Angular Variation of Applicators in LDR-ICBT

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Abstract: Effect of angular variation to dose received and its clinical correlation was studied in 36 ca.cervix patients. Angular variation results in dose variation but its impact needs to be studied.

Keywords: CA Cervix, LDR ICBT, Angular variation.

INTRODUCTION

Brachytherapy is derived from the Greek word "brachios" which means "short" [1]. Brachytherapy is based on the principles of both radiotherapy and surgery. It has evolved independently with many different techniques, treatment regimens and planning methods. Intracavitary Brachytherapy (ICBT) forms an integral part of radiotherapy, which is employed in the treatment of carcinoma cervix patients combined with teletherapy. ICBT was first performed by Margaret cleaves [2] in 1903 which involves placement of uterine tandem and vaginal ovoids. It can be delivered either as Low Dose Rate (LDR) based or High Dose Rate (HDR) based system with the help of manual or remote after loading of Caesium 137 and Iridium 192 sources. In our institute we employ the manual after loading LDR Brachytherapy system with Cesium 137 sources. LDR Brachytherapy involves delivery of radiation at a continuous rate of 0.4-2 Gy/hr and this means that the delivery of the required dose will require around 24 to 30 hours. The ICBT procedure is done in the operation theatre (OT). The applicators are placed in the uterine and the vaginal cavity. Then the patient is shifted to the Brachytherapy ward for simulation and after loading of Cesium 137 source following which the patient needs to lie down in the same supine position for the prescribed duration of 20-30 hours. Due the long treatment time, soakage of vaginal packing and patient movement these can result in angular variation of applicators. These are the few reasons why some advocate HDR brachytherapy [3]. The purpose of this study is to evaluate the angular movement and to determine the actual dose difference to critical structures and finally the clinical outcome.

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MATERIALS AND METHODS

Estimation of Sample Size

The estimation of sample size is based on the study "Positional stability of Sources during low dose rate Brachytherapy for carcinoma cervix" [4]. The sample size is estimated based on 5% significance level and with an error of 0.3 and the sample size is 36.

Inclusion Criteria

(a) Any age.

(b) Carcinoma cervix patients receiving brachytherapy treatment with LDR-ICBT.

Exclusion Criteria

(a) Carcinoma cervix patients receiving palliative radiotherapy.

(b) Patients receiving interstitial Brachytherapy.

Method of Statistical Analysis

The following methods of statistical analysis have been used in this study.

1. One way Analysis of Variance (Anova)

2. Univariante analysis of the dichotomous variables encoded was performed by means of the Chi square test with Yates correction if required.

3. Pearson Correlation technique used to test the direction and strength of the relationship between angle and point, rectal and dose variation.

Method of Collection of Data

36 consecutive carcinoma cervix patients who underwent Low Dose Rate Intracavitary Brachytherapy

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were the subjects of the study. Post treatment localization radiographs were obtained for comparative analysis. EUA (Examination under Anesthesia) was performed to assess the response of growth and to decide whether the ICBT was suitable for the patient. After the ICBT procedure Patient is transferred to a stretcher with the help of a lift board and shifted to the recovery room then to the Brachytherapy simulator room. Orthogonal X-rays are taken and the different measurements necessary for calculation of magnification are recorded. The center of the cross wires are marked on the patient skin and the patient is shifted to the Brachytherapy treatment room where manual after loading of Caesium sources is done. Here the patient has to lie down in supine position for an average of 24-26 hours. Once the treatment is completed as decided after going through the dose distribution on the TPS (Treatment Planning System) the patient is shifted back to the simulation room for post treatment X-rays. Care was taken to make sure that orthogonality is maintained and the skin marks along with the measurements matched to those of pretreatment recordings in order to avoid any kind of error.

Localization images were a set of orthogonal antero-posterior and lateral radiographs. Reference planes (x,y,z) were defined for each set of images by using patients bone landmarks in this way evaluation of the changes In position of applicators relative to fixed bony landmarks in the patient were done. The x reference plane is defined as a line passing through the symphysis pubis on the antero-posterior radiograph. The y reference plane is defined as the line passing through the centre of pubic symphysis and the vertebra. The z reference plane as the line passing parallel to the table and the anterior most point of vertebra or the pubic symphysis and these reference planes were maintained in both the radiographs i.e. one taken before and after the treatment. Measurement of the values of all the variables in all the planes and then reproducing them onto the after X-ray were done in order to exactly calculate the positional and dose variations if any. The reference points or variables used to evaluate the effect of applicator movement on doses were Point A, Point B, Point P, and Alfa and Beta angles, bladder and rectal points. These patients were followed up and they were evaluated for the presence of sequalae in terms of rectal reactions and bladder reactions. They were graded as per the RTOG criteria.

Point A: It is 2 cms lateral to the midline of the intra uterine canal and 2 cms cephalad to the lateral vaginal fornices.

Point B: 5 cms to the right and the left of the patient midline in the transverse plane.

Point P: 6 cms right and left of the patient's midline in the transverse plane.

Rectal Point: 0.5cm posterior to the posterior vaginal wall.

Bladder Point: falls on the surface of a Foleys balloon.

Alfa angle: the angle formed between intrauterine tube and the vaginal axis at the os marked in the LAT radiograph.

Beta angle: the angle between axis of vagina and intrauterine tube measured at os marked from AP radiograph (Figure **1**).

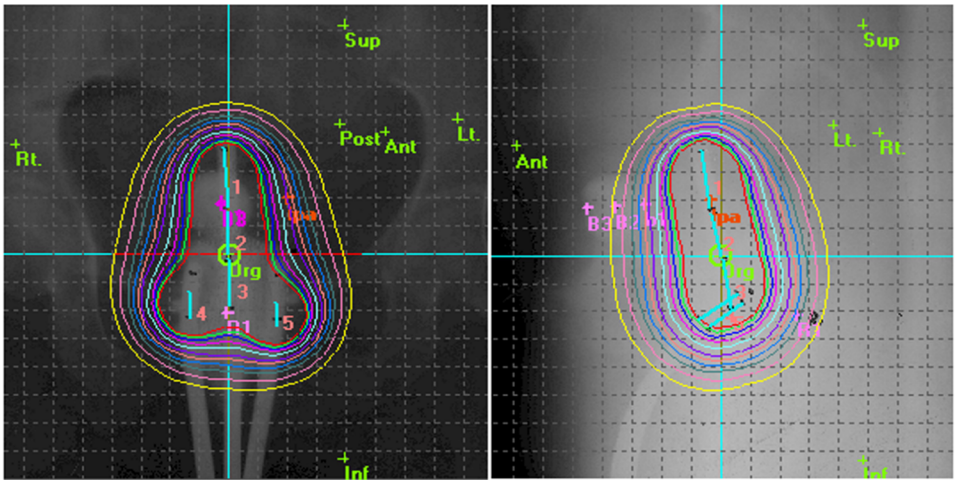

Figure 1:

Table 1:

	N	Mean	Median	Mode	Std. Deviation	Min	Maxi
Age	36	54.47	53.50	55	10.20	32	76

RESULTS

Age Distribution

The study group (n=36) consisted females in the age group ranging from 32-76 with a mean of 54 and median of 53 (Table **1**).

Stage of Disease

The study group had a spectrum of stages from IB to IVB with variable frequencies as depicted in the table below. The most common stage which the patient suffered from is stage IIIB accounting for 52% of the cases.

Angular Variation of Applicators

Of the 36 patients angular variation was studied in terms of alfa angle and beta angle. Alfa angular variation ranged from 0-8degrees and beta angle variation from 2-8 degrees (Tables **2** & **3**).

Table 2:

Alfa Angle	Frequency	Percent
0-2	17	47.2
3.5	15	41.7
6-8	4	11.1
Total	36	100.0

Table 3:

Beta Angle	Frequency	Percent
0-2	3	8.3
3.5	24	66.7
6-8	9	25.0
Total	36	100.0

Correlation between Alfa Angle and Dose Variation

Alfa angle was measured in the present study to substantiate the observation that even in the absence of the variation in position of applicators there can be variation in dose. This will also help to show that applicators not only vary in position but also there can be presence of rotation of the applicators. Though variation in dose at point A, B, P was recorded it was not statistically significant when correlated with the Alfa angle as shown in the table below (Table **4**).

Correlation between Beta Angle and Dose Variation

In the present study the relation between beta angle with dose variation at R2 is statistically significant with a p value of 0.002 (Table **5**).

Correlation between Angles and Point A, B, P and Rectal Dose Variation

In order to tabulate the positive results and to substantiate them Pearson correlation was calculated which showed that rectal dose variation had a positive relationship with beta angle and point A dose variation with values of 0.575 and 0.792 respectively (Table **6**).

Correlation between Toxicity and Point A, B, P Dose Variation

The values were not statistically significant.

DISCUSSION

Management of carcinoma cervix involves multimodal approach with each specialty paying utmost attention. The mode of failure in carcinoma cervix is loco regional more than the distant metastases. This is where radiotherapy has a special role to play with brachytherapy forming the backbone to deliver a high dose to the tumor while respecting the tolerance of critical organs. In these patients 72 pairs of orthogonal films both pre and post ICBT were studied. Quantification of the data was as per ICRU 38 and ABS guidelines. Variation in terms of angles namely Alfa and Beta were analyzed along with variation in terms of displacement at point A, point B, point P, rectal points and bladder points with respect to the bony pelvis. Of the 36 patients the mean age was 54 years with a range of 32-76. Most of these patients were of stage III B i.e. 52% of the total. These patients had a median follow up of 6.75 months. As per the treatment protocol followed at our institute which is in cognizance to the

Table 4:

	Alfa Angle	N	Mean	Std. Deviation	Min	Max	'F' value	'P' value
Point A dose variation (%)	0-2	17	15.65	7.60	6	30	.254	.777
	3-5	15	14.27	7.13	5	28		
	6-8	4	13.25	4.43	9	18		
Point B (%)	0-2	17	2.32	1.27	1	5	.528	.595
	3-5	15	1.93	1.00	1	4		
	6-8	4	2.38	1.38	1	4		
Point P (%)	0-2	17	1.38	.85	0	3	.555	.580
	3-5	15	1.10	.72	0	3		
	6-8	4	1.38	.75	1	2		
Rectum 1 (%)	0-2	17	4.12	1.76	2	8	.856	.434
	3-5	15	3.40	1.64	1	7		
	6-8	4	4.25	1.50	3	6		
Rectum 2 (%)	0-2	17	4.657	2.760	1.0	10.0	.562	.576
	3-5	15	3.900	2.140	1.0	9.0		
	6-8	4	3.500	1.915	2.0	6.0		

Table 5:

	Beta Angle	N	Mean	Std. Deviation	Min	Max	'F' value	'P' value
Point A dose variation (%)	0-2	3	14.00	5.29	10	20	1.000	.379
	3-5	24	13.83	6.82	6	30		
	6-8	9	17.67	7.86	5	30		
Point B (%)	0-2	3	2.00	.87	2	3	2.060	.143
	3-5	24	1.94	1.03	1	4		
	6-8	9	2.82	1.41	1	5		
Point P (%)	0-2	3	1.27	.64	1	2	2.708	.081
	3-5	24	1.08	.65	0	3		
	6-8	9	1.76	.97	1	3		
Rectum 1 (%)	0-2	3	3.33	.58	3	4	1.157	.327
	3-5	24	3.63	1.56	1	6		
	6-8	9	4.56	2.13	2	8		
Rectum 2 (%)	0-2	3	2.333	.577	2.0	3.0	7.613	.002
	3-5	24	3.604	1.961	1.0	9.0		
	6-8	9	6.444	2.506	2.0	10.0		

world data these patients received 46 Gy of external bean radiotherapy to the pelvis. After a gap of 2 weeks they underwent ICBT procedure to a dose of 30 Gy- 32 Gy to point A. This was based on whether patients had midline shielding at the end of 40Gy.

Angular Variation of Applicators

There has been paucity of data in terms of angular variation in LDR Brachytherapy. In our study we could find on an average angular variation of 3degrees of Alfa angle and 4degrees of Beta angle. This becomes

Table 6:

Correlation								
		Alfa Angel	**Beta Angel**	**Point A dose variation (%)**	**Point B (%)**	**Point P (%)**	**Rectum 1 (%)**	**Rectum 2 (%)**
Alfa Angel	Pearson Correlation 'P' value N	1.000 -	0.55 .749	-.048 .780 36	.081 .638 36	.045 .793 36	-.006 .974 36	-.091 .596 36
Beta Angel	Pearson Correlation 'P' value N			.182 .289 36	.356(*) .033 36	.363(*) .030 36	.299 .076 36	.575(**) .000 36
Rectum 1 (%)	Pearson Correlation 'P' value N	-.006 .947 36	.299 .076 36	.792(**) .000 36	.811(**) .000 36	.791(**) .000 36		.681(**) .000 36
Rectum 2 (%)	Pearson Correlation 'P' value N	-.091 .596 36	.575(**) .000 36	.690(**) .000 36	.674(**) .000 36	.651(**) .000 36		

*Correlation is significant at the 0.05 level (2-tailed).
**Correlation is significant at the 0.01 level (2-tailed).

all the more important due to the observation of angular variation in the absence of applicator displacement in nearly 5 cases.

Variation in Dose

Dose to point A variation has been studied by many radiation oncologists like Corn, Ljuggeren [5], Pham [6], Rutten and Dutta [7]. These studies showed dose variation of 2%, 35%, 8% and 20%. This is wide range for the fact that some of the studies were done with radium source and some with iridium and cesium sources.

In our study we found an average variation of 14% which is well within the data shown in the above mentioned studies. We also assessed the variation in dose at point B and point P in order to make out the differences at the lymph node areas. Corn and his colleagues showed this variation to be 1.7% & 0.9% respectively. In the present study we encountered a variation of 2% and 1% at point B and point P respectively.

As per the guidelines there is only one rectal point but in our study we have tried to include two rectal points in order to assess rectal morbidity. This is based on the studies done by Deshpande and Lahtinen. Studies done by Corn and Pham have shown a difference of 3% and 10% respectively. In our study we could find 3.5% variation in the dose to rectum. As far as bladder dose variation is considered our study showed on an average 9.3% and the results of other studies by Corn and Pham 1.9% and18% respectively.

Toxicity Profile

The incidence of toxicity as per the world literature after LDR Intracavitary Brachytherapy is 20 %(moderate) and 5.3 %(severe) at the end of 5 years. Combined rectal and bladder toxicity in our study is 16% with a maximum follow up of 18 months. It is imperative to analyze the incidence of rectal and bladder toxicity and its correlation if any to the angular variations. Though there is paucity of data with respect to analysis of correlation between dose variation and toxicity there have been ample number of studies on critical organ dose and morbidity. Deshpande, Kapp, Lahtinen and Stryker [8] have shown that dose to critical organ and toxicity is directly proportional and also the relation between the dose to critical organ and the measured dose at the respective points.

Correlation of Toxicity and Variation

There are no studies in LDR Brachytherapy who have studied this aspect of correlation in a prospective form due to the shorter period of follow up. Our study aimed at providing some light in to this aspect with a reasonable follow up period to assess the reactions.

There was a positive correlation between Alfa angle and point A dose variation and also with rectal dose. The chances of rectal toxicity with point A dose variation is statistically significant. Among the two rectal points variation at R2 seems to be statistically significant in terms of resultant toxicity and this is in concordance with the studies done by Deshpande at TMH hospital. Though there was a relation between

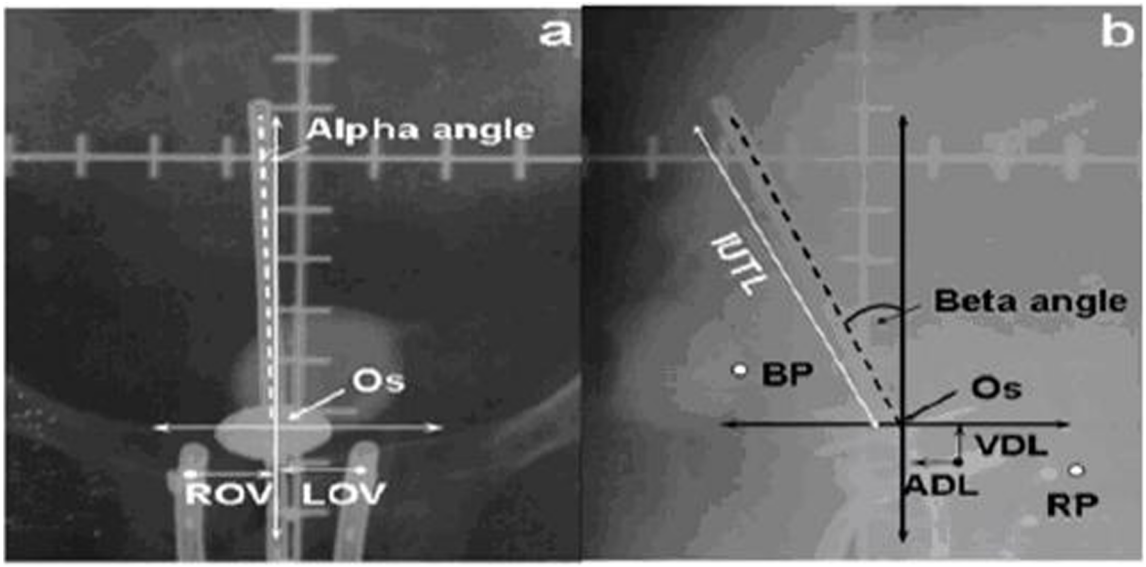

Figure 2:

bulkiness of the disease and the resultant Variations it was not statistically significant as shown by some of the studies done by Eifel and Kim *et al.* [9]. Though the study was powered to know the correlation between these attendant alterations in dose to the clinical outcome of the disease the follow up period was too short to predict the exact figures in terms of survival. This study was done with a worst case scenario thinking that whatever alterations occurred did occur just after the loading of the sources. With the present technology further analysis is needed to exactly quantify at what stage of the treatment duration the variation occurred.

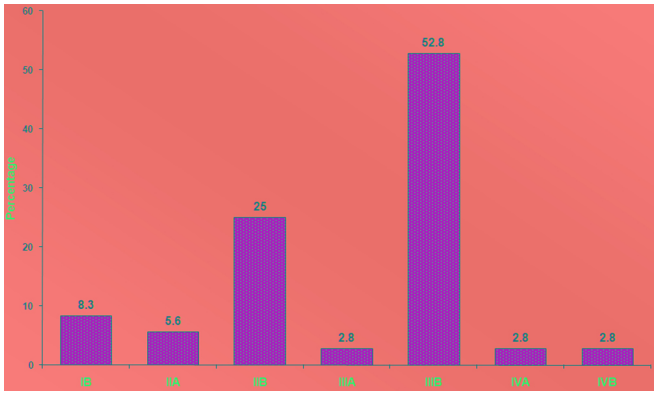

Figure 3:

Though HDR Brachytherapy is suggested as an alternative there can be gross variations if planning is not done for individual fractions and meticulous QA will be the need of the hour. Further studies with longer follow up period are necessary to substantiate the relationship between variations in applicator position and clinical outcome

CONCLUSIONS

Angular variation of applicators does occur during low dose rate intracavitary brachytherapy which results in dose variation to critical organs but the impact on cure needs to be studied. The proponents of HDR brachytherapy quote this as one of the reasons to choose HDR but one has be meticulous in planning during HDR brachytherapy and planning needs to be done during each session and fraction. Some of the steps that can minimize the variation during LDR-ICBT are

- Ensure adequate sedation is used for patients comfort and to achieve better geometry of the applicators.
- Be aware of various geometric variations that can occur

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