VOLUME-7, ISSUE-11, NOVEMBER-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Oncology

INTER FRACTION SET UP ERRORS AND ORGAN MOTION IN CARCINOMA RECTUM- ROLE OF IMAGE GUIDANCE

Dr Shailley A S

ABSTRACT

Introduction- New technological advances in radiation have its own limitations. We give large Planning Target Volume (PTV) margins to overcome set up errors and organ motion which in turn lead to more organs at risk toxicity. If there is quantification of set up errors and organ motion PTV margins can be reduced accordingly which is possible with image guidance. Here we are evaluating the role of image guidance by assessing bone shifts and interfraction urinary bladder motion in pelvic radiotherapy for Carcinoma Rectum.

Material and methods- Six patients of Carcinoma Rectum from December, 2014 to June, 2015 who gave consent for treatment with Image Guided Radiotherapy were taken for interfraction set up errors. 10 pre treatment CBCT scans per patient were analyzed. Values were registered on three principal axes, left-right(x), supero-inferior (y) and antero posterior (z) axes values for inter-fraction set up errors. Amongst organs at risk we have evaluated urinary bladder and assessed interfraction motion by the differences in bladder volume and translation of the bladder wall in three dimensions in comparison to the baseline PCT.

Results- Mean (standard deviation) bone shifts noted were 0.34± 0.26 cm, 0.34± 0.13 cm and 0.22 ± 0.10 cm in x, y and z axis respectively. There was an overall decrease in mean CBCT bladder volume compared to PCT bladder volume. However the difference between PCT mean (214.42±84.17) and CBCT mean (203.80±83.71) was not statistically significant (p=0.706). Maximum movements were seen in superior direction of bladder wall.

Conclusion- Prescribed PTV margins are able to cover set up errors and organ motion, however exceptional errors need to be addressed on time.

- During treatment patient should be periodically followed up and patients' dietary, bowel and bladder habits and weight loss should be observed and noted.

Alternate day CBCT is a good option especially patient with frequent change in bowel and bladder habits.

Adaptive strategies based on first and second week CBCTs should be undertaken.

The effect of organ motion on adjacent organs warrants further studies.

KEYWORDS : Apo-B, Andrographis paniculata and Syzygium polyanthum, dyslipidemia

INTRODUCTION

Rectal cancer along with colon constitutes 6.1% of total cancers and 9.1 % mortality. It is the third most frequent cancer in males all over the world. [1] Population based time trend studies show a rising trend in the incidence of Colorectal cancer in India. [2]

Radiation is an integral part of the treatment besides chemotherapy and surgery. New technological advances in radiation act as double edge sword i.e. if not delivered correctly may lead to appalling results due to its limitations. To overcome organ at risk toxicity we give restricted Planning Target Volume (PTV) margins and to overcome set up errors and organ motion we need to give large PTV margins which in turn lead to more toxicity for normal structures in the treatment field. We have to find a mid way out of the two. That emphasizes the need for randomized data in our set of patients for organ motion and set up errors considering patient variables along with technical issues.

The small bowel, large bowel and urinary bladder are the most important organs at risk (OAR) in pelvic radiation. Geographical miss is another important flaw to be considered. Numerous studies are quoted till date of set up errors and bladder motion separately in pelvic malignancies on outcome. [3-5] These parameters have been looked in totality with set up errors and organ motion in every patient to decide patient specific PTV margin in our study.

MATERIAL AND METHODS

Patient Selection

Prospective single institution evaluation study of 7 carcinoma rectum patients from 19 to 75 years of age for interfraction set up errors and organ motion. Patient having confirmed histopathological diagnoses including all stages except metastatic disease from December, 2014 to June, 2015 and underwent External beam radiotherapy (EBRT) by IGRT technique were included in the study.

Immobilization Protocol

For each patient a custom immobilization cast (orfit industries, Belgium) was fabricated in supine position covering abdomen and pelvis and indexed on the treatment couch. Knee rest and arm rest were used based on patient comfort. Moving lasers were used to assist in set up.

Ct Simulation

For all patients planning CT (PCT) was done on dedicated CT simulator Machine (24 Slice Somatom Sensation Open with wide bore (82cm) with software version of Siemens CT 2007S). The scans were acquired from the top of L1 to 3cm below ischial tuberosity, with a slice thickness of 3 mm. Bladder protocol was followed with all patients were instructed to void urine and drink 300 ml of water for reproducible bladder filling 40-50 minutes before scanning (PCT scan) and treatment. At time of planning bowel distension was assessed, if more than usual then appropriate measures like laxatives were used and subsequently planned.

treatment planning, prescription, implementation and verification

After transferring the PCT data sets were transferred to Eclipse treatment planning system (Version 10.0 of Varian Medical System, Palo, Alto, CA), Gross tumor volume (GTV) and clinical target volume (CTV) were taken as per guidelines. [6] PTV was the margin added for set-up error and organ motion. PTV was the CTV expanded by margins as per our institutional protocol, 0.5cm axially and 1cm in cranio-caudal direction.

Dose prescribed was 45Gy in 25 fractions over 5 weeks with simultaneous integrated boost (SIB) to gross disease up to 50Gy. VMAT plans were generated in the Eclipse Treatment Planning System (version 10) using 6MV photons. Anisotropic Analytical Algorithm (AAA v 10) was used. After plan evaluation, treatment commencement was done on Novalis Tx Linear Accelerator. For treatment verification CBCT were acquired on first 3 days of treatment and twice weekly thereafter, at least 10 pre treatment CBCT scans were taken per patient.

Organ Motion And Set Up Error Quantification

The patients' planning CT and the current CBCT scan were registered using the bony anatomy and setup error was calculated. Both bone auto fusion followed by manual bone match was done

and after soft tissue matching (set up + organ motion) rectal filling and bladder filling was noted simultaneously and necessary couch correction (online correction) was applied. Inter-fraction set up error values were registered for three principal axes, in left-right(x), supero-inferior (y) and antero posterior (z) axes. The axes used for these shifts define positive shifts from anterior to posterior, right to left, and superior to inferior.

Bladder volume was calculated by outlining it on every CBCT image for each patient. Differences in bladder volume and translation of the bladder wall in three dimensions in comparison to the baseline PCT was assessed for interfraction motion. Cranio-caudal and antero-posterior displacements was assessed in PCT mid-line sagittal imaging and lateral displacements by mid-bladder image in coronal plane.

Statistical Methods

The overall set up error was calculated for individual patients based on CBCT imaging. For the magnitude of set up error values, absolute values of position errors were considered for calculation. Statistical analysis was performed using Wilks'Lambda test for intra-patient variation while Huynh Feldt test was used for inter-patient variation among 7 subjects. Dunett T test was used for urinary bladder volume and rectal diameter variation. Discrete variables are reported as frequency, proportion and continuous variables as mean +/- standard deviation (SD). All statistical analysis were done using SPSS (version17) software.

Results and observations

Six patients of Carcinoma Rectum in the age group of 30 to 65 years were enrolled with the mean age of 47 years. All cases were stage III and planned for preoperative chemo- radiation.

Bone Shifts

Mean bone-shifts were calculated and given in table 1 in x (right-left), y (supero-inferior) and z (antero-posterior) axes (Table 1). Mean bone shifts were noted within range of 0 to 2.3cms. In one patient there was unexpected bone shift of 2.3cm in x axis, so median was taken and variability was analyzed across subsequent CBCT of each carcinoma rectum patients. Maximum mean shift was seen in y axis and x axis.

Table 1: Mean, median and range of bone shifts along x(right-left),y(supero-inferior) and z(antero-posterior)axes in 6 carcinoma rectum patients over 60 CBCTs

CBCT No	X	Range	Median	Y	Range	Median	Z	Range	Median
1	0.22 ± 0.18	0-0.4	0.25	0.33 ±0.36	0.1-1.0	0.15	0.18 ± 0.12	0-0.3	0.2
2	0.20 ± 0.15	0.1-0.5	0.15	0.32 ±0.26	0-0.6	0.3	0.20 ± 0.11	0.1-0.4	0.2
3	0.38 ± 0.38	0.1-1.1	0.3	0.55 ±0.42	0-1.0	0.55	0.25 ± 0.10	0.1-0.4	0.25
4	0.05 ± 0.08	0-0.2	0	0.30 ±0.19	0.2-0.5	0.3	0.20 ± 0.23	0-0.6	0.15
5	0.23 ± 0.23	0-0.5	0.25	0.37 ±0.15	0.2-0.5	0.4	0.15 ± 0.15	0-0.4	0.15
6	0.27 ± 0.20	0.1-0.6	0.2	0.47 ±0.22	0.1-0.8	0.45	0.20 ±0.14	0-0.4	0.2
7	0.38 ±0.38	0-1.2	0.3	0.25 ±0.23	0.1-0.7	0.15	0.17 ±0.20	0-0.4	0.1
8	0.41 ±0.35	0.1-1.1	0.34	0.25 ±0.23	0-0.7	0.15	0.27 ± 0.16	0-0.5	0.25
9	0.35 ±0.59	0.1-1.7	0.3	0.37 ±0.44	0-1.2	0.25	0.32 ± 0.17	0-0.5	0.2
10	0.50 ± 0.82	0.2-2.3	0.3	0.23 ±0.15	0-0.4	0.2	0.22 ± 0.15	0-0.4	0.2
Mean ± SD	0.34 ± 0.26 cm			0.34± 0.13 cm			0.22 ± 0.10 cm		

Organ motion

Urinary bladder movement was measured in anterior, posterior, right, left, superior and inferior directions with respect to baseline planning CT scan in carcinoma rectum (Table 2& Figure 1). Maximum movements were seen in superior followed by anterior direction and minimum movements was in inferior direction.

Patient No	Anterior	Posterior	Right	Left	Superior	Inferior
1	0.46	0.47	0.76	0.38	1.18	0.31
2	0.70	0.39	0.35	0.32	0.98	0.42
3	0.41	0.42	0.37	0.09	0.99	0.05
4	0.78	0.12	0.08	0.08	0.86	0.12
5	0.15	0.01	0.03	0.05	0.19	0.03
6	0.25	0.26	0.06	0.14	0.74	0.00
Mean ± SD	0.46± 0.25	0.28 ± 0.18	0.28 ±0.28	0.17±0.14	0.82±0.34	0.15±0.17

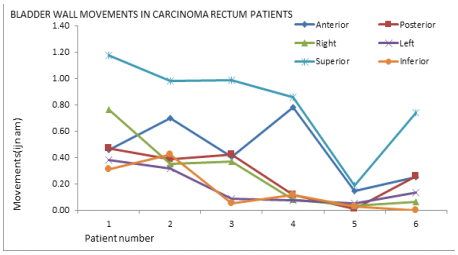

Fig.1: Urinary bladder mean movement(deviation) in three axes(anterior, posterior ,right ,left ,superior and inferior) in carcinoma rectum patients (6 patients) over 60 CBCTs.

We also did CBCT-wise analysis of these patients for measuring volume in each subsequent CBCT. Following were the variation in urinary bladder volume over 60 CBCTs of carcinoma rectum patients.

Table 4: Urinary bladder volume in carcinoma rectum patients (6 patients) over planning CT and 60 CBCTs.

Patient no	PCT	1	2	3	4	5	6	7	8	9	10	Mean ± SD
1	164.76	87.66	177.14	100.57	197.91	110.95	76.89	63.37	50.82	56.72	71.45	99.35
2	113.20	195.97	152.43	227.17	152.67	150.34	115.68	134.81	109.82	151.53	101.85	149.23
3	323.42	185.35	249.52	169.28	343.44	193.76	125.53	154.8	216.75	203.32	219.99	206.17
4	252.57	302.81	373.36	295.15	201.99	366.31	132.37	474.01	296.43	225.3	265.24	293.30
5	147.86	152.57	179.68	269.33	187.55	110.85	168.41	194.1	129.82	126.32	117.66	163.63
6	284.74	251.18	310.55	211.98	349.65	371.15	257.27	447.93	373.2	269.24	269.24	311.14
Mean ± SD	214.42±84.17	PCT mean (214.42±84.17) Vs Mean CBCT (203.80±83.71) p=0.706 Not significant										203.80±83.71

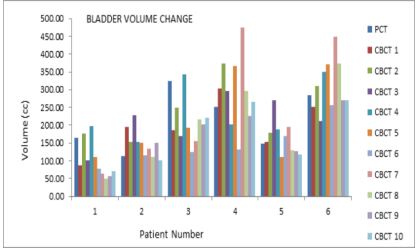

Fig 2: Urinary bladder volume in carcinoma rectum patients (6 patients) over 60 CBCTs.

Four patients had increase in mean CBCT volume. There was an overall decrease in mean CBCT bladder volume compared to PCT bladder volume. However the difference between PCT mean (214.42±84.17) and CBCT mean (203.80±83.71) was not statistically significant(p=0.706)(table 4).

DISCUSSION

We assessed bone shift in carcinoma rectum patients separately, mean (standard deviation) bone shifts noted were 0.34 ± 0.26 cm, 0.34 ± 0.13 cm, 0.22 ± 0.10 cm in x, y and z axis respectively(Table 2,figure 1). A study by Tournel et al analyzed ten patients of carcinoma rectum who were treated with tomotherapy and underwent MVCT scanning before and after 10 treatments. Based on bony landmarks, movement of patients during treatments was limited to 0.245 cm, 0.199 cm, and 0.109 cm in the lateral, longitudinal, and vertical direction, respectively.[7] Maximum shifts were seen in right-left direction(x axis) followed by supero-inferior direction. In our study we had maximum shifts in both right-left direction and supero-inferior direction. Weight loss and cast loosening may be the probable cause of these shifts.

There was an exceptional error of 2.3 cm in last CBCT of one patient of carcinoma rectum in right direction, probably due to skin mark fading as reported by technologist. The other probable reason of this is weight loss which is more frequent in carcinoma rectum cases due to altered bowel habits and diarrhea on and off leading to cast loosening and subsequent set up errors.

Other factors that could result in set-up error include the type of immobilization used, laser alignment and localization, machine factors, expertise and experience of therapists, and patient anxiety and co-operation.

In order to improve bladder volume consistency, many study fixed the water drinking protocol as ours by specifying the volume of liquids to be consumed and timing of liquid consumption before treatment. [8,9] Although we didn't quantify impact of bladder filing on adjacent organs but bladder filling can influence adjacent organ motion e.g. bowel, uterus, cervix and prostate.

These variations in bladder filling were most probably due to pre-hydration status. If the patient is dehydrated, then bladder protocol had shown reduced volume comparatively. Also on the day of concurrent chemotherapy when the patient is hydrated with IV fluids, there is expected increase in volume of bladder. Thus even after setting bladder protocol, it occasionally needs to be individualized. Patient should be well hydrated and preferably radiation should be given at same time everyday to minimize volume variation.

In a study by Mcbain et al, the dominant direction of bladder expansion was primarily in the superior (cranial) and secondarily in the anterior (forward) direction. [10] Studies on bladder wall movements in pelvic malignancies except carcinoma bladder are scarce. In another study by Yee et al, they analyzed 262 CBCT images were obtained from 10 bladder cancer patients. [11] There was maximum shift in anterior wall which was statistically significant. Maximum movements were seen in superior and minimum movements were seen in inferior wall which is in agreement with above studies.

Our set up errors and organ motion are within our prescribed PTV but protocol need to be individualized in certain patients.

Conclusion Imaging is important during radiotherapy treatment for monitoring and evaluation. Our bone match results are within prescribed institutional PTV margins but exceptional errors need to be addressed on time. Organ motion i.e. bladder, mean movements are within our prescribed PTV margins, but protocol for these need to be individualized and adaptive strategies are proposed based on first and second week CBCTs. Patient follow up during treatment is must and should be frequent to assess patients dietary, bowel and bladder habits and weight loss during treatment. Frequent CBCT required for patients with altered bowel and bladder habits. For PTV margin reduction, we require further studies to quantify the effect of organ motion on adjacent organs.

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