Bladder Filling Variation in Cancer Cervix Patients Treated by Image Guided Radiation Therapy

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Abstract: Variable bladder filling during radiotherapy for carcinoma cervix significantly affects the position of target volumes to be treated. This directly impacts the precision with which advanced radiotherapy plans are delivered using specific margins to target volumes. The aim is to study mean bladder volumes and mean range of bladder motion in all three dimensions in patients of carcinoma cervix treated with Image guided radiation therapy (IGRT), and compare them to the baseline planning Computed tomography (CT) scans. For this, a total number of 25 patients/ 150 CT scans, i.e. 25 planning scan and 125 CBCT (cone-beam CT) were analyzed. The bladder volumes and bladder wall dimension were analyzed using offline views of CBCT imaging, conducted weekly for cervix cancer patients, thus adding considerable understanding to the bladder wall motions. The mean bladder volume for all 25 patients was 263.41 cc with standard deviation of 110.174 cc. When mean CBCT bladder volumes of each patient were compared to their respective planning CT bladder volumes, *P* was found to be insignificant (p=0.25), showing consistent bladder filling or reproducibility during treatment. The mean ± standard deviation of bladder's transverse, anteroposterior and supero-inferior dimension was 9.55 ± 0.923 cm; 6.92 ± 2.387 cm and 7.22 ± 0.967 cm. The mean supero-inferior bladder diameter had significant variation from that of the planning CT (7.84 ± 2.749 cm vs 6.92 ± 2.387) with p = 0.018. This study shows that more liberal margins should be considered in supero-inferior dimensions and considerable lesser margins could be given on the lateral sides, as there is less displacement in transverse diameter.

Keywords: Cervix cancer, Bladder filling, Cone Beam CT, Image Guided Radiation Therapy.

INTRODUCTION

Chemoradiation is the standard treatment approach for cancer cervix patients. For radiotherapy planning, most of the centers follow conformal techniques with either three dimensional conformal radiotherapy (3DCRT) or Intensity modulated (IMRT) or Volumetric modulated arc radiotherapy (VMAT). With advancement in technology, image guidance has been utilized using cone beam CTs before every treatment delivery. These CBCTs help in positioning the patient daily in accordance to the planning CT scan taken as baseline, on which radiation plans are made. Other than utilizing these scans for bone to bone matching, the major use of these scans have been in conforming the bladder filling, as strict bladder protocols are given to these patients before planning CT scans and before daily treatments [1,2]. When bladder filling in daily CBCTs matches the bladder filling in planning CTs, radiation treatment is delivered. This study has been conducted to retrospectively analyze the bladder filling variations in cancer cervix patients treated at our centre with image guided radiation therapy (IGRT), so that necessary changes can be taken in the treatment protocols according to the results. Although several studies have examined bladder filling variations during pelvic radiotherapy, most have relied on linear bladder diameters and limited imaging data, often focusing on prostate rather than cervical cancer patients. There is limited literature evaluating three dimensional bladder reproducibility using serial CBCTs during concurrent chemoradiation for carcinoma cervix, especially in the context of a standarized bladder filling protocol in routine Indian settings. The present study addresses this gap by performing weekly volumetric assessments of bladder filling on CBCTs throughout the course of treatment, and by statistically comparing these planning CT bladder volumes to determine reproducibility.

MATERIAL AND METHODS

The study is a retrospective analysis of 25 cancer cervix patients treated with chemoradiation from Jan 2025 to June 2025, where radiation has been delivered using IGRT. All these patients were given bladder protocol before planning CT scan. All patients were advised to come in the morning after four hour fasting. They were asked to void, and then asked to drink 1 L of water in 15 minutes. After 40 minutes of finishing water intake, a planning CT scan was taken with contrast. Planning CT images were then sent to the Eclipse treatment planning station (TPS), where contouring of normal organs at risk i.e bladder, rectum, small bowel and bone marrow was done, along with contouring of target volumes (tumor and lymph nodes) according to RTOG guidelines for cancer cervix [3]. All bladder

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volume contouring and bladder measurements were performed by a single radiation oncologist to ensure consistency and to avoid inter observer variability. All contours were reviewed by a second radiation oncologist in random cases, and any discrepancy was resolved by consensus. 3DCRT or VMAT plans were made for these patients. CBCTs were taken weekly for these patients before each radiation delivery to confirm the accurate bladder filling and bone matching.

For this study, first planning CT scan was opened. Bladder volume was measured and Bladder wall measurements were noted down in transverse direction, superior-inferior direction (longitudinal) and anterior posterior direction, with respect to the uterus, in coronal and saggital views. Then bladder contouring was done in 5 CBCTs of every patient, done on the first day of every week of radiation therapy. Again on all these CBCTs, same bladder measurements were noted down.

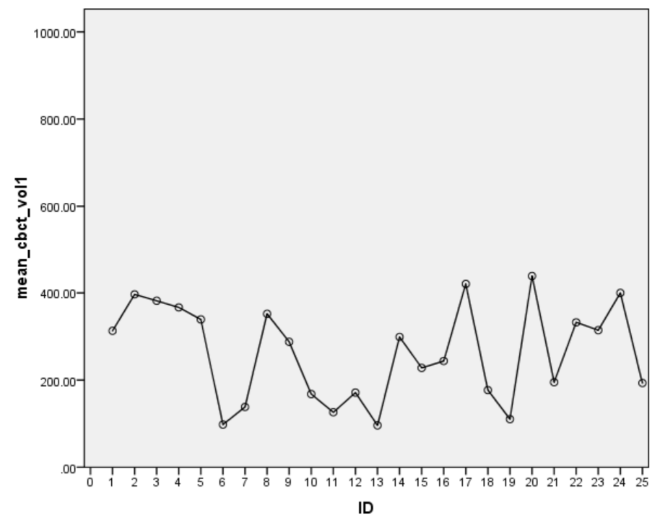
For statistical analysis, SPSS v 23 [4] has been utilized. Descriptive stats have been used to calculate mean and standard deviation, maximum, minimum and range of bladder volumes and bladder dimensions in the three dimensions. Paired T test was used to compare means. Chi square test was used to find patients with significant bladder dimension variations compared to planning CT scans. $P < 0.05$ was considered as significant.

RESULTS

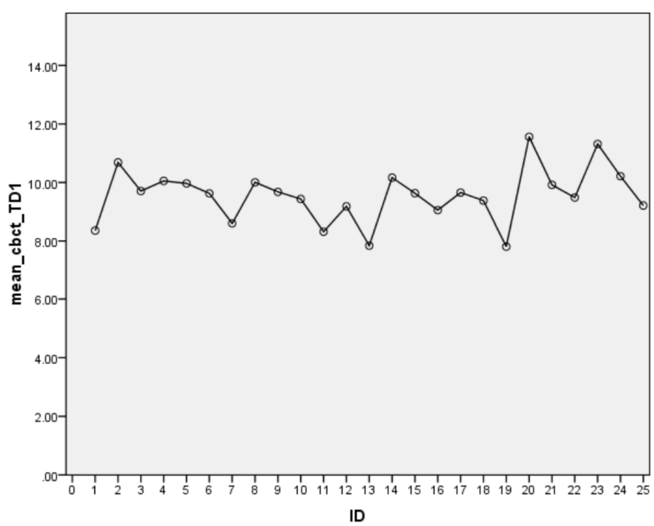
A total number of 25 patients of cervical cancer underwent planning CT scan, then weekly CBCT scan, therefore minimum of 5 CBCTs were performed for each patient. Total 25 planning CTs and 125 CBCTs were analyzed. Urinary bladder was contoured in all 125 scans by same radiation oncologist and bladder volume was measured. Also, the bladder measurements were taken in all three maximum dimensions; transverse, superoinferior, and anteroposterior diameter. All these parameters were compared with the planning CT scan, considering it as baseline.

The mean bladder volume of all 5 CBCTs in each of the 25 patients was calculated. Maximum mean bladder volume was 438.66 cc and minimum mean bladder volume was 96.02 cc Graph **1**. The mean bladder volume in all 125 CBCTs was 263.41 ± 110.174 cc.

As shown in Graph **2**, patients had maximum mean transverse diameter of 11.56 cm and minimum transverse diameter of 7.81 cm. The mean transverse diameter of bladder in all 125 CBCTs was 9.55 ± 0.923 cm. 52 % of patients (*n* = 13) fall in between mean range of 9 to 10 cm, while 48 % (*n* =12) patients extend beyond this mean. This shows that there is moderate inter fraction variation in the transverse bladder dimension among patients.

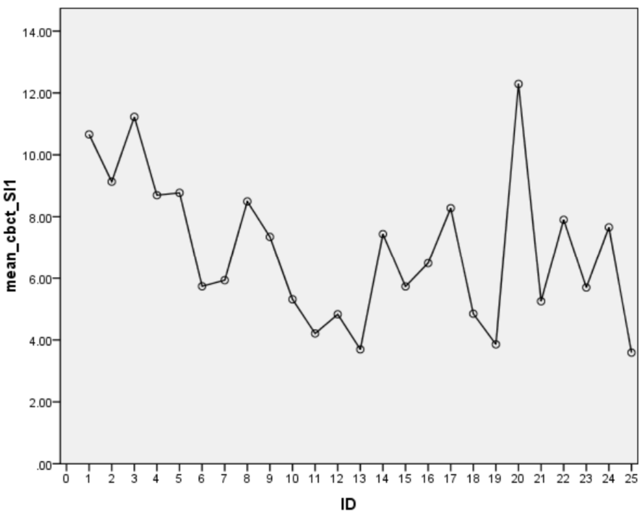


Graph 1: Mean bladder volume of 5 CBCTs of 25 patients.



Graph 2: Mean bladder transverse diameter of 5 CBCTs of 25 patients.

Graph **3** shows that maximum mean as observed in superoinferior dimension was 12.29 cm and minimum mean was 3.59 cm. The mean superoinferior diameter of all 125 CBCTs was 6.92 ± 2.387 cm. 56 % (*n* = 14) patients fall in mean range of 4 to 8 cm, while 44 % (*n* =11) patients extend beyond this mean. This shows that there is significant inter fraction variation in the supero inferior bladder dimension among patients.



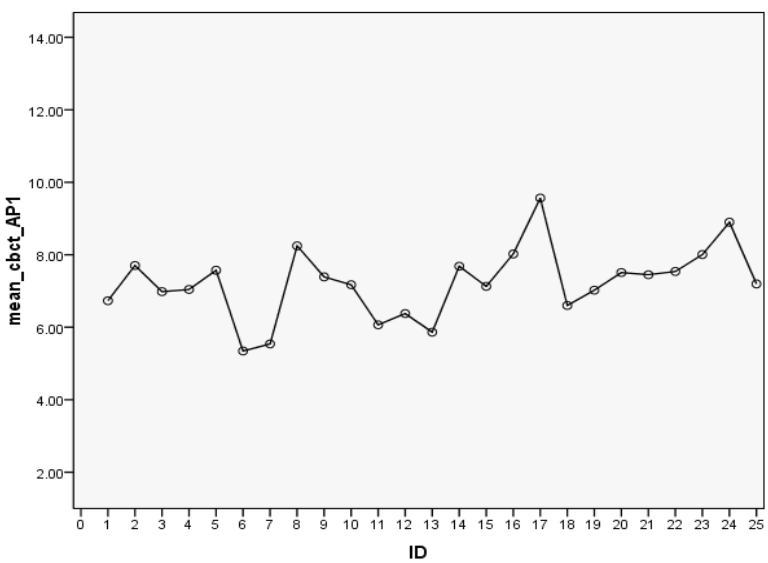
Graph 3: Mean bladder supero-inferior diameter of 5 CBCTs of 25 patients.

As shown in Graph **4**, the maximum mean anteroposterior diameter was 9.56 cm and minimum mean anteroposterior diameter was 5.34 cm. The mean anteroposterior diameter of all 25 CBCTs was 7.22 ± 0.967 cm. About 40 % (*n* =10) patients fall in mean range of 7 – 8.5 cm and 60 % (*n* =15) extend beyond this mean. This shows that there is moderate inter fraction variation in the antero posterior bladder dimension among patients.

When the mean CBCT bladder volumes of each patient were compared to their respective planning CT bladder volumes, using paired T test analysis, *P* was found to be insignificant (p 0.25). This signifies that the bladder filling was reproducible and consistent throughout the treatment, compared to the planning CT scans.

Similarly, the mean bladder diameter in all the three dimensions was calculated in all 5 CBCTs in each 25 patients. These means were compared to the bladder dimensions in all three directions, in baseline planning CT scans for each patient to test for significance. The mean supero inferior bladder diameter had significant variation from that of the planning CT as shown in Table **1**.

Table **2** shows the maximum and minimum mean diameters in each dimension, along with the most common mean range in 25 patients, along with number



Graph 4: Mean bladder antero-posterior diameter of 5 CBCTs of 25 patients.

Table 1: Mean ± Standard Deviation of Bladder Volume and Bladder Wall Movements in all 25 Patients in Planning CT and all 25 CBCTs

	Planning Ct Mean	Planning Ct Standard Deviation (Sd)	Cbcts Mean	Cbcts Standard Deviation (Sd)	P Value
Bladder Volume (Cc)	289.86	166.730	263.41	110.174	0.25
Transverse Diameter (Td) Cm	9.85	1.540	9.55	0.923	0.18
Supero-Inferior(Si) Cm	7.84	2.749	6.92	2.387	0.018
Antero-Posterior (Ap) Cm	7.27	1.415	7.22	0.967	0.48

Table 2: Bladder Diameter in 25 Patients in all Three Dimensions

	Maximum Mean Diameter	Minimum Mean Diameter	Range	Most Common Mean Range (Cm)	P Value Significant In	P Value
Transverse Diameter (Td) Cm	11.56	7.81	3.75	9 - 10	13/25	0.002
Supero-Inferior (Si) Cm	12.29	3.59	8.7	4 – 8	14/25	0.007
Antero-Posterior (Ap) Cm	9.56	5.34	4.22	7 – 8.5	10/25	0.005

of patients having significant *P* value calculated by chi square test, with maximum bladder wall dimension range in supero inferior direction.

DISCUSSION

Precision of delivering radiotherapy to the contoured target volumes in cervical cancer patients is affected by variation in bladder and rectal filling during radiotherapy [5]. Though bladder filling protocols have long been used to assure reproducible bladder filling, still there are various factors which can affect the above protocols. The most important ones are patient related factors like daily variation in hydration status prior to giving bladder filling protocol, timing of fluid intake, fluctuations in bladder capacity during treatments, anxiety or co morbidities like diabetes that can increase urgency leading to premature voiding. Other are treatment related factors like waiting time before treatment, longer set up times, adaptive planning especially when CBCT s show inadequate filling. There are certain physiological factors also like diurnal variations in urine production by kidneys and overfilled rectum which can compress bladder. Last are the institutional or logistical factors like consistency of staff guidance and protocol flexibility.

Though the bladder filling variations can never be controlled to null, still, in the present study, the attempt has been made to find out how much bladder filling variation occurs during radiotherapy and also, in which dimension the bladder filling is maximum. This can help us to decide whether in certain dimension, target volumes need to be given generous margins and where we require strict margins.

We conducted weekly CBCTs in our patients compared to daily CBCTs, in accordance with the institutional protocol. Though we did not analyze the dosimetric data to calculate radiation doses received by each CBCT, still we wanted to avoid unwanted radiation doses. Many centres [6,7,8] though are doing daily CBCTs. Wang *et al*. [9] in his study in 2008, found that the a patient can receive 17.7 mGy dose while doing CBCT pelvis, which is almost negligible compared to radical radiation dose (50–76 Gy).

Also, when the mean CBCT bladder volumes of each patient were compared to their respective planning CT bladder volumes, using paired T test analysis, *P* was found to be insignificant (p 0.25). This implies that reproducible bladder filling could be achieved while treating the patients on daily basis, and is comparable to planning CT bladder volumes.

In our study, the mean bladder volume in all 125 CBCTs was 263.41 ± 110.174 cc, ranging from maximum 438.66 cc to minimum 96.02 cc. The mean transverse diameter of bladder in all 125 CBCTs was 9.55 ± 0.923 cm. The mean superoinferior diameter of all 125 CBCTs was 6.92 ± 2.387 cm. The mean anteroposterior diameter of all 25 CBCTs was 7.22 ± 0.967 cm. The standard deviation is maximum in supero inferior direction and when compared to planning ct volumes, this variation is significant. This implies that while contouring the target volumes, we need to give generous margins along the supero inferior direction.

Yee *et al*. 2010 [6] analyzed bladder filling variation in 10 bladder cancer patients using daily CBCTs. In his study maximum shift was seen in anterior bladder wall with mean shift of -0.5 cm.

Another study conducted in 15 patients of bladder cancer by Fokdal *et al*. 2004 [10], found maximum bladder wall movements in anterior and cranial directions.

In our study also, bladder wall movements were studied in all three dimensions; transverse, supero inferior (longitudinal), and anteroposterior diameter. 13 of the 25 (52%) patients showed significant changes in transverse diameter followed by superoinferior diameter which showed significant changes in 14 of the 25 (56%) patients. In anteroposterior transverse diameter, only 10 of the 25 (40%) patients showed significant changes. Although the number of patients with significant changes was more in transverse diameter, variation was seen more in superoinferior diameter with a range of 8.7 cm as compared to transverse diameter which has range of 3.75 cm and anteroposterior diameter which has range of 4.22 cm as shown in Table **1**.

Jhingran *et al*. 2012 [8], implanted fiducial markers in 24 patients of carcinoma cervix and found maximum movements in anteroposterior direction, next in superior–inferior direction and least in the transverse direction. Mean diameter for 25 patients in our study was 9.55, 6.92, and 7.22 cm in transverse, supero inferior dimension and anteroposterior respectively. Standard deviation was 0.923, 2.387, and 0.967 cm in above directions respectively, and these results were consistent with above‑mentioned studies.

In a study by Shah *et al* 2019 [11], 26 patients with different pelvic malignancies had undergone twice wekly CBCTs. The mean bladder volume for 26 patients was 183.07 cc with standard deviation of 90.43 cc. The mean +/- standard deviation of transverse, anteroposterior and longitudinal diameter was 8.35+/-1.03, 6.69+/-1.05 and 5.59+/-1.79 cm. The study concluded wider margins in on the lateral side, and more liberal margins in anteroposterior dimension and longitudinal dimensions.

In a study by Nanda *et al* (2024) [12], a total of 90 CBCT scans were analyzed in 15 cervical cancer patients (6 CBCTs for each patient). The mean bladder volume for all 15 patients was 183.346 cc with a standard deviation of 107.66 cc (p value = 0.792). Maximum transverse, anteroposterior and craniocaudal diameter was 10.975 cm, 8.273 cm and 10.493 cm while minimum was 6.30 cm, 4.936 cm and 3.711 cm respectively. The mean standard deviation of transverse, anteroposterior and craniocaudal diameter was 8.634 cm +/- 1.153 cm, 6.088 cm +/- 0.908 cm and 5.38 cm +/- 1.69 cm respectively.

The results of our study were in concordance with those of above mentioned studies. However on studying the literature further, we found that most other studies [13-15] focused on dosimetric effects of bladder volume changes in IGRT of cervical cancer patients. This is one of the limitation of our study as studying the dosimetric impact on normal organ sparing and target volume coverage can justify the CTV to PTV margin design, and can help guide adaptive planning. But studying the dosimetric correlation with bladder filling variations is beyond the scope of this study

The other limitations of this study are small sample size and retrospective design. The most important constraint is weekly CBCTs done in our study compared to daily CBCTs done by most other studies, which can be a potential source of bias.

Our study shows that to decide margin reduction for target volumes during image‑guided radiation therapy (IGRT) in cervical cancers, and to avoid geographical miss, its important to understand the variations in bladder wall movements and also ensure adequate and reproducible bladder filling protocols [16,17]. Daily CBCT imaging though is ideal to achieve reproducibility, still if not feasible in routine setting, decision to go for weekly/twice/thrice weekly CBCTs should be based on institutional studies and protocols. This study showed considerable reduction of margin could be done on the lateral sides, as there is less displacement on transverse diameter and more generous margins should be considered in superoinferior dimension.

CONCLUSION

This retrospective study was done to analyze bladder filling variation which can occur, despite following a strict bladder filling protocol. The most significant variation was seen in superoinferior (longitudinal) direction, indicating the need of generous margins required in this direction, compared to the other two dimensions.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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