

# Modeling correlation indices between bladder and Foley's catheter balloon dose with CT-based planning using limited CT slices in intracavitary brachytherapy for carcinoma of cervix

## ABSTRACT

**Purpose:** To derive and validate an index to correlate the bladder dose with the catheter balloon dose using limited computed tomography (CT) slices.

**Materials and Methods:** Applicator geometry reconstructed from orthogonal radiographs were back-projected on CT images of the same patients for anatomy-based dosimetric evaluation. The correlation indices derived using power function of the catheter balloon dose and the bladder volume dose were validated in 31 patients with cervical cancer.

**Results:** There was significant correlation between International Commission on Radiation Units (ICRU)-38 balloon reference dose ( $D_r$ ) and the dose received by 25% bladder volume ( $D_{25}$ ) ( $P < 0.0001$ ). Significant correlation was also found between the reference dose of mid-balloon point ( $D_m$ ) and the dose to  $D_{25}$  ( $P < 0.0001$ ). Average percentage difference [ $100 \times (\text{observed index} - \text{expected index}) / \text{expected index}$ ] of observed value of  $I'_{25}$  (index for the dose to  $D_{25}$  bladder with respect to mid-balloon reference point) from that of expected value was 0.52%, when the index was modeled with reference dose alone.

Similarly the average percentage difference for  $I'_{10cc}$  (index for the dose to 10 cc volume of bladder with respect to mid balloon point) was 0.84%. When this index was modeled with absolute bladder volume and reference dose, standard deviation of the percentage difference between observed and expected index for  $D_m$  reduced by approximately 2% when compared to  $D_r$ .

**Conclusion:** For clinical applications, correlation index modeled with reference dose and volume predicts dose to absolute volume of bladder. Correlation index modeled with reference dose gives a good estimate of dose to relative bladder volume. From our study, we found  $D_m$  to be a better indicator of bladder dose than  $D_r$ .

**KEY WORDS:** Back-projection, balloon dose, bladder dose, carcinoma cervix, correlation indices, intracavitary brachytherapy

## INTRODUCTION

Brachytherapy in combination with external-beam radiotherapy is a standard treatment modality for carcinoma of cervix. Historically, brachytherapy treatment planning was empirical and based on one of the three systems namely the Stockholm system,<sup>[1]</sup> the Paris system,<sup>[2]</sup> and the Manchester system<sup>[3]</sup> using traditional radiographs for planning. As these systems use two-dimensional methods for treatment planning, estimation of critical organ dose may be underestimated, leading to fallacious representation of the dose- complication relationship. The International Commission on Radiation Units and Measurements report-38 (ICRU-38) was thought to be the first comprehensive report which gave reasonable estimates of the dose-volume relationship in intracavity

brachytherapy for carcinoma cervix.<sup>[4]</sup> However, more than 20 years after its publication, it has been recognized that some of its concepts failed to gain widespread acceptance, while others failed the test of time and have not been able to find a place in clinical practice.<sup>[5,6]</sup> With the advent of innovative diagnostic tools, such as computed tomography (CT) scans" there has been a constant endeavor to integrate these diagnostic tools for three dimensional treatment planning to individually adapt dose distribution to the target volume.<sup>[7]</sup>

Available literature reveals a lack of a dose-response relationship in terms of bladder and rectal complications.<sup>[8-10]</sup> Few studies have reported that the point of maximum dose is not be represented by the dose to bladder neck, but is usually situated proximal to the applicator sources.<sup>[10,11]</sup> Studies

Arun S Oinam,  
Jayant Sastri Goda,  
Sidharth Dubey,  
Anup Bhardwaj,  
Firuza D Patel

Department of  
Radiotherapy,  
Postgraduate Institute of  
Medical Education and  
Research, Chandigarh-160  
012, India

### For correspondence:

Dr. Arun S. Oinam,  
Department of  
Radiotherapy, PGIMER,  
Chandigarh-160  
012, India. E-mail:  
oarunsingh@rediffmail.  
com

comparing conventional x-ray- and CT-based brachytherapy planning showed gross variations between the maximum bladder dose ( $D_{max}$ ) calculated from CT images and the ICRU-38 reference bladder dose ( $D_{ref}$ ) calculated from orthogonal radiographs.<sup>[12-17]</sup> While Ultrasound Scans have shown that the maximum computed bladder dose to be 2-8 times higher than the ICRU dose<sup>[12]</sup>; similar discrepancies were also seen with CT scans, with variations in the maximum calculated bladder dose with respect to the ICRU point dose.<sup>[15]</sup> These studies do not mention the reasons for the variations observed in the ratio of bladder  $D_{max}$  and bladder  $D_{ref}$ . Again, the dosimetry on specific points of Foley's catheter balloon with conventional radiographic technique based on ICRU-38 dosimetric recommendation may give fallacious results that may not be the true representation of the dose received by bladder.<sup>[18]</sup> The shortcomings of radiographic planning necessitated a study for correlating the balloon dose with the actual bladder dose, using CT-based planning with minimum variation of patient repositioning. This correlation could help us to better predict the actual bladder dose from the balloon dose calculated from conventional radiographs. The semi-empirical formula developed for these correlations can be utilized to review the old dosimetric data of conventional radiographic-based plans and the radiographic-based plans of the center which does not have the CT based brachytherapy planning facility for clinical correlations.

In this present study, our main objective was to correlate the bladder dose with the Foley's catheter balloon dose. Moreover, we tried to find the most suitable dose point on the balloon for predicting the actual dose received by the bladder. Thus, to estimate the bladder dose from the balloon dose, we developed a semi-empirical equation to generate a correlation index which is a function of the dose received at different dose points on the balloon and the bladder volume. We then tried to validate the correlation indices with our clinical cases.

## MATERIALS AND METHODS

### Patients and brachytherapy technique

Thirty-one patients with biopsy-proven squamous cell carcinoma of the cervix were selected for this prospective study. Intracavity application was done with a rigid and fixed PGI Applicator<sup>®</sup> (Postgraduate Institute, India) in patients suitable for intracavity radiotherapy (ICRT).<sup>[19]</sup> Uterine tandem lengths of either 4 or 6 cm, depending on the patient's uterine length, with inter ovoids spacing of 2.0 cm and 2.5 cm, respectively, were used. The application was done with optimal gauze packing to maintain the geometry of the applicator. The patients were treated with a low-dose-rate (LDR) brachytherapy machine (Selectron LDR, Nucletron<sup>®</sup>, Holland). Based on institutional protocol, an LDR equivalent dose of 3500 cGy at 50 cGy/h was delivered to point A of the classical Manchester system in a single fraction after a gap of 2 weeks following whole-pelvis radiotherapy of 4600 cGy in 23 fractions.

### Radiographic simulation, acquisition of CT axial image, and treatment planning

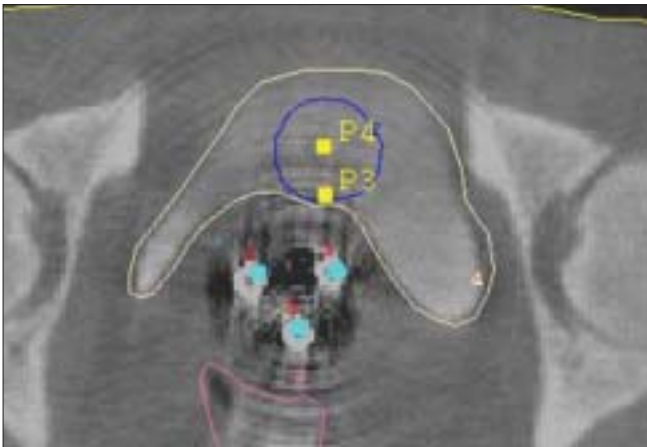
Radiographic simulation was done after filling the balloon with 7cc of contrast as per ICRU-38 recommendations.<sup>[4]</sup> Orthogonal anteroposterior and lateral radiographs were taken with the central axis of the films aligned to the intersection of uterine tandem and colpostats. This intersection point was taken as reference point 'R,' and three fiducial points corresponding to this reference point were marked on the patient's skin using laser lights (sagittal, coronal, and vertical lasers of simulator). CT axial images were acquired on Simulator CT (Phebus of Mecaserto<sup>®</sup>, France) after careful alignment of the laser light with the patient's midline and the reference plane after acquiring the orthogonal radiographs. As CT data acquisition takes around 8 min, care was taken to reduce patient movement during the scan. CT data with 3-mm slice thickness and 5-mm spacing were acquired over the region around the bladder and the colpostats. The field of view (FOV) was chosen from 2 cm above the tip of tandem in the cranial direction to about 2 cm below the colpostats in the caudal direction. During the image acquisition, the bladder was filled with 42 cc of diluted contrast (ratio of contrast: distilled water was 1:5) to delineate the bladder wall for studying the effect of bladder volume on bladder dose, while the Foley's catheter balloon was filled with 7 cc of distilled water to delineate the balloon. Then the CT axial images were transferred to the three-dimensional treatment planning system through a local area network. The bladder and Foley's catheter balloon were delineated in PLATO image processing system (version 2.7, Nucletron<sup>®</sup>, Holland).

### Reconstruction of applicator geometry using back-projection method

The applicator geometries were reconstructed from orthogonal radiographs using the catheter-tracking method and were saved in the library folder by defining at least three points, called Anchor<sup>TM</sup> points, on these catheters, corresponding to the respective catheters points on the axial CT images. The same applicator geometry from the library folder was back-projected on the 3D CT image of each patient by digitizing these anchor points on the corresponding CT slices. The dosimetric and positional accuracy of this technique has been well documented (mean calculated error of  $1.3 \pm 0.3$  mm) in the literature.<sup>[20]</sup> Anatomy-based dose calculations were performed on CT datasets using Brachytherapy Software (Brachytherapy version 14.2.5). Evaluation software (EVAL 3.0) of PLATO TPS (Nucletron, Holland)<sup>TM</sup> was used to calculate individual organ dose-volume histograms (DVH).

### Proposed theory of correlation of bladder with balloon dose

The balloon lies inside the bladder and can be clearly delineated on radiographs as well as in CT images. Usually the bladder takes a crescentic shape and more or less envelopes the cervix and the vaginal cavity due to residual urine and the compact vaginal packing [Figures 1, 2, 3 and 4]. This shape and volume

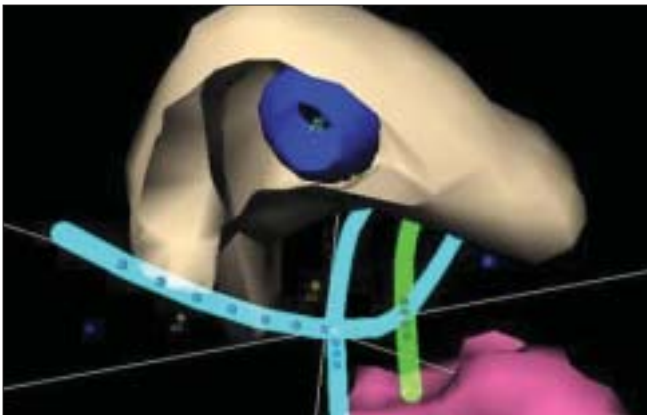


**Figure 1:** The ICRU bladder reference point (P3) and balloon mid-reference point (P4) inside the blue-colored contour of the spherical balloon on a CT transverse slice. The white-colored crescent-shaped contour anterior to the applicator points represents the bladder

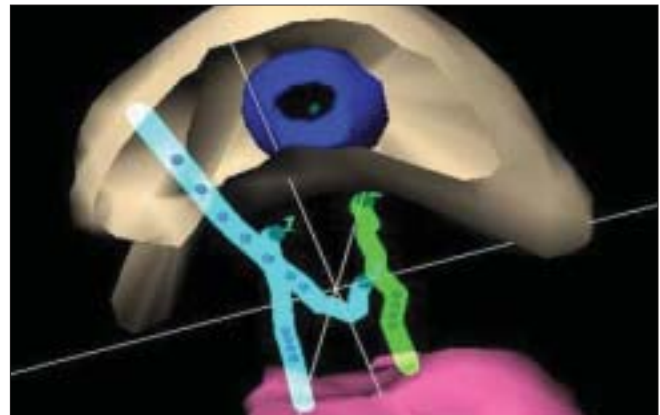
of the bladder affect the dose received by bladder during the brachytherapy dose calculations, which depends on the radius of curvature of dose distribution and the dose rate. The ratio of bladder dose and balloon dose varies inversely



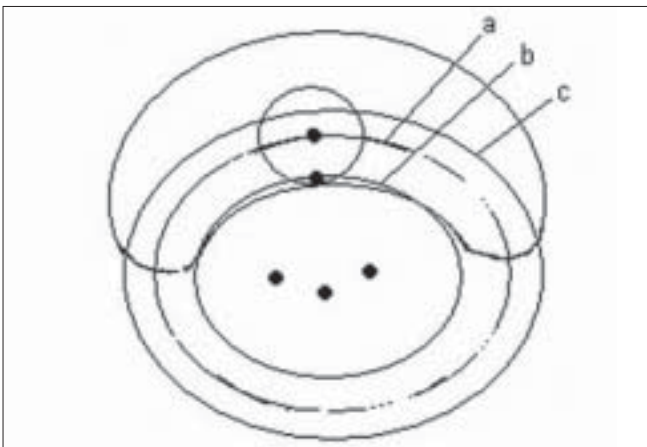
**Figure 2:** (Left panel) 3D image of brachytherapy catheters shown in sky blue, bladder in white, rectum in pink and the balloon in blue colour. The blue pear shaped volume represents the 100% isodose surface. (Right panel) represents the CT transverse slice along the plane of the applicator tip



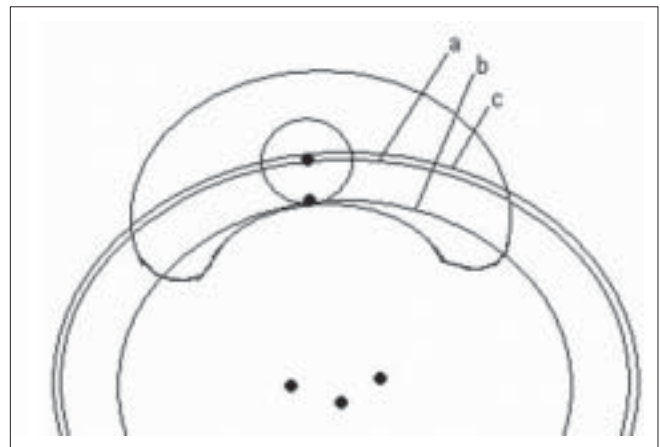
**Figure 3a:** The applicator reconstruction with back-projection method on CT image which displays a smooth reconstruction of applicators



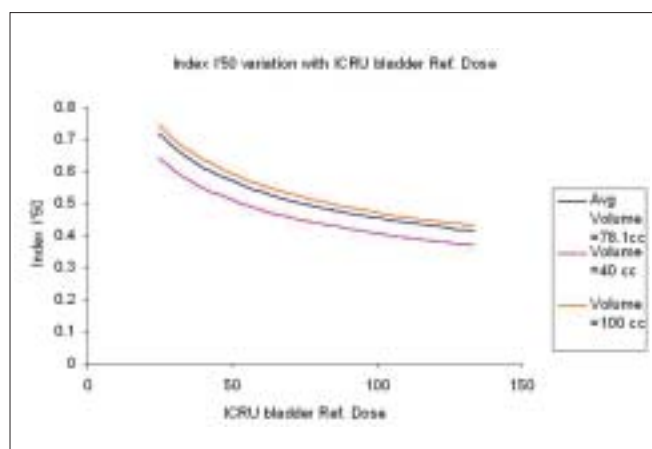
**Figure 3b:** The applicator reconstruction with catheter tracking on CT image showing a zig-zag reconstruction of catheters



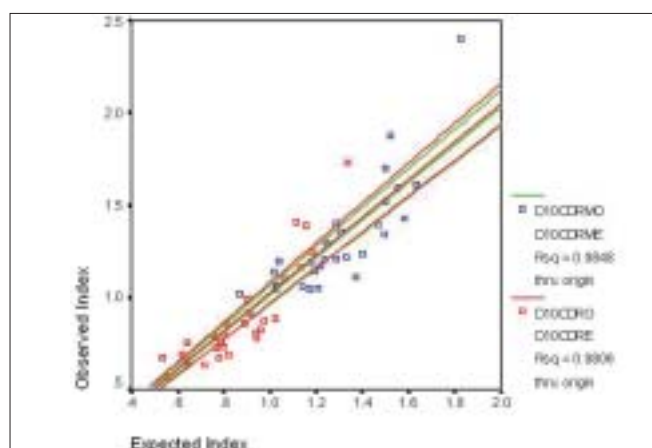
**Figure 4a:** Isodose curves on a distended bladder, which is nearer to the applicators. Correlation Index with reference to this position is  $D_c / D_a$ .  $D_b$  = Isodose passing through ICRU bladder reference point).  $D_a$  = Isodose passing through ICRU balloon mid reference point).  $D_c$  = Isodose which covers 50% volume of bladder



**Figure 4b:** Isodose curves on the distended bladder which is farther away from the applicators. Correlation Index with reference to this position is  $D_c / D_a$ . The value of correlation index in 4b is greater than 4a.  $D_b$  = Isodose passing through ICRU bladder reference point).  $D_a$  = Isodose passing through ICRU balloon mid reference point).  $D_c$  = Isodose which covers 50 % volume of bladder

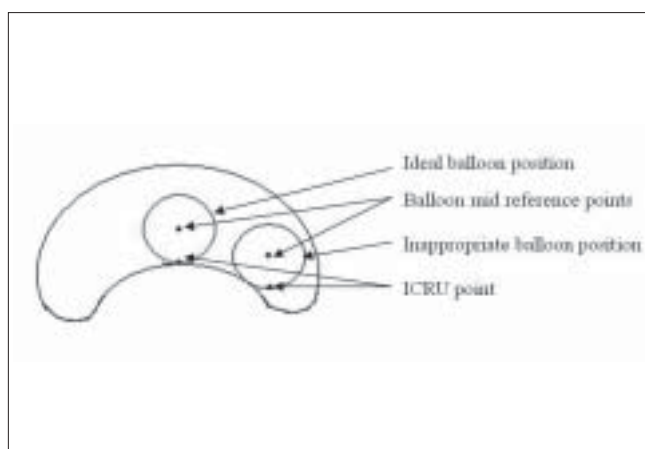


**Figure 5:** The index I'50 changes against the ICRU reference dose for different bladder volumes of 100 cc (orange color), 40 cc (sky blue color), and 78.1 cc (dark blue color)



**Figure 7:** Scatter plot of Expected vs Observed Index with Correlation coefficient and 95% CI. The red squares (i.e.D10CDRO) represent the observed values of I10cc (Dr), the central red color line (i.e.D10CDRE) represents the expected values of I10cc (Dr), and surrounding red lines represent 95% CI. Blue color squares (i.e.D10CDRMO) represent the observed values of I'10cc (Drm) and the central green lines (i.e.D10CDRME) represents the expected values of I10cc (Drm) and surrounding green lines represent 95% CI.

with respect to changes in the dose rate of balloon [Figure 4]. Again, this index value (ratio of bladder dose and balloon dose) changes with the volume and shape of the bladder. The dose to the relative and absolute bladder volume varies with the bladder volume and the reference dose. Figures 4a and 4b show the variation in the ratio of the dose to 50% bladder volume and the ICRU reference dose ( $D_{50}/D_r$ ). In intracavitary brachytherapy planning with radiographic films, the balloon outline can be clearly visualized in both anteroposterior and lateral radiographs; this enables us to define patient-specific points on the balloon surface that represents the limited outline of the balloon. Based on ICRU-38 recommendations, the bladder dose is represented by these specific points. However,



**Figure 6:** The variation in Foley's balloon position inside a crescent-shaped bladder, resulting in shift of ICRU reference point relative to the bladder wall. The blue color circle represents an appropriately positioned balloon with the posterior-most point and midpoint representing ICRU point and mid-balloon point. The black color circle represents the inappropriately positioned balloon with the ICRU point (posterior-most point) and mid-balloon reference point

in CT-based brachytherapy planning, it is impossible to mark these points on limited images as there is missing data within successive slices. Therefore, in our study, we defined the ICRU reference points and the mid-reference point of the balloon by slice interpolation.

#### Definitions of correlation indices

##### 1. Indices with respect to ICRU reference points:

$$I_{50} = D_{50}/D_r$$

$$I_{25} = D_{25}/D_r$$

$$I_{10cc} = D_{10cc}/D_r$$

$$I_{6cc} = D_{6cc}/D_r$$

##### 2. Indices with respect to mid-reference points:

$$I'_{50} = D_{50}/D_{rm}$$

$$I'_{25} = D_{25}/D_{rm}$$

$$I'_{10cc} = D_{10cc}/D_{rm}$$

$$I'_{6cc} = D_{6cc}/D_{rm}$$

Where

- $D_{50}$ : Dose which covers the 50% volume of bladder
- $D_{25}$ : Dose which covers 25% volume of bladder
- $D_r$ : Dose to ICRU dose point of balloon, i.e., posterior points of balloon
- $D_{rm}$ : Dose to mid-reference point of balloon
- $D_{6cc}$ : Dose to 6 cc volume of bladder
- $D_{10cc}$ : Dose to 10 cc volume of bladder

The above measured index values of all the patients are fitted on the following mathematical model of index, which is a function of dose and volume, as follows:

$$I(D, V) = D^c \cdot V^{c1} \quad (1)$$

Where  $V$  = absolute bladder volume,  $D$  = reference dose (ICRU reference dose or mid-balloon reference dose), and  $c_0$  and  $c_1$  are exponentials of  $D$  and  $V$ , respectively; these exponentials are found out by using least square curve-fitting of measured index values in Equation 1. When these measured index values are fitted with reference dose by power function using the following equation, the modeled index is given by:

$$I(D) = b_0 \cdot D^{b_1} \quad (2)$$

Where  $b_0$  is a constant multiplication factor and  $b_1$  is the exponential of  $D$ .

### Statistical analysis

Statistical analysis was done using SPSS, version 10.0. Regression correlation (least square line-fitting) was used to correlate the balloon dose and the dose received by the relative and absolute volume of the bladder. The accuracy of the estimated bladder dose was analyzed by finding the mean, standard deviation, 95% confidence intervals (CI), and range of percentage difference of the measured correlation indices from the calculated indices which was normalized to the calculated indices [i.e.,  $100 \times (\text{measured indices} - \text{calculated indices}) / \text{calculated indices} \%$ ]. Paired sample  $t$ -test was also used to find out the statistical significance of the difference between the ICRU reference dose and the dose to absolute volume.

### RESULTS

Figure 1 shows the crescent-shaped bladder injected with diluted contrast media. Inside this crescent-shaped bladder, the image of the Foley's catheter balloon filled with distilled water is delineated. P3 and P4 in this figure represent the ICRU-38 bladder reference point and balloon mid-reference point, respectively. Figure 2a shows the back-projection of applicators geometry on the 3D CT image. This back-projection method for autoprediction of catheter geometry adjusts the tips of the catheters and interpolates catheters geometry in between the CT slice images according to the stored geometry of catheters as shown in Figures 2a and b. The digitization of catheters with the catheter tracking method cannot reproduce the same applicators geometry on the 3D CT image due to unavailability of CT axial data at these points. The difference between these reconstructions of catheters using the catheter tracking method and back-projection method is shown in Figures 3a and 3b. There was smooth reconstruction of catheters using the back-projection method [Figure 3a], which was not possible with the catheter tracking method [Figure 3b]. The crescent shape of the bladder and the distance of the bladder from the applicator sources changes the ratio of the dose which covers the 50% volume of bladder and the dose of ICRU-38 bladder reference point [Figure 4a and 4b]. The changes in the values of the dose ratio can be noticed from these figures. In higher ICRU-38 bladder reference dose, this ratio is smaller, as shown in Figure 4a. Figure 4b shows the increase in the ratio for lower ICRU-38 bladder reference doses. The same changes of index

variation were observed as shown in Figure 5. Furthermore, the ICRU-38 bladder reference point defined by anteroposterior and lateral radiographs may not represent the bladder wall for inappropriate balloon position. This may lead to a large variation of the index defined with ICRU-38 reference dose as compared with the index defined with mid-balloon reference dose as shown in Figure 6. A statistically significant correlation was found between balloon reference dose ( $D_r$ ) and the dose to 25% bladder volume ( $D_{25}$ ),  $P < 0.0001$ . A significant correlation was also seen between mid balloon point ( $D_{mm}$ ) and dose to 25% bladder volume ( $D_{25}$ ),  $P < 0.0001$ . These correlation coefficients gave us the idea regarding the applicability of defining the correlation indices for the estimation of bladder dose from the balloon dose. The constants and exponents of power functions of the above equations were derived by the least square curve-fitting program written in Microsoft Excel® using the dose and volume parameters given in Tables 1 and 2. These semi-empirical equations can be used to predict the dose to the different volumes of the bladder using the constants and exponents given in Tables 1 and 2. A scatter plot was drawn through origin to show the degree of dispersion between the calculated index and the observed index values [Figure 7].

### Variation of modeled index values of relative bladder volume from the observed values

When the index was modeled with reference dose  $D_r$  and bladder volume using Equation 1, the average difference and the standard deviation of the differences between the measured index value from the calculated value (percentage difference =  $100 \times (\text{measured values} - \text{calculated values}) / \text{calculated values}$ ) were, respectively, 2.2% and 17.4% for both  $I_{50}$  and  $I_{25}$  [Table 3]. Modeling Equation 2 with reference dose  $D_r$  only, the average percentage differences between measured and calculated index values for  $I_{50}$  and  $I_{25}$  was 0.69% and 0.64%, respectively, and the respective standard deviations were 12% and 11.8% [Table 4]. The correlation indices for various dependent parameters with respect to  $D_{mm}$  also showed similar variations [Tables 3 and 4].

On comparing the indices with respect to  $D_r$  and  $D_{mm}$ , the dispersion in the calculated values from the observed values of the indices for  $D_{mm}$  was reduced by 2% compared to  $D_r$ . These show the improvements of dose predictions to relative volume using Equation 2 when modeled with reference dose only.

### Variation of modeled index values from the observed values with respect to absolute bladder volume

When the absolute volume was taken into consideration for defining the indices modeled with reference dose and volume (Equation 1), the indices which are modeled with volume and reference dose  $D_{mm}$  show minimum variations between observed and calculated values of index [Tables 3 and 4]. The average percentage differences between observed and calculated index values for  $I'_{10cc}$  was 0.84% (SD = 11.5%), for  $I'_{6cc}$  it was 0.94% (SD = 13.5%), and for  $I'_{1cc}$  it was 2.31% (SD = 23.0%) with respect to  $D_{mm}$  [Table 3]. However, when these

**Table 1: Modeled parameters of relative bladder volume indices**

Index	Ref. dose	Dependent parameter	b0	b1	c0	c1
$I_{25}$	$D_r$	Dose and volume			-0.29	0.20
		Dose	5.79	-0.51		
$I'_{25}$	$D_{rm}$	Dose and volume			-0.18	0.17
		Dose	4.93	-0.41		
$I_{50}$	$D_r$	Dose and volume			-0.33	0.16
		Dose	4.94	-0.54		
$I'_{50}$	$D_{rm}$	Dose and volume			-0.22	0.14
		Dose	4.31	-0.45		

$I_{25} = D_{25}/D_r$ ,  $I'_{25} = D_{25}/D_{rm}$ ,  $I_{50} = D_{50}/D_r$ ,  $I'_{50} = D_{50}/D_{rm}$ ,  $D_r$  = ICRU reference dose;  $D_{rm}$  = balloon mid-reference dose; b0 = constant multiplying factor of Equation 2; b1 = exponential constant of reference dose of Equation 2; c0 and c1 = exponential constant of reference dose and volume of Equation 1

indices were modeled with reference dose alone (Equation 2) the percentage variation in dispersion was larger for the above indices.

When the Indices with respect to reference dose  $D_r$  were compared to that of  $D_{rm}$ , there was significant reduction in the average and spread of variation. The mean percent difference reduced from 1.11% (SD = 13.36%) to 0.84% (SD = 11.52%) respectively for 10 cc Index [Tables 3 and 4].

**DISCUSSION**

Brachytherapy for carcinoma cervix has become more sophisticated with the advent of CT-based planning. Conventional radiographs provide limited information concerning the spatial relationship between the bladder and the implanted sources using radioopaque markers. Evaluating a plan based on two-dimensional dose computations at selected bladder points may result in suboptimal clinical decisions, with adverse effects on therapeutic outcome. Computerized axial tomography scan is an efficient method for volumetric delineation of organs and the approach is based on volumetric dose computations on a series of transverse CT images using the 3D treatment planning system.<sup>[21]</sup> This allows dose evaluation for different bladder volumes. In our study, we utilized the CT axial images from Simulator CT for the reconstruction of 3D images and applied the back-projection technique to reconstruct the applicator geometry.

The basic idea of the back-projection technique was to avoid the adjustment of the tips of applicators, which enables autocorrection of missing data of catheters within the CT images.

The inherent disadvantage of ICRU bladder reference ( $D_r$ ) point in estimating the actual bladder dose is that there occur large variations in the ratio of maximum bladder dose to ICRU reference dose. These variations could be attributed to changes in applicator positioning. The observations were further corroborated by other studies which analyzed the dose received by 3% volume of bladder ( $D_3$ ).<sup>[22]</sup> The mean dose to  $D_3$  was 1.28 times higher than the mean ICRU bladder point dose. Literature reviews also showed large variations between the ratio of the maximum bladder dose to ICRU reference dose (range: from 1.01 to 3.59).<sup>[13-14,16]</sup> In our study, the average observed dose to 1 cc volume of bladder was 1.4 times the ICRU reference dose (SD = 0.45; range 0.95-2.95) as shown in Table 5. A study evaluating 60 patients and 93 applications reported that the estimated dose to ICRU bladder point was significantly lower than the dose received by 2 cc volume of bladder ( $D_{BV2}$ ) ( $P < 0.001$ ); the mean difference was 680 cGy ( $\pm 543$  cGy).<sup>[23]</sup> This study concluded that the ICRU reference point may not be a reasonable surrogate for estimating the dose to absolute (2 cc) bladder volume, which confirms our observations. Moreover, the ICRU bladder reference point received significantly lesser dose when compared to 1 cc volume of bladder ( $P = 0.032$  by paired 't' test) and the mean

**Table 2: Modeled parameters of absolute bladder volume indices**

Index	Ref. dose	Dependent parameter	b0	b1	c0	c1
$I_{10cc}$	$D_r$	Dose and volume			-0.41	0.36
		Dose	8.08	-0.54		
$I'_{10cc}$	$D_{rm}$	Dose and volume			-0.32	0.33
		Dose	6.75	-0.44		
$I_{6cc}$	$D_r$	Dose and volume			-0.35	0.34
		Dose	6.55	-0.46		
$I'_{6cc}$	$D_{rm}$	Dose and volume			-0.25	0.31
		Dose	5.40	-0.35		
$I_{1cc}$	$D_r$	Dose and volume			-0.24	0.31
		Dose	6.90	-0.38		
$I'_{1cc}$	$D_{rm}$	Dose and volume			-0.11	0.27
		Dose	5.08	-0.24		

$I_{10cc} = D_{10cc}/D_r$ ,  $I'_{10cc} = D_{10cc}/D_{rm}$ ,  $I_{6cc} = D_{6cc}/D_r$ ,  $I'_{6cc} = D_{6cc}/D_{rm}$ ,  $I_{1cc} = D_{1cc}/D_r$ ,  $I'_{1cc} = D_{1cc}/D_{rm}$   
 $D_r$  = ICRU reference dose;  $D_{rm}$  = balloon mid-reference dose; b0 = constant multiplying factor of Equation 2; b1 = exponential constant of reference dose of Equation 2; c0 and c1 = exponential constant of reference dose and volume of Equation 1.

**Table 3: Comparison between observed and expected values of indices for  $D_r$  and  $D_{rm}$  and 95% confidence interval of percentage difference between observed and expected values for  $D_r$  and  $D_{rm}$  in case of dose and volume modeling**

Volume of index $I_x$ or $I'_x$	$D_r$				$D_{rm}$			
	Mean of difference (%)	SD of difference (%)	Lower bound	Upper bound	Mean of difference (%)	SD of difference (%)	Lower bound	Upper bound
50%	2.18	17.36	-4.42	8.79	1.90	15.80	-4.10	7.92
25%	2.14	17.37	-4.47	8.75	1.80	15.44	-4.07	7.68
10 cc	1.11	13.36	-3.97	6.19	0.84	11.52	-3.54	5.22
6 cc	1.22	15.16	-4.54	7.00	0.94	13.46	-4.18	6.06
1 cc	3.08	26.97	-7.18	13.34	2.31	23.09	-6.47	11.10

Difference =  $100 \times (\text{measured values} - \text{calculated values}) / \text{calculated values} (\%)$

**Table 4: Comparison between observed and expected values of indices for  $D_r$  and  $D_{rm}$  and 95% confidence interval of percentage difference between observed and expected values for  $D_r$  and  $D_{rm}$  in case of dose modeling**

Volume of index $I_x$ or $I'_x$	$D_r$				$D_{rm}$			
	Mean of difference (%)	SD of difference (%)	Lower bound	Upper bound	Mean of difference (%)	SD of difference (%)	Lower bound	Upper bound
50%	0.689	12.00	-3.87	5.25	0.573	10.90	-3.57	4.72
25%	0.644	11.80	-3.84	5.13	0.515	10.28	-3.39	4.42
10 cc	1.089	15.99	-4.99	7.17	0.955	14.86	-4.70	6.61
6 cc	1.39	18.25	-5.56	8.33	1.19	17.03	-5.29	7.67
1 cc	2.62	26.11	-7.31	12.56	2.09	23.34	-6.78	10.97

Difference =  $100 \times (\text{measured values} - \text{calculated values}) / \text{calculated values} (\%)$

**Table 5: Index statistics showing distribution of different indices in the whole population**

Index	Mean	SD	Median	Lower bound	Upper bound	Minimum	Maximum
$I_{50}$	0.536	0.15	0.489	0.479	0.594	0.37	0.96
$I_{25}$	0.719	0.19	0.661	0.646	0.793	0.51	1.26
$I_{10cc}$	0.881	0.27	0.790	0.777	0.985	0.57	1.73
$I_{6cc}$	0.997	0.30	0.894	0.885	1.110	0.69	2.05
$I_{1cc}$	1.436	0.45	1.298	1.265	1.608	0.95	2.94
$I'_{50}$	0.796	0.16	0.768	0.734	0.859	0.54	1.18
$I'_{25}$	1.069	0.20	1.022	0.991	1.145	0.78	1.56
$I'_{10cc}$	1.307	0.31	1.209	1.189	1.424	0.92	2.40
$I'_{6cc}$	1.482	0.34	1.387	1.351	1.613	1.11	2.84
$I'_{1cc}$	2.132	0.53	1.980	1.930	2.334	1.51	4.06

difference was 713 cGy ( $\pm 726$  cGy). This prompted us to do a study to find out a better parameter to estimate the actual bladder dose. In this study, we compared the dose to the ICRU reference point ( $D_r$ ) with a point inside the balloon ( $D_{rm}$ ). The ICRU points defined on the orthogonal radiographs may not represent points on the bladder wall for inappropriate balloon positions [Figure 7], resulting in underestimation of the dose to 1 cc of bladder by 0.75 (95% CI = 0.67–0.81). Other studies have shown similar results, with underestimation of dose to 2 cc of the bladder wall (overall mean ratio of ICRU bladder reference point dose to the 2 cc of bladder wall dose by  $0.9 \pm 0.4$ ).<sup>21</sup> However, the uncertainty in predicting the dose to lesser bladder volume increases due to the variation of applicator positions. In our study, the average variation of the modeled index with respect to  $D_{rm}$  ( $I'_{10cc}$ ) from the observed value was 0.84%, with a spread of 11.32% [Table 3]. However, these uncertainties are reduced when the reference dose ( $D_{rm}$ ) is taken at the midpoint of the balloon for all indices [Tables 3 and 4]. As the radial distance from the balloon midpoint and the bladder wall in which the balloon is sitting with respect

to sources are almost fixed, this results in better correlation of bladder dose. Moreover, the variation in the shape of the bladder due to nonuniform packing and presence of variable amount of residual urine causes a change in the relative and the absolute volume of bladder enclosed by a particular isodose level [Figures 1 and 4]. This nonuniformity is reflected in large variations in the dose to smaller volume of bladder, resulting in large estimates in the SD. Hence, for dosimetric purposes and for better clinical correlation of radiation reactions, we suggest the use of larger volumes of bladder and mid-balloon reference point ( $D_{rm}$ ) rather than the use of smaller volumes and the ICRU reference point ( $D_r$ ).

## CONCLUSION

The correlation index modeled with the reference dose was found to be a satisfactory index for predicting dose to relative volume of bladder (e.g., 25% and 50% of bladder volume). Furthermore, the mid-balloon reference point ( $D_{rm}$ ) was found to correlate better with the bladder dose. These indices can

also be used with reasonable accuracy for predicting the dose to larger bladder volumes. However, these correlation indices need to be validated prospectively in a large series of patients under normal clinical conditions (i.e., when the bladder has been catheterized) using multislice CT scanners with faster image acquisition capabilities. For dosimetric purposes, we suggest the use of larger volumes of bladder and the mid-balloon reference point ( $D_{rm}$ ), rather than using smaller volumes and the ICRU reference point ( $D_r$ ), where the variations in dose estimation is much larger.

## REFERENCES

- Heymen J. The so called Stockholm method and the results of treatment of uterine cancer at radium hemmet. *Acta Radiol* 1935;16:129-48.
- Pierquin B. *Precis de curietherapie, endocurietherapie et plesiocurietherapie*. Paris: Masson; 1964.
- Meredith WJ, editor. *Radium dosage: The Manchester system*. 2<sup>nd</sup> ed. Edinburgh: E and S. Livingstone 1967.
- ICRU report 38: Dose and volume specification for reporting intracavitary therapy in gynaecology. Bethesda: International commissioning on Radiation units and measurements; 1985.
- Grigsby PW, Williamson JF, Clifford Chao KS, Perez CA. Cervical tumour control evaluated with ICRU 38 reference volumes and integrated reference air kerma. *Radiother Oncol* 2001;58:19-23.
- Pötter R, Van Limbergen E, Gerstner N, Wambersie A. Survey of the use of ICRU 38 in recording and reporting cervical cancer brachytherapy. *Radiother Oncol* 2001;58:11-8.
- Schoeppel SL, LaVigne ML, Martel MK, McShan DL, Frass BA, Roberts JA. Three dimensional treatment planning of intracavitary gynaecologic implants: Analysis of ten cases and implications for dose specifications. *Int J Radiat Oncol Biol Phys* 1994;28:277-83.
- Orton CG, Wolf-Rosenblum S. Dose dependence of complication rates in cervix cancer radiotherapy. *Int J Radiat Oncol Biol Phys* 1986;12:37-44.
- Pourqueir H, Delard R, Achiulle E, Daly NJ, Horiot JC, Keiling R, *et al.* Quantified approach of the analysis and prevention of urinary complications in radiotherapeutic treatment of cancer of the cervix. *Int J Radiat Oncol Biol Phys* 1987;13:1025-33.
- Cunningham DE, Velkley JA, Velkley DE, Chung CK. Routine clinical estimation of rectal, rectosigmoidal, and bladder doses from intracavitary brachytherapy in the treatment of carcinoma of the cervix. *Int J Radiat Oncol Biol Phys* 1981;7:653-60.
- Stueckelschweiger GF, Arian-Schad KS, Poier E, Poschauko J, Hackl A. Bladder and rectal dose of gynecologic high dose rate implants: Comparison of orthogonal radiographic measurements with *in vivo* and CT-assisted measurements, *Radiology* 1991;3:889-94.
- Barillot I, Horiot JC, Maingon P, Bone-Lepinoy MC, Vaillant D, Feutray S. Maximum and mean Bladder dose defined from ultrasonography: Comparison with the ICRU reference in gynaecological brachytherapy. *Radiother Oncol* 1994;30:231-8.
- Kuipers TJ, Visser AG. Technical aspects of bladder dosimetry in intracavity irradiation in cervix carcinoma. *Radiother Oncol* 1987;7:7-12.
- Schoeppel SL, Lavigne ML, Martel MK, McShan DL, Frass BA, Roberts JA. Three dimensional treatment planning of intracavitary gynaecologic implants: Analysis of ten cases and implications for dose specifications. *Int J Radiat Oncol Biol Phys* 1994;28:277-83.
- Hunter RD, Wong F, Moore C, Notley HM, Wilkinson J. Bladder base dosage in patients undergoing intracavity therapy. *Radiother Oncol* 1986;7:189-97.
- Kapp KS, Stueckelschweiger GF, Kapp DS, Hackl AG. Dosimetry of intracavitary placements for uterine and cervical carcinomas: Results of orthogonal films, TLD and CT assisted techniques. *Radiother Oncol* 1992;24:137-46.
- Tan LT, Warren J, Freestone G, Jones B. Bladder dose estimation during intracavity brachytherapy for carcinoma cervix using line source system. *Br J Radiol* 1996;69:953-62.
- Ling CC, Schell MC, Working KR, Jentzsch K, Harisiadis L, Carabell S, *et al.* CT-assisted assessment of bladder and rectum dose in gynecological implants. *Int J Radiat Oncol Biol Phys* 1987;13:1577-82.
- Patel FD, Negi PS, Sharma SC, Kapoor R, Singh DP, Ghoshal S. Dose rate correction in MDR brachytherapy in cancer cervix treatment. *Radiother Oncol* 1998;49:317-23.
- Fellner C, Potter R, Knocke TH, Wambersie A. Comparison of radiography- and computed tomography-based treatment planning in cervix cancer in brachytherapy with specific attention to some quality assurance aspects, *Radiother Oncol* 2001;58:53-62.
- Wachter Gerstner N, Wachter S, Reinstadler E, Fellner C, Knocke TH, Wambersie A, *et al.* 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. *Radiother Oncol* 2003;68:269-76.
- Kim RY, Pareek P. Radiography-based treatment planning compared with computed tomography (CT)-based treatment planning for intracavitary brachytherapy in cancer of the cervix: Analysis of dose-volume histograms. *Brachytherapy* 2003;2:200-6.
- Christopher EP, Mathew P, Gregory M, Chronoski, Anuja J, John H, *et al.* 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. *Int J Radiat Oncol Biol Phys* 2005;62:131-7.

**Source of Support:** Nil, **Conflict of Interest:** None declared.