

To Compare Dose Volume Histograms of Computed Tomography Based 3-Dimensional Treatment Planning with International Commission on Radiation Units and Measurements (ICRU)-38 Point Doses to Bladder and Rectum in High Dose Rate Intracavitary Brachytherapy in Carcinoma Cervix: Experience from a Tertiary Care Cancer Institute of India

Abhishek Purkayastha, Arumugham Balraj, Saurabh Jaiswal, Virender Suhag, Sachin Taneja, and Mayuri Jain

Department of Radiation Oncology, Command Hospital (Southern Command), Pune, India

Correspondence should be addressed to Virender Suhag, Department of Radiation Oncology, Command Hospital (Southern Command), Pune, India

Received: December 01, 2021; Accepted: December 15, 2021; Published: December 22, 2021

ABSTRACT

OBJECTIVES

To share our institutional experience of comparing radiation-dose variations at organs-at-risk (bladder and rectum) between dose-volume-histograms of computed-tomography based 3-dimensional treatment planning and International Commission on Radiation Units and Measurements (ICRU)-38 reference-point in carcinoma cervix patients treated with high-dose-rate intracavitary brachytherapy.

METHODS

From July 2019 to October 2021, 33 patients were treated with 99 fractions of intracavitary-brachytherapy after chemoradiotherapy. The ICRU bladder and rectum-point doses along with four additional rectal-points were recorded. The dose-volume-histograms and minimum doses to the highest irradiated 2cc volume of bladder and rectum were recorded (D2cc) for all 33 fractions. Retrospectively, mean D2cc of bladder was compared with the mean ICRU bladder-point and mean rectum D2cc was compared to mean ICRU rectal-Point-And rectal-DMax.

RESULT

At D2cc mean bladder-dose was 5.27 ± 0.97 Gy and 4.23 ± 1.34 Gy at DICRU-38. The mean bladder D2cc dose differed significantly from the mean dose at the ICRU reference point ($p=0.001$). At D2cc mean dose to the rectum was 3.92 ± 1.46 Gy, 4.78 ± 1.54 Gy at DICRU-38 and 4.94 ± 1.58 Gy at D_{Max} . The mean D2cc rectal-dose differed significantly from the doses at the ICRU reference point ($p = 0.001$). On average, bladder received 78% and rectum received 57% of the prescribed dose.

Citation: Abhishek Purkayastha, To Compare Dose Volume Histograms of Computed Tomography Based 3-Dimensional Treatment Planning with International Commission on Radiation Units and Measurements (Icru)-38 Point Doses to Bladder and Rectum in High Dose Rate Intracavitary Brachytherapy in Carcinoma Cervix: Experience from a Tertiary Care Cancer Institute of India. *Cancer Med J* 5(2): 62-69.

CONCLUSION

The bladder dose assessed by DVH criteria were higher than ICRU point doses whereas rectum doses were lower. Dose to 2cc volume of bladder and rectum differed significantly than ICRU point dose. Neither bladder nor rectal ICRU dose/maximal point dose to the rectum is an acceptable substitute to the dose received by 2cc volume of rectum.

KEYOWRDS

Carcinoma cervix; High-dose-rate intracavitary brachytherapy; Dose-volume-histograms; ICRU-38

INTRODUCTION

The evolution of brachytherapy started with discovery of X-rays in 1895 by Wilhelm Roentgen and Henri Becquerel recognizing emitted radiation in 1896. Treatment with radium-therapy was commenced by Danlos and Bloch in 1901, Finze, Wickham and Degrais in 1909 culminating into today's image-based volumetric brachytherapy [1]. For gynaecological malignancies, intracavitary brachytherapy (ICBT) was implemented by Stockholm-method (1914) and Paris-system (1919). Over decades, radium (Ra226) remained the only radionuclide for brachytherapy till the discovery of manufactured or artificial radioactivity in 1934. Introduction of remote-afterloading devices and new radionuclides analogues of Ra226 like cobalt (Co60), caesium (Cs137), gold (Au198) and iridium (Ir192), the most widely used radioactive-source have revolutionized the field of brachytherapy [2]. Carcinoma cervix is the second most common cause of cancer-deaths in Indian women and 1/4th of the world's cervical cancer-deaths [3]. The curative and survival outcome of these patients have improved significantly with brachytherapy, especially with high-dose-rate (HDR) technique due to greater radiation-exposure protection, reproducible applicator positioning and dose-optimization compared to low-dose-rate (LDR) brachytherapy [4].

Traditionally, 2-dimensional (2D) orthogonal film-based treatment planning has been the work-horse of brachytherapy with dose prescribed to Point-A, a point described with respect of the inserted applicators.

International Commission on Radiation Units and Measurements (ICRU) standardized dose-reporting system with ICRU-38 report based on reference-points like parametrium (lymphatic trapezoid of Fletcher), lateral pelvic walls (pelvic-wall point), organ at risk (OAR) like bladder (bladder point) and rectum (rectal point). Introduction of computed tomography (CT) based 3-dimensional (3D) brachytherapy treatment planning with applicators in-situ has provided greater precision regarding prescription Point-A and target coverage in relation to surrounding OARs. Treatment planning with slice-by-slice 3D-reconstruction using dose volume histograms (DVH) to optimize dose distribution to target and OARs at high-risk (HR) or intermediate-risk (IR) for recurrence was recommended in the Groupe Européen Curiethérapie-European Society of Therapeutic Radiation Oncology (GEC-ESTRO) guidelines by Porter et al., [5] which has been advocated by American Brachytherapy Society (ABS) guidelines [6-8]. GEC-ESTRO and ABS prescribes iso-equivalent doses of 80-90Gy for HR-clinical-target-volume (CTV), 60Gy for IR-CTV, 80-90Gy for bladder and 70-75Gy for rectum while dose for 2cc of tissue volume (D2cc) for the OARs are calculated at 2Gy per fraction. 3D-planning may increase the efficacy of ICBT by validating whether the calculated DVH covers the CTV and spares the OARs. Earlier studies have recorded disparity between ICRU-38 reference-points and volumetric CT-based 3D planning in determining late complications to OARs like radiation-cystitis and radiation-proctitis [9-12] and postulated that these points cannot be best representative of each other [13-16].

MATERIALS AND METHODS

Study Design, Inclusion and Exclusion Criteria

From July 2019 to October 2021, 97 cases of histologically confirmed carcinoma cervix were registered for treatment in the department of radiation oncology of our tertiary care cancer institute. 54/97 (55.7%) cases belonged to stage-II/III requiring definitive concurrent chemoradiotherapy (CCRT) followed by ICBT, 21/97 (21.6%) were post-operative cases requiring adjuvant RT and central vaginal cylinder brachytherapy and remaining 22/97 (22.7%) were metastatic. All 54 patients belonging to stage-II/III received upfront external beam radiotherapy (EBRT) to a dose of 50.4 Gy in 28 fractions at 1.8 Gy per fraction as per our institutional protocol along with 5-6 cycles of cisplatin. This retrospective study included 33/54 patients who completed 99 ICBT fractions according to the inclusion criterions and remaining were not considered as per exclusion criterions. Inclusion criterions: (1) stage-II/III carcinoma cervix; (2) upfront non-metastatic; (3) received 50.4 Gy EBRT; and (4) received all three fractions of ICBT with prescription dose of 7 Gy to Point-A; (5) completed the entire treatment protocol within 8 weeks - 10 weeks. Exclusion criterions: (1) Metastatic cases; (2) operated cases; (3) received 6 Gy to Point-A; (4) could receive either one or two fractions of ICBT due to non-tolerability, chemotherapy induced haematological derangements, intra- and post-procedural haemorrhage, anaesthesia contraindications; incorrect applicator insertions; dosimetric variations and self-default or non-compliance.

BRACHYTHERAPY TECHNIQUE

ICBT was started after a week of completion of CCRT in all the patients after being deemed fit in pre-anaesthesia check-up. Each ICBT insertion was performed under spinal-anaesthesia (SA), however general-anaesthesia (GA) was used when there was either contraindication or failure to SA. On table per-vaginal/per-speculum

examination was done to know the status of residual disease and vaginal friability. A Foley catheter was inserted into the bladder and 10cc of radio-opaque contrast was injected into the balloon to identify ICRU bladder-point. The length of the uterine cavity was determined using the uterine sound. Special attention was paid to avoid perforation. After determining the intrauterine dimensions, dilatation was performed. This enables a final decision on the type of applicator, length, curvature of central tandem (15-degree, 30-degree, 45-degree) and size of ovoids (mini, half and full) to be used depending on tumour diameter, topography and physics related considerations. The applicators used were Fletcher Williamson Special set tandem and ovoids. The intrauterine catheter or the central tandem was inserted through the cervical-os into the uterine cavity. A flange (stopper) on the central tandem was used to measure the length of the uterine cavity in images and preventing perforation at the uterine fundus.

The vaginal applicators or ovoids were introduced gently and pushed into the fornices. The axis of the vaginal part of the applicator was usually placed as perpendicular to the axis of the intrauterine part. Radiopaque gauze soaked with saline water and lignocaine was used for anterior and posterior packing of the vagina to fix the applicators in place and to push the bladder and rectum away. A flexible tube with radiopaque markers were also inserted into the rectum and positioned near the anterior rectal wall to calculate the dose at specific points inside the rectum in addition to the ICRU rectum reference point. Two orthogonal radiographs (anterior-posterior and lateral) were taken with isocentric reference zig in supine position with the thighs together (brachytherapy treatment position). The patient was then transferred to the CT scan centre where scan of the pelvis was performed with the patient in a supine position using 3-mm slices and exported digitally to the Oncentra Brachytherapy Treatment Planning System (TPS) Version 4.5. CT scan of the patient in same position with implants on were performed

immediately. After the image acquisition procedures, position of the applicator including the packing, the bladder balloon, and the rectal marker were verified.

CT BASED 3D TREATMENT PLANNING

A ICBT treatment plan was generated by the chief medical physicist and radiological safety officer (RSO) and dosimetrist in collaboration with the treating radiation oncologist. The rectum was contoured from the lowest level of the ischial tuberosities (right or left) till it connected anteriorly with the sigmoid. The bladder was contoured from the base of the contrast-filled Foley catheter balloon to the superior most aspect of the bladder or dome of bladder. Careful analyses of the coronal and sagittal views were also done to properly delineate these structures. Reconstruction of catheters was done, and Point-A and B defined on planning system (Figure 1).

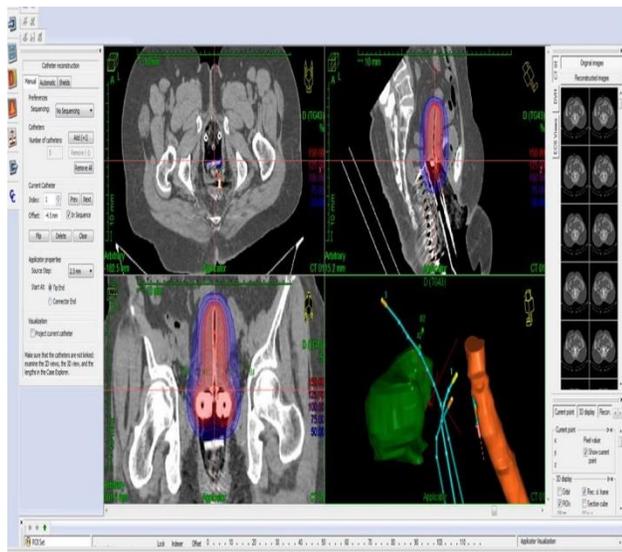


Figure 1: Axial, coronal and sagittal planes with pear shape dose distribution around the tumour volume. Catheter reconstructed, OARs contoured and Point A1, A2, B1 and B2 defined as per The Manchester System on Oncentra Brachytherapy Treatment Planning System Version 4.5.

Point-A has the significance to represent paracervical triangle. It's defined as a point 2 cm lateral to the centre of cervical canal and 2 cm from the mucous membrane of the lateral fornix in the plane of the uterus. A keel or cervical stopper placed at the external cervical-os serves an identifiable reference point on a radiograph. In treatment

plans Point-A was specified at 2 cm above and 2 cm lateral to the cervical stopper of the intrauterine tube at the external os. Point-B was defined as a point 2 cm up from the external cervical-os and 5 cm lateral at patient's midline.

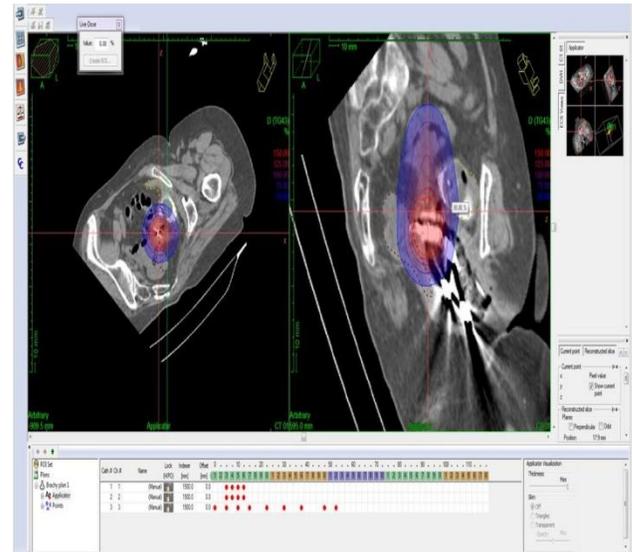


Figure 2: Pear shape dose distribution after determination and activation of dwell positions of source in the applicator tubes, may be a standard or manual source distribution, but is optimized to get more than 90-95% of prescribed dose to Point A.

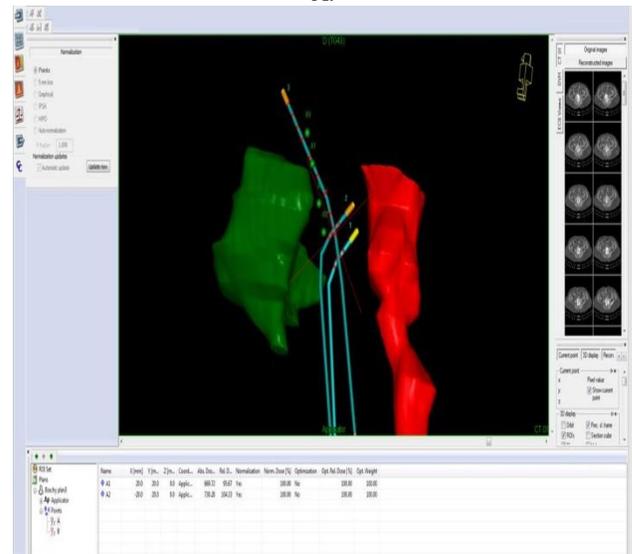


Figure 3: Manual optimization of the treatment plan with various loading patterns and dwell times to achieve 90-95% of prescribed dose to Point A.

One hundred percent of prescribed dose 7Gy was normalized at Point-A which gave a pear-shaped dose distribution around the target volume. As per our centre's

protocol, not less than 90% of prescribed dose is accepted at point-A (Figure 2).

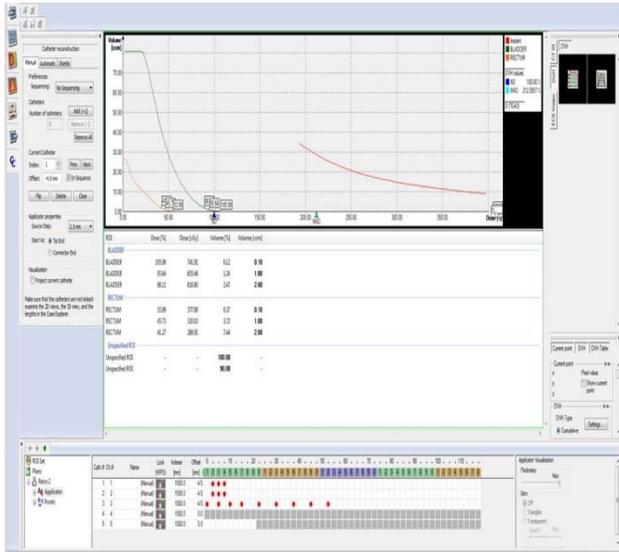


Figure 4: Dose volume Histogram generated on Oncentra Brachytherapy TPS Version 4.5 displays doses to the tumour volumes (0.1cc, 1cc and 2cc). Value of dose to the tumour volume 2cc i.e. D2cc is taken for this study. Plans are optimized to achieve D2cc less than 80% for bladder and rectum.

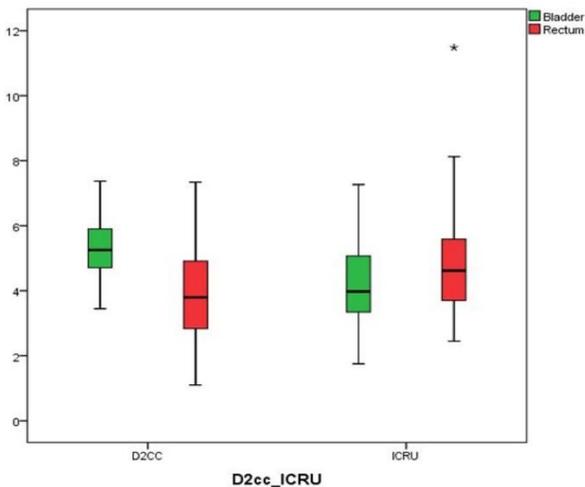


Figure 5: Box and Whisker plot box generated with existing datasets of D2CC and ICRU point's values in respect of OARs (bladder and rectum) is displaying the minimum (0th percentile), the maximum (100th percentile), the sample median (50th percentile), and the first (25th percentile) and third quartiles (75th percentile), depicts the dose differences in D2CC and ICRU points.

Point-B should not get more than 30%-35%. Rectum and Bladder should not get more than 80%-85% of prescribed dose in general. Manual optimization of the plan was carried out with various loading patterns and dwell times

and an optimal plan fulfilling criteria of the dose prescription and dose constraints was achieved (Figure 3). The DVHs were calculated using Oncentra Brachy TPS ver 4.5 Brachytherapy planning system (Figure 4). For each fraction minimum dose to the irradiated 2cc volume of rectum and bladder were determined (D2cc). Volumetric D2cc doses to the Bladder and rectum were then compared with the doses at the bladder and rectum ICRU points (DICRU). Doses at Additional rectum points were determined at 3 mm and 6 mm above and below the ICRU rectum Point-A and the maximum dose to rectum (D_{Max}) was found as the highest recorded dose among these five rectum points. For determining the incomplete sublethal damage repair of both cancer cells and normal cells after being treated with ionizing radiation, linear-quadratic (LQ) model was used to calculate the total iso-effective dose for all 33 patients receiving EBRT and 3 fractions of ICBT using α/β value of 10Gy for tumour and α/β value of 3Gy for OARs (α and β = constants in LQ model in radiobiology). Treatment of the patients carried out on micro-Selectron Digital after-loading HDR Unit version 3.1.5.500.

STATISTICAL ANALYSIS

All quantitative data were expressed as mean standard deviation (SD) and qualitative in terms of percentage. The statistical comparison between two groups for quantitative variables was assessed by Student-T test. The two tailed p-value <0.05 was considered as statistically significant. SPSS version 22.0 (SPSS Inc., Chicago, USA) was used for the analysis. To assess the precision of the estimate 95% confidence-intervals (CI) for all estimated probabilities were calculated.

RESULTS

We retrospectively analyzed a total of 99 complete intra-uterine insertions in 33 patients of carcinoma cervix who received EBRT followed by ICBT from July 2019 to October 2021. Dose of 7Gy was prescribed to Point-A for

all 99 insertions. The result of our study has been shown in Table 1. The total prescribed dose was 79.31Gy α/β 10. The mean dose to the bladder was 5.27 ± 0.97 Gy for D2cc and 4.23 ± 1.34 Gy at DICRU. The mean bladder D2cc dose differed significantly from the mean dose calculated at the ICRU reference point ($p = 0.001$). The mean difference was 1.03 (95% Confidence interval = 0.71-1.36). The mean EQD2 was 75.12 ± 5.94 Gya/ β 3 for D2cc and 67.85 ± 8.03 Gya/ β 3 at DICRU. The mean difference was 7.26 (95%CI=3.78-10.79). This difference was statistically significant ($p=0.001$). The mean ratio of D2cc bladder to DICRU bladder was 1.33. In the majority of applications, the maximum dose point was not the ICRU point.

OAD	Dose parameters	Mean dose for each radiation fraction (Gy)	Mean iso-effective dose 2Gy per fraction (Gy)	P value
Bladder	D _{ICRU}	4.23±1.34	67.85±8.03 α/β 3	0.001
	D _{2cc}	5.27±0.97	75.12±5.94 α/β 3	
Rectum	D _{ICRU}	4.78±1.54	72.18±10.66 α/β 3	0.001
	D _{max}	4.94±1.58	73.48±11.19 α/β 3	
	D _{2cc}	3.92±1.46	65.94±8.18 α/β 3	

D_{2cc}= Dose to 2cc volume
D_{max}= Dose to maximum rectal point
D_{ICRU}= Dose to ICRU point

Table 1: Summary of all 99 fractions of HDR brachytherapy in this study.

The mean dose to the rectum was 3.92 ± 1.46 Gy for D2cc, 4.78 ± 1.54 Gy at DICRU and 4.94 ± 1.58 Gy at D_{Max}. The mean rectal D2cc dose differed significantly from the mean dose calculated at the ICRU-38 reference point ($p=0.001$); The mean difference was 0.86 (95% Confidence interval = 0.44-1.28). The mean EQD2 was 65.94 ± 8.18 Gy α/β 3 for D2cc, 72.18 ± 10.66 Gy α/β 3 at DICRU and 73.48 ± 11.19 Gy α/β 3 for D_{max}. The mean difference was 6.23 (95%CI = 1.56-10.91) which was statistically significant ($p = 0.001$). The mean ratio of D2cc rectum to DICRU rectum was 0.84 and the mean ratio of D2cc rectum to D_{Max} rectum was 0.81 for all individual fractions. On an average, the rectum received 57% and bladder received 78% of the prescribed dose. Box and whisker plot was drawn to determine for means in D2CC and ICRU doses for bladder and rectum (Figure 5).

DISCUSSION

The use of HDR brachytherapy has revolutionized the treatment of carcinoma cervix with significant increase in

survival rates and reduction in local recurrence. However, HDR ICBT brings about both long and short-term adjacent tissue injury due to large dose per fraction. Therefore, to assess the normal-tissue dose tolerance more accurately, CT or magnetic resonance imaging (MRI) guided treatment planning with the brachytherapy applicators in situ is the most recommended. As per ICRU-38 recommendations the bladder point is localized using a Foley catheter, with the balloon filled with 7cc of a radiopaque fluid. The bladder point is obtained on the lateral radiograph on a line drawn antero-posteriorly through the centre of the balloon, at the posterior surface while on the frontal radiograph, the bladder point is marked at the centre of the balloon. The rectal point on the lateral radiograph is located on a line drawn from mid-point of the ovoids 5 mm behind the posterior vaginal wall. Point-A is defined as a point 2 cm lateral to the central canal of the uterus and 2 cm up from the mucous membrane of the lateral fornix, in the axis of the uterus. Point-B is defined as being in the transverse axis through Points-A, 5 cm from the midline. In 3D CT-based planning system, D2cc is the most widely used parameter for bladder and rectal doses. [5,6] Although uncertainty exists between D2cc and ICRU rectal-point with respect of radiation-proctitis, [14] studies by Pelloski et al., [16] Kiristis et al., [17] and Wachter-Gerstner et al., [18] described close interrelationship between them. In 3D-planning CT/MRI helps to define the 100% isodose-line which can cover the residual tumor volume and prescribe a DVH parameter like D2cc (dose received by 2cc of normal tissue volume). In 3D-planning the aim is to provide a good coverage of the involved region with a normalized therapy dose (EQD2) \geq 80-90 Gy prescribed to either Point-A or D90 to enhance local tumor control. [19] As per ABS guidelines, the EQD2 for D2cc bladder is 90 Gy and rectum is 70-75 Gy [6,7,20].

In our study, the dose to the 2cc volume of bladder and the ICRU point dose did differ significantly ($p = 0.001$) (Table 1). Our study suggests that the bladder ICRU dose is not an

acceptable replacement to the dose received by 2cc volume of rectum (D2cc) as the mean ratio of D2cc bladder to DICRU bladder was 1.33 and the mean difference was 1.03. Similarly, Kim et al., [15] and Pelloski et al., [16] had also observed significant difference between the two doses. However, Kirisits et al., [17] reported a good correlation between D2cc and DICRU of bladder. By using the LQ model to calculate the dose received by tumour, we have come to the conclusion that our dose to Point-A was largely 99% of the recommended 80Gy. This study observed that the rectal ICRU dose (DICRU) is also not an acceptable representative to the dose received by 2cc volume of rectum (D2cc) as they differed significantly ($p = 0.001$) (Table 1) as the mean ratio of D2cc rectum to DICRU rectum was 0.84 while the mean ratio of D2cc rectum to D_{Max} rectum was 0.81 and the mean difference was 0.86. This is in accordance with previous studies by Vinod et al., [9] Kim et al., [15] and Pelloski et al., [16]. We further recorded that maximal point dose to the rectum (D_{Max}) is also not an acceptable substitute to the dose received by 2cc volume of rectum (D2cc), although Deshpande et al., [21] and Mahanshetty et al., [22] described non-significant

correlation between the maximum rectal dose point (D_{Max}) and ICRU rectal Point-A (DICRU). From our data, the rectum on average received 57% and the bladder received 78% of the prescribed dose and this would result in an expected doses received by the rectum and bladder. This study also observed that the radiation doses received by the critical OARs are higher in case of bladder (5.27 ± 0.97 Gy for D2cc Vs 4.23 ± 1.34 Gy at DICRU) and lower in case of rectum (3.92 ± 1.46 Gy for D2cc vs. 4.78 ± 1.54 Gy at DICRU and 4.94 ± 1.58 Gy at D_{Max}). To conclude, treatment planning for ICBT with DVHs by 3D CT based planning may be advantageous compared to ICRU point doses by 2D orthogonal planning as the former allows the oncologist to prescribe an optimal dose escalation in the target without delivering excess dose to the OARs thus resulting in reduced incidence of radiation induced adverse effects. Also, the estimated dose to the ICRU bladder point may not be a reasonable surrogate for the D2cc of bladder. Similarly, the dose to the ICRU rectal point/ maximal dose point does not appear to be a reasonable substitute for the D2cc of rectum.

REFERENCES

1. Rivard MJ, Venselaar JL, Beaulieu L (2009) The evolution of brachytherapy treatment planning. *Medical Physics* 36(6): 2136-2153.
2. Henschke U, Hilaris BS, Mahan GD (1963) After loading in interstitial and intracavitary radiation therapy. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* 90: 386-395.
3. Reichheld A, Mukherjee PK, Rahman SMF, et al. (2020) Prevalence of cervical cancer screening and awareness among women in an urban community in South India - A cross sectional study. *Annals of Global Health* 86(1): 30.
4. Stewart AJ, Viswanathan AN (2006) Current controversies in high-dose-rate versus low-dose-rate brachytherapy for cervical cancer. *Cancer* 107(5): 908-915.
5. Potter R, Haei-Meder C, Van Limbergen E, et al. (2006) Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. *Radiotherapy and Oncology* 78(1): 67-77.
6. Viswanathan AN, Beriwal S, De Los Santos JF, et al. (2012) American brachytherapy society consensus guidelines for locally advanced carcinoma of the cervix. Part II: High-dose-rate brachytherapy. *Brachytherapy* 11(1): 47-52.

7. Viswanathan AN, Moughan J, Small W Jr, et al. (2012) The quality of cervical cancer brachytherapy implantation and the impact on local recurrence and disease-free survival in radiation therapy oncology group prospective trials 0116 and 0128. *International Journal of Gynecological Cancer* 22(1): 123-31.
8. Nag S, Beth E, Thomadsen B, et al. (2000) The American brachytherapy society recommendations for high-dose-rate brachytherapy for carcinoma of the cervix. *International Journal of Radiation Oncology, Biology, Physics* 48: 201-211.
9. Vinod SK, Caldwell K, Lau A, et al. (2011) A comparison of ICRU point doses and volumetric doses of organs at risk (OARs) in brachytherapy for cervical cancer. *Journal of Medical Imaging and Radiation Oncology* 55(3): 304-310.
10. Takenada T, Yoshida K, Tachiri S, et al. (2012) Comparison of dose-volume analysis between standard Manchester plan and magnetic resonance image-based plan of intracavitary brachytherapy for uterine cervical cancer. *Journal of Radiation Research* 53(5): 791-797.
11. Tan LT, Coles CE, Hart C, et al. (2009) Clinical impact of computed tomography-based image-guided brachytherapy for cervix cancer using the tandem-ring applicator - the Addenbrooke's experience. *Clinical Oncology* 21(3): 175-182.
12. Wachter-Gerstner N, Wachter S, Reinstadler E, et al. (2003) Bladder and rectum dose defined from MRI based treatment planning for cervix cancer brachytherapy: Comparison of dose-volume histograms for organ contours and organ wall, comparison with ICRU rectum and bladder reference point. *Radiotherapy and Oncology* 68(3): 269-276.
13. Lee LJ, Viswanathan AN (2012) Predictors of toxicity after image-guided high-dose-rate interstitial brachytherapy for gynecologic cancer. *International Journal of Radiation Oncology, Biology, Physics* 84: 1192-1197.
14. Kang HC, Shin KH, Park SY, et al. (2010) 33D CT-based high-dose-rate brachytherapy for cervical cancer: Clinical impact on late rectal bleeding and local control. *Radiotherapy and Oncology* 97(3): 507-513.
15. Kim RY, Shen S, Duan J (2007) Image-based three-dimensional treatment planning of intracavitary brachytherapy for cancer of the cervix: Dose-volume histograms of the bladder, rectum, sigmoid colon, and small bowel. *Brachytherapy* 6(3): 187-194.
16. Pelloski CE, Palmer M, Chronowski GM, et al. (2005) Comparison between CT-based volumetric calculations and ICRU reference-point estimates of radiation doses delivered to bladder and rectum during intracavitary radiotherapy for cervical cancer. *International Journal of Radiation, Oncology, Biology and Physics* 62(1): 131-17.
17. Kirisits C, Potter R, Lang S, et al. (2005) Dose and volume parameters for MRI-based treatment planning in intracavitary brachytherapy for cervical cancer. *International Journal of Radiation, Oncology, Biology and Physics* 62(3): 901-911.
18. Wachter-Gerstner N, Wachter S, Reinstadler E, et al. (2003) Bladder and rectum dose defined from MRI based treatment planning for cervix cancer brachytherapy: Comparison of dose-volume histograms for organ contours and organ wall, comparison with ICRU rectum and bladder reference point. *Radiotherapy and Oncology* 68(3): 269-76.
19. Dimopoulos JC, Lang S, Kirisits C, et al. (2009) Dose-volume histogram parameters and local control in magnetic resonance imaging guided cervical cancer brachytherapy. *International Journal of Radiation, Oncology, Biology and Physics* 75(1): 56-63.
20. Georg P, Lang S, Dimopoulos JC, et al. (2011) Dose-volume histogram parameters and late side effects in magnetic resonance image-guided adaptive cervical cancer brachytherapy. *International Journal of Radiation, Oncology, Biology and Physics* 79(2): 356-362.
21. Deshpande DD, Shrivastav SK, Pradhan AS, et al. (1997) Dosimetry of intracavitary applications in carcinoma of the cervix: Rectal dose analysis. *Radiotherapy and Oncology* 42(2): 163-166.
22. Mahantshetty U, Tiwana MS, Jamema S, et al. (2011) Additional rectal and sigmoid mucosal points and doses in high dose rate intracavitary brachytherapy for carcinoma cervix: A dosimetric study. *Journal of Cancer Research and Therapeutics* 7(3): 298-303.