Section: Radiotherapy

Original Research Article

AN OBSERVATIONAL DOSIMETRIC STUDY OF ASSESSMENT OF DOSES TO SIGMOID COLON, SMALL BOWEL AND RECTUM IN CT BASED BRACHYTHERAPY IN CARCINOMA CERVIX AT A TERTIARY CANCER INSTITUTE

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ABSTRACT

Background: Assessment of doses to sigmoid colon, small bowel, and rectum in CT-based brachytherapy for carcinoma cervix and to observe the D2cc of sigmoid colon, D2cc of the rectum and D2cc of the small bowel.

Materials and Methods: Prospective study done in Department of Radiotherapy from March 2022 to March 2024, 50 registered women with non-metastatic cervical cancer treated with definitive concurrent chemo-radiotherapy followed by HDR intracavitary brachytherapy who met inclusion criteria were enrolled.

Results: The median age of the whole group was 50.5 years, the majority of them were in their 5th (38%) or 4th (30%) decade. Pathologically, all were squamous cell carcinoma. 50. For the rectum, the D2cc doses did not differ significantly from the doses calculated at the ICRU reference point (p=0.625); the mean difference was 10cGy (±13cGy). However, for the bladder, the doses calculated at the ICRU reference point were significantly higher than the D2cc doses (p=0.0001). The mean difference was 107cGy (±7cGy).

Conclusion: Study suggests that rectum ICRU reference points can be surrogate markers for D2cc.but not for bladder and hence reporting should be preferably be done in volumetric method rather than reference point doses.

Keywords: Minimum dose to the highest irradiated 2 cc volume (D2cc), equivalent dose in 2 Gy fractions (Dmax), External Beam Radiotherapy (EBRT), International Commission on Radiation Units and Measurements (ICRU).

INTRODUCTION

Cervical carcinoma is the seventh most frequent cancer globally, accounting for 3.1% of all cancer cases in all age categories. Cervical carcinoma is the fourth most prevalent cancer in women worldwide, accounting for 604,127 cases (6.5%). Carcinoma cervix is the second most common cancer in women in India, accounting for 123907 cases in 2020, or 9.7% of all malignancies in both sexes. In contrast, females account for 18.3%. In FIGO STAGE IA, surgery has been the basis of treatment; however, in STAGE IB or higher, definitive management is considered concomitant. chemoradiotherapy. Radiotherapy requires a combination of external beam radiotherapy and brachytherapy.[1,2]

Intracavitary brachytherapy has evolved significantly from the use of radium to the use of artificial radionuclides, after loading techniques, steeping source technologies, and computer imaging and technology. These resulted in the application of novel dosage rate techniques (LDR, HDR). Conventional brachytherapy relies on clinical evaluation and 2D point-based planning, which uses fixed bone landmarks and orthogonal X-ray images for dosage calculations and prescriptions regardless of tumour size or shape. This causes inadequate target coverage, insufficient dosage delivery, and therapy failure for bigger asymmetrical tumours. Dosages are prescribed to certain points. The dose for the tumour is prescribed to point A, and for the bladder and rectum, the dose is prescribed to reference points defined by the International Commission on Radiation Units and Measurements (ICRU). Radiograph-based planning is easy and cost-effective, hence it is still utilized for dosage reporting.

Dose prescription is based on tumour volume rather than a predetermined common point. This results in better conformal plans. 3D imaging using MRI is ideal for volume-based planning. MR-based applications are still being adopted at varying rates across institutions. When an MRI is not accessible, CT is an option.[3,4] CT does not provide a distinct clinical target volume but can identify nearby OARs and determine the dose distribution. Ulceration, fistula, and restricted telangiectasia are some of the complications associated with brachytherapy. These are frequently associated with small volumes obtaining large absorbed dosages. Brachytherapy has a steep dose gradient. The dose recorded at a single site does not reflect the amount the organ receives. Depending on the application, D2cc may be located in different parts of the OAR. This study evaluates three-dimensional computed tomography dose-volume parameters for high-dose-rate intracavitary brachytherapy of cervical cancer.

MATERIALS AND METHODS

Prospective study done in Department of Radiotherapy from March 2022 to March 2024, 50 registered women with non-metastatic cervical cancer treated with definitive concurrent chemo-radiotherapy followed by HDR intracavitary brachytherapy who met inclusion criteria were enrolled in the research.

Inclusion Criteria

Age 30-70yrs, Eastern cooperative oncology group 1 and 2, Positive biopsy for squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, Stage IIA-IVA carcinoma cervix patients according to FIGO staging system, Patients with an adequate vagina, adequate for comfortable insertion of applicators

Exclusion Criteria

Immunocompromised patients and HIV positive patients, Post hysterectomy status, Patients with narrow vagina and poor symmetry, Stage IVB carcinoma cervix, Eastern cooperative oncology group 3 and 4.

All women in the trial received 50 Gy EBRT, which was subsequently evaluated for response and appropriateness for pleasant application insertion. The brachytherapy operation was carried out under SEDATION in the lithotomy position. A Foley catheter was placed into the bladder, and 7cc of radio-opaque contrast was injected into the balloon to help locate the ICRU bladder reference point. A comprehensive gynaecological examination was conducted, and tumour factors were examined. The length of the uterus cavity was measured using a uterine sound. The applicators utilized were CT/MR compatible tandem and ovoid. Betadine-soaked gauze is used to pack the vagina, hold the applicators in place, and push the bladder and rectum out. The patient was sent to the CT simulation suite. A CT scan of the pelvis was done with the patient in a supine posture using 3-mm slices and digitally uploaded to the brachytherapy planning system. The rectum's outer wall was contoured inferiorly 5 cm from the anal verge and ends superiorly before connecting anteriorly with the sigmoid, following RTOG contouring guidelines. The bladder's outer wall was contoured from the base of the contrast-filled Foley catheter balloon to the superior aspect of the bladder (dome of the bladder). The sigmoid colon was defined and contoured as the bowel above the rectum to the level of the lumbosacral interspace. The tiny bowel was described as the bowel that did not include the sigmoid colon or rectum in the pelvic.

A radiopaque rectal probe of 10cm in length is placed into each rectum. Manual optimization of the plan began with a typical loading pattern and dwell times, and tweaks were performed until an ideal plan outcome was achieved. As much as possible, the bladder dose was kept below 80% and the rectal dose below 60%. The DVH values were calculated. The lowest dose to the most irradiated 2 cc area of the rectum. The average is determined for the ICRU rectum point, D2cc rectum doses, sigmoid, small bowel, bladder ICRU point, and bladder D2cc doses.

Statistical analysis: EPI info software with Descriptive statistics is used. Data represented as frequency table with percentage. Values represented as mean ± standard deviation. To compare means, use the Student paired T-test and Pearson's correlation coefficient.

RESULTS

Among the study population, majority belong to 51-60yrs of age (38%) followed by 41-50 years (30%), 31–40 years (16%) ,61-70 years (12%)and 21-30 years (4%). Median age of the study population is 50.5 years.

Table 1: Distribution of patients based on age

Age Group	Frequency	% of Total Patients
21-30	2	4
31-40	8	16
41-50	15	30
51-60	19	38
61-70	6	12
Stage		
IVA	1	2.00%
IIIC1	2	4.00%
IIIB	13	26.00%
IIIA	2	4.00%
IIB	18	36.00%
IIA2	11	22.00%
IIA1	3	6.00%
Histopathology		
PD SCC	4.00%	2
MD SCC	18.00%	9
LCNK SCC	60.00%	30
LCK SCC	6.00%	3
K SCC	6.00%	3
INV SCC	6.00%	3

Among the study population, majority belong to FIGO stage IIB (36%) followed by IIIB (26%), IIA2 (22%), IIA1 (6%), IIIA& IIIC1 (both 4%) and IVA (2%). Among the study population, all patients were diagnosed with squamous cell carcinoma. Majority of them are large cell non keratinizing (60%) followed by moderately differentiated (18%), large cell keratinizing (6%), keratinizing (6%), invasive (6%) and poorly differentiated (4%).

Table 2: Bladder doses and their means with p values and correlation coefficient

	Mean	SD	Pearson correlation	P Value
ICRU bladder point dose Gy)	4.370	1.078	0.763	0.00012
D 2cc bladder (Gy)	5.477	1.631		
ICRU bladder point dose Gy)	4.370	1.078	0.700	<0.0001
D 0.1cc bladder (Gy)	7.589	2.372		

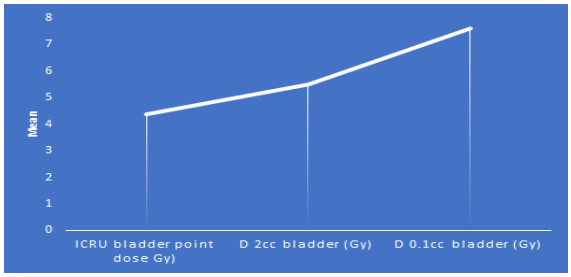

Figure 1: Mean Bladder doses

Mean ICRU bladder point dose are 4.370±1.078, mean D2cc bladder dose are 5.477 ± 1.631 pearson correlation coefficient is 0.76 (p= 0.0001). Mean ICRU bladder point dose is 4.370± 1.078 mean D0.1cc volume dose are 7.589±2.372 pearsons correlation coefficient is 0.700 ($p=2.65*10^{-32}$).

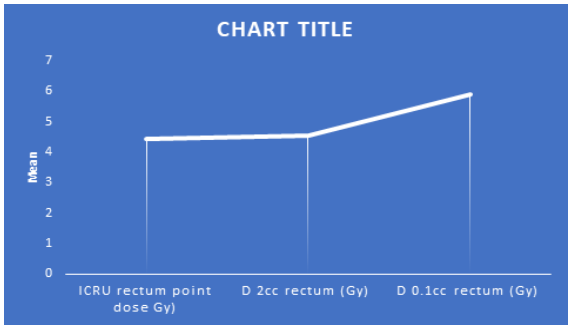

Figure 2: Mean Rectum doses

Table 3: Rectum doses and their means with correlation coefficient and p value

	Mean	SD	Pearson correlation	P Value
ICRU rectum point dose (Gy)	4.435	1.101	0.654	0.625
D 2cc rectum (Gy)	4.538	0.995		
ICRU rectum point dose (Gy)	4.435	1.101	0.672	$2.67*10^{-8}$
D 0.1cc rectum dose (Gy)	5.923	1.362		

Mean ICRU point rectum dose is 4.435± 1.101, mean D2cc volumetric dose is 4.538±0.995 with pearson correlation coefficient of 0.654 (p=0.625). Mean rectum point dose is 4.435 ±1.101 and D0.1cc rectum volumetric dose is 5.923±1.362 with pearsons correlation coefficient of 0.672 ($P=2.67*10^{-8}$).

Table 4: Sigmoidcolon and small bowel doses and their means with correlation coefficient and p value

	Mean	SD	Pearson correlation	P Value
ICRU sigmoidcolon point dose (Gy)	4.291	1.086	0.721	0.453
D 2cc sigmoidcolon (Gy)	5.953	1.486		

ICRU small bowel point dose (Gy)	3.0882	1.338	0.672	
D 0.2cc small bowel dose (Gy)	4.403	2.024		

Mean sigmoid colon volumetric dose D2cc is 4.291±1.086 and D0.1cc is 5.953±1.486.
Mean small bowel volumetric dose D2cc is 3.0882±1.338 and D0.1cc is 4.403±2.024
50 ICRT applications were studied; an FSD after loading tandem was used with ovoids. The mean doses to the ICRU reference points and the mean minimal doses delivered to various small volumes of the maximal organ dose.
For the rectum, the D2cc doses did not differ significantly from the doses calculated at the ICRU reference point (p=0.625); the mean difference was 10cGy (±13cGy). However, for the bladder, the doses calculated at the ICRU reference point were significantly higher than the D2cc doses (p=0.0001). The mean difference was 107cGy (±7cGy).

DISCUSSION

This study included carcinoma cervix patients with median age of 50.5 years. Age- specific incidence of cervical cancer increases rapidly, usually reaching a peak at 40–50 years of age, followed by a plateau and a variable decline thereafter. Although a high prevalence of HPV exists worldwide, peaking at ages 25 to 35 years, <15% of exposed women develop persistent infection, results in dysplasia, whereas the majority of women clear the infection within 2 years. Cervical cancer may develop 10 to 20 years after initial exposure to HPV. Thus the usual peak of incidence can be seen around 40-50 years of age. Mitchell et al,[5] showed that Comorbid conditions in the elderly (>70 years) resulted in diminished ability to undergo intracavitary brachytherapy. Tumor recurrence and death from cervical cancer were more common in the elderly group.
Major bulk of the study is contributed by stage IIA, IIB, IIIB. Histologically all were diagnosed with squamous cell carcinoma. Large cell non keratinizing (60%) is the most common subtype in this study. 90% of tumors are squamous cell carcinoma. Squamous cell carcinoma is divided into three types: large-cell keratinizing, nonkeratinizing, and small cell carcinomas. Based on degree of differentiation divided into well, moderately, or poorly differentiated. no significant correlation of survival or tumor behavior attributed to degree of differentiation.
All patients were treated with external beam radiotherapy of 50 Gy in 25 fractions with 2 Gy per fraction followed by high dose rate brachytherapy of 7 Gy per fraction for 3 fractions, one week apart to a total intracavitary brachytherapy dose of 21Gy. After the applicators were placed per vaginally and vaginal packing was done, Ct simulation was done and simulated images were imported into planning systems. Then the bladder, rectum, sigmoid colon and small bowel were contoured. Using brachytherapy planning systems, a dose of 7 Gy is prescribed to point A, ICRU point doses and volumetric dose were measured.
Mean ICRU bladder dose M= 4.3704 (SD=1.078) was numerically smaller than D2cc M=5.477(SD=1.631) bladder volumetric dose. To the test the hypothesis that ICRU bladder point dose is comparable to either D2cc, an independent sample student T test was performed. T test was associated with a statistically significant effect of p=0.0001. Pearsons correlation coefficient was 0.76 for D (ICRU) vs D2cc. Mean bladder D2cc dose differed significantly from the mean dose at the ICRU reference point (p=0.0001) with a mean difference of 1.07Gy and ICRU bladder point has weak positive correlation with D2cc (r=0.763, p=0.0001).
Mean ICRU bladder point dose M= 4.3704 (SD=1.078) was numerically smaller than D0.1cc M=7.589(SD=2.372) bladder volumetric dose. To the test the hypothesis that ICRU bladder point dose is comparable to either D0.1cc, an independent sample student T test was performed. T test was associated with a statistically significant effect of p=2.65*10-32. Pearsons correlation coefficient was 0.700 for D(ICRU) vs D0.1cc. Mean ICRU point dose differed from D0.1cc with positive correlation this observation is statistically significant.
Mean ICRU rectum dose M= 4.435 (SD=1.101) was numerically smaller than D2cc M=4.538(SD=0.995) rectum volumetric dose. To the test the hypothesis that ICRU rectum point dose is comparable to D2cc, an independent sample student T test was performed T test was associated with a statistically not significant effect of p=0.625 Pearsons correlation coefficient was 0.654 for D (ICRU) vs D2cc. Mean rectum D 2cc dose does not largely differ numerically from the mean dose at the ICRU reference point, with mean difference of 0.10Gy (statistically not significant p=0.625). Thus ICRU rectal point can be used as a surrogate to D2cc but with a positive correlation (r.0.654). Mean ICRU rectum dose M= 4.435(SD=1.101) was numerically smaller than D0.1cc M=5.923(SD=1.362) rectum volumetric dose. An independent sample student T test was performed T test was associated with a statistically significant effect of p=2.67*10-8. Pearsons correlation coefficient was 0.672 for D (ICRU) vs D0.1cc. Mean ICRU point dose differed largely from D0.1cc (mean difference is 1.48Gy) with significant p-value but with a positive correlation(r=0.672).
Mean calculated for D2cc sigmoid colon M=4.291(SD=1.086), and mean calculated for D0.1cc of sigmoid colon M=5.953(SD=1.486). Mean calculated for D2cc small bowel m=3.088(SD=1.338), and mean calculated for D0.1cc of small bowel M=4.403(SD=2.024)
The results of this study suggest during cervical cancer treatment the ICRU bladder reference point is an NOT AN acceptable surrogate for the maximal radiation dose delivered to the bladder. In this study,

the D2cc was more than the ICRU reference dose always and was greater than the ICRU dose by 1.25-fold. Various studies have the same findings . Ling et al,[6] and Schoeppel et al,[7] conducted two small studies that concluded that the ICRU bladder reference doses two to three times underestimated D2cc. This study found no significant difference between dose to the 2cc volume of rectum and the ICRU point dose. The mean difference was 0.10Gy and the ratio of D2cc/D(ICRU)was 1.0. The DICRU also did correlate positively with D2cc (r=0.654). Similar results are seen in studies done by Vinod et al,[8] pelloski et al,[9] Kim et al.[10] This study suggests that the rectal ICRU reference point dose can be used an acceptable surrogate to the dose received by 2cc volume of rectum. Results from the study suggests that ICRU rectal reference points can be surrogate markers for D2cc.but not for bladder. Hence reporting in volumetric method is better than point based. Inaccurate estimates of doses to OAR may be contributing factors for the poor correlation between the dose and late complications. Image-based 3-D volumetric calculations will undoubtedly improve accuracy. Our study showed that the mean D2 dose was also higher in the area of sigmoid colon D2cc.

The anatomical definition of the rectosigmoid junction has not been consistent between studies as well as upward displacement of cervix and vaginal fornix during intracavitary application, which may account for variations in reported 3-D volume doses. In our study, the definition of the rectosigmoid junction was defined at the level of the top of two femoral heads, rather than more commonly used definition in which the junction occurs where the sigmoid colon curve off from the rectum.

We used our definition simply because the anatomical landmark is more consistent. Data from Cheng et al,[11] also have suggested that a proximal rectal dose is a better estimation of maximal dose than the ICRU rectal point. Colonoscopic findings of radiation colitis were correlated with the proximal rectum, the area with maximal rectal dose.

In this study, a CT-compatible applicator was used for 3-D planning. Most CT or magnetic resonance imaging-compatible applicators have no internal shielding in the colpostats. Therefore, a higher dose of radiation around OAR near the applicator is a concern.

However, the current design of the shielding is to reduce dose to ICRU bladder and rectum points, less likely to areas of D2 dose which are more likely higher locations compared to the ICRU reference points. In the past, the calculation of OAR was limited to only bladder and rectum due to the inability to visualize sigmoid colon and small bowel. Therefore, no data are available regarding the sigmoid colon and small bowel around the uterus, which may receive higher doses than the rectum. Today, routine use of CT simulation and 3-D TP allows us to evaluate DVHs for any OAR, such as the sigmoid colon and small bowel. Our study showed that the sigmoid colon received the highest mean D2 dose compared to the rectum and small bowel. This was not recognized in the past.

Depending on the anatomical definition of rectum, the area of proximal rectum or sigmoid colon is often inside the pear-shaped high isodose area of ICBT Furthermore, the upper half of the rectal wall and sigmoid colon is technically impossible to push away by vaginal packing. It is useful to contrast the whole rectal wall up to the sigmoid colon and calculate the dose at that area. In the bladder, the area of the high-dose region is also more cranially located than the ICRU reference point because the posterior wall is closer to the higher pear- shaped isodose lines, especially in cases of a distended bladder. Therefore, imaging of the bladder and rectum must duplicate treatment conditions as closely as possible. In our study, each loop of small bowel was contoured. However, some authors contoured the outermost limit of all small bowel rather than individual bowel loops, considering constant movement of the bowels. Our study indicated that the mean maximum volume dose of small bowel was not as high as expected.

Some possible explanations include the radiation source in the tandem were not all the way against the fundus of the uterus in many cases and/or also the anisotropic effect of the intrauterine radioactive source at the uterine fundus. Brachytherapy for cervical cancer has impressively progressed in the last decade through the introduction of image-guided brachytherapy. Image-guided brachytherapy is the new gold standard for cervix cancer brachytherapy. Traditionally, intracavitary brachytherapy treatment planning and technique is done using 2D orthogonal film-based approach. 2d based planning prescribed dose 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 .Point based reporting is based on points representing parametria, pelvic side walls and rectum and bladder, these point do not act as a best surrogate marker.

Between reference points and volumetric image-based 3D dose calculation, there are inconsistencies and they cannot best estimate late complication to organs at risk in studies done by Vinod et al,[8] pelloski et al,[9] van derberg et al,[12] fellner et al,[13] Jason et al,[14] kiristis et al,[15] tan et al.[16] Conformal treatment is possible with 3D image based brachytherapy, as it integrate the anatomy, tumor factors, and response of tumor to EBRT. 3D spatial reconstruction of tumor applicators and normal tissue is possible, enabling delineation of tumor and 0AR accurately and thus conformal dose to tumor can be prescribed while respecting normal tissue tolerance. Takenaka T et al,[17] Point A prescription may over treat small tumors but may result in suboptimal dose distribution for larger tumors. As the imaging modalities are improved, improvement in quality of dose prescription in brachytherapy can lead to a better clinical outcome and reduced late radiation toxicities. Tan LT et al,[18] 96% pelvic control rate and 3- year cancer- specific survival of 81% was reported in 3 yr experience with CT image guided

brachytherapy using tandem and ring. Implementation of a CT-based tandem-ring HDR brachytherapy technique along with individual dose adaptation has resulted in a significant 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

Kirchheiner et al,[19] Impairment of quality of life in relation to treatment related morbidity becomes an increasingly important concern when choosing oncological- treatment strategies. If the late complications are minimized, there will be a better quality of life for cancer cervix survivors. There are variations in mean doses with the other studies.it can be due to many uncertainties as bladder and rectum are hollow organs and their filling status will alter their positions and thus can change the dose received by that organs. Any variations in contouring can cause inter and intra observer variations. Contouring in CT films is quite difficult as the contrast and tandems cause lot of artifacts which interfere in our contouring and delineation of structures. Radiopaque markers are usually not recommended as they distort the rectal wall position. Rigid rectal probe is used in this study. Based on clinical research and understanding of biological mechanisms, OAR dose volume constraints should evolve with time . this will help in development of treatment techniques. Further research is needed to assess clinical complications and volume attributing to the complication, to evaluate and minimize the complications.[20]

Strengths of the study: Effectiveness of point based planning dose reporting in OARs is assessed. Assessing whether to shift to volume based planning in cervix intracavitary brachytherapy

Limitations of this study: Only one fraction of intracavitary brachytherapy was simulated, imported and planned. Doses were not equated to EQD2, hence total dose comparison was not done. Clinical correlation was not taken into account contouring on CT images

Recommendations for future: A larger study in similar to determine the clinical outcome, tumor control and toxicity to organs at risk will be worthwhile for resource-appropriate practice. To further correlate the complications for better understanding of dose constraints. However, special attention should also be given to the areas of proximal rectum and sigmoid colon due to more frequent high D2 dose in these areas in addition to the ICRU reference rectal point dose.

CONCLUSION

Bladder D2cc was more than the ICRU reference dose and was greater than the ICRU dose by 1.25-fold. No significant difference between dose to the 2cc volume of rectum and the ICRU point dose and ratio of D2cc/D(ICRU) was 1.0. The DICRU also did correlate positively with D2cc (r=0.654). Results from the study suggests that rectum ICRU reference points can be surrogate markers for D2cc.but not for bladder and hence reporting should be preferably be done in volumetric method rather than reference point doses. Contouring on Ct images poses a challenge as the applicator artifacts obscure the tissue delineation. MR compatible applicator with MR imaging will better help delineate tumor. As bladder and rectum are hollow organs, their filling status varies thus simulation and planning should be done for every brachytherapy session. Oars sigmoid colon and small bowel around the uterus, which may receive higher doses than the rectum.

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