based tandem-ring HDR brachytherapy technique in conjunction with individual dose adaptation has resulted in a significant improvement in local control without increasing the risk of serious toxicity. These studies signify a real improvement in the therapeutic ratio by use of image guided brachytherapy.

According to our institution's protocol, the EBRT prescription is 48.6Gy in 27 fractions and delivered in 6 weeks. The HDR brachytherapy is 7Gy in 3 fractions prescribed to Point A, given at week 4, 5 and 6 of EBRT. Sometimes large tumour volume necessitated us to delay the start of HDR brachytherapy. However, the total treatment duration is still kept to less than 8 weeks, in keeping with ABS recommendation (Nag et al., 2000). To calculate the total dose given in the whole treatment, our institution used dose reduction factor of 0.65 to convert HDR doses to LDR equivalent doses. Therefore, the total dose prescribed to point A is equal to 80.1Gy. The GYN-GEC ESTRO working group had recommended the use of linear quadratic (LQ) model for incomplete mono-exponential sublethal damage repair to compare the effects of different dose rate and fraction sizes of EBRT and brachytherapy (Potter et al., 2006). Different time dose schedules cause different biologic effects, the doses have to be biologically weighted to be comparable. The calculation intended to provide a more appreciable meaning of the dose given to the tumour and organs at risk for quantifying treatment expectations. The calculation of total dose in this study used quantitative radiobiological approach; the results are given in isoeffective (equivalent) doses in 2-Gy fractions.

We found significant difference between dose to the 2cc volume of rectum and the ICRU point dose. The mean difference was 0.84 Gy and the $D_{2cc}$ was on average 1.25 times higher than DICRU. The DICRU also did not correlate well with $D_{2cc}$. The variation of dose was much larger for the $D_{2cc}$, with a standard deviation of 1.2 Gy *vs* 0.6 Gy for DICRU; evaluated for the individual fractions. The same result was observed if the mean total isoeffective doses in 2-Gy fractions were calculated for 18 patients who completed all the EBRT and brachytherapy components, with a standard deviation of 7 Gy for $D_{2cc}$ *vs* 3 Gy for DICRU. The mean total isoeffective dose in 2-Gy fractions of $D_{2cc}$ to the rectum was $68.52\pm7.24Gy_{\alpha/\beta3}$ and it was 77% from prescribed dose to point A. This result is not in good agreement with other studies. Other CT based studies who also studied the difference between $D_{2cc}$ and DICRU, did not find significant difference between the two doses (Pelloski et al, 2005; Kim et al., 2007; Vinod et al., 2011). Our study suggests that the rectal ICRU dose is not an acceptable surrogate to the dose received by 2cc volume of rectum. In contrast, the maximal point dose to the rectum correlates well with the dose received by 2cc volume of rectum. These maximum point doses were mostly (47%) reported in the vicinity of 6 mm superior to the ICRU rectal points and only 25% the maximal dose is the ICRU dose. This is not in agreement with studies done by Deshpande (1997) and Mahanshetty (2008) where they reported the maximum rectal dose point was the ICRU rectal point and found no significant difference the two points. Our result however is in good agreement with a study done by Jason C and colleague (2003), who reported the maximal rectal dose during ICBT was at the proximal rectum and found correlation between the maximal rectal doses with rectal complications. In our study, the dose to the 2 cc volume of bladder and the ICRU point dose did not differ significantly. The mean difference was 0.17 Gy. The DICRU correlated well with $D_{2cc}$ for bladder. The variation of dose was comparable between the two doses, with a standard deviation of 2 Gy for DICRU *vs* 1.9 Gy for $D_{2cc}$; evaluated for the individual fractions. Two studies have reported a good correlation between $D_{2cc}$ and DICRU of bladder (Kirisits et al., 2005). However, prior to our study, there were also two studies which observed significant difference between the two doses (Pelloski et al., 2005; Kim et al., 2007).

By using the linear-quadratic model to calculate the dose received by tumour, we have come to the conclusion that our dose to Point A was 77.5 Gyαβ10; less than the recommended 80 Gy. To achieve the recommended 80 Gy, we have to either prescribe 7.5 Gy for each fraction for three fractions or to add another HDR brachytherapy fraction with minimal dose of 6.2 Gy per fractions. However, from our data, the rectum on average received 77% and the bladder received 92% from the prescribed dose and this would result in an expected higher doses receive by the rectum and bladder than our normal dose constraint Table 3.

These basic equations of the LQ model are used to calculate the physical dose for each brachytherapy fraction needed to arrive at a given total isoeffective dose for the whole treatment (EBRT+ICBT). When we applied this to our dose fractionation of 48.6 Gy in 27 fractions for EBRT with our institution's dose constraints for bladder (75 Gy) and rectum (70 Gy) respectively, the physical dose constraints per fraction HDR brachytherapy for rectum is 4.91 Gy and bladder is 5.53 Gy. In this study, our data suggest that OARs doses assessed by DVH criteria were higher than ICRU point doses. The estimated dose to the ICRU bladder point may be a reasonable surrogate for the $D_{2cc}$ of bladder and rectal $D_{Max}$ for $D_{2cc}$ of rectum. In contrast, the dose to the ICRU rectal point does not appear to be a reasonable surrogate for the $D_{2cc}$ of rectum.

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