International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 9; Issue 01 (B); January 2020; Page No.20949-20953
DOI: http://dx.doi.org/10.24327/ijcar.2020.20953.4105

Research Article

A STUDY OF IMPACT OF METHODS OF DELINEATION OF HOLLOW ORGANS ON DOSE VOLUME PARAMETERS IN PROSTATE CANCER INTENSITY MODULATED RADIATION THERAPY

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ARTICLE INFO

Article History:
Received 24th October, 2019
Received in revised form 19th November, 2019
Accepted 25th December, 2019
Published online 28th January, 2020

Key words:

IMRT (Intensity Modulated Radiation Therapy), prostate cancer, bladder wall, rectal wall

ABSTRACT

Objectives: In irradiation of pelvic malignancies by IMRT (Intensity Modulated Radio Therapy) technique, bladder and rectum toxicities have been a major concern. Rectum and bladder are routinely being contoured as solid organs. However, there is inclusion of the wastes also which leads to incongruity in the evaluation of dose volume parameters. The intention of this study is to evaluate the differences in dose volume parameters of prostate cancer IMRT depending on the method of contouring of bladder and rectum.

Materials and Methods: In this retrospective study, we included 50 patients of carcinoma prostate treated with IG- IMRT (Image Guided- Intensity Modulated Radiotherapy) at our institute. We delineated bladder and rectal walls and compared the dose volume parameters of these solid organs with their walls.

Statistical analysis: Paired t-test has been used for statistical analysis.

Results: This study revealed statistically significant differences in the dose volume parameters used to assess the acute and chronic toxicity of bladder and rectum, when corresponding walls were delineated, which received higher doses as compared to the solid organs.

Conclusions: The results of this study have been well supported by the available literature in the sense that method of contouring bladder and rectum may produce significant differences in the estimation of doses received by these hollow organs which may in turn lead to inaccurate assessment of the acute and chronic toxicities pertaining to these OARs (Organ At Risk).

INTRODUCTION

During the past few decades, there has been a rapid progress in the field of Radiation Oncology and the advent of Intensity Modulated Radiotherapy (IMRT), which was further augmented by Image Guidance, has allowed dose escalation beyond levels feasible with previous techniques. Several dose escalation studies have shown improved biochemical control rates for prostate cancer. However, this therapeutic gain has been associated with the morbidity of Organ At Risk (OAR) in proximity like bladder and rectum[1]. Both these OARs are hollow tubular structures but they are contoured as solid organs and the predictive value of the resultant DVH is questionable. However, radiobiologically the critical structure is the wall of these organs and not the contents (urine and faeces). Hence, contouring these organs as solid organs can lead to inaccurate estimation of the risk of adverse events. ICRU 83 has also emphasized the importance of delineating the wall rather than the whole organ in cases of tubular structures[2]. In this study, we have delineated rectal and bladder wall and compared the Dose Volume Histogram (DVH) of these structures to rectum and bladder, drawn as solid organs.

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MATERIALS AND METHODS

Patient selection

This is a retrospective observational study in which fifty patients of Carcinoma prostate diagnosed from 2012 to 2016 and treated with Radical Radiotherapy at our institute have been included. Inclusion criteria were- histologically proven adenocarcinoma prostate, whole pelvis irradiation with IMRT. Exclusion criteria were metastatic disease, prior history of pelvic irradiation.

CT simulation

All patients had undergone Radiotherapy planning CT scans performed with a helical CT scanner (Phillips Brilliance 64) in supine position with a slice thickness of 2 mm. Institutional bladder filling protocol was followed in which the patients were instructed to void the urine, 40 minutes prior to CT scan and then drink 600ml of water. No routine laxatives were advised unless the patient had complaint of constipation. Patients were simulated in supine position and were

immobilized using a 4 clamp abdomino-pelvic thermoplastic mould (ORFIT^{TM}). The CT image dataset was registered in the Treatment Planning System (ECLIPSE^{TM} version 8.6.15, Varian Medical Systems, USA) and these images were used for contouring, planning and evaluation.

Treatment planning

Clinical Target Volume encompassed prostate, seminal vesicle and pelvic lymph nodes. Planning Target Volume (PTV) was generated with isotropic margins of 5 mm except in supero-inferior direction (8mm). Rectum and bladder were delineated as solid organs according to RTOG contouring guidelines. Other OARs were bilateral femoral heads, bowel bag and genitalia. A dose of 76Gy/38fr for the PTV (prostate and seminal vesicles) and 62.7Gy/38fr to the pelvic lymph nodes was prescribed. Patients were treated on a dual energy linear accelerator (9& 15 MV VARIAN ix) using 9 field dynamic IMRT with coplanar beams at 40 degree interval. Prescribed dose covered 95% of the PTV and the OAR doses were kept within tolerance limits recommended by QUANTEC.

Delineation of bladder and rectal walls

Rectal and bladder walls were delineated in retrospect in all the selected patients. An inside margin of 3 mm was given to both the organs (Fig I a, b, c). The resultant new DVH was analyzed to compare the dose received by both the OARs drawn as solid organs as well as walls.

Various parameters analyzed were

Rectal and rectal wall- Maximum dose, mean dose, V30, V50, V60, V65, V70, V75
Bladder and bladder wall- Maximum dose, Mean dose, V65, V70, V75

Statistical analysis

All the data was entered in the Microsoft Word Excel sheet 2007 version and the statistical analysis was performed using SPSS software version 20 for the descriptive analysis and statistical tests of significance. The mean and percentages were calculated for each clinical parameter and paired t test of statistical significance was used to compare mean and maximum doses received by bladder & bladder wall and rectum & rectal wall as well as the volumes exposed to different doses. Statistical significance was set at $p< 0.05$.

Table I Comparison between mean and maximum doses of Rectum & Rectum Wall and Bladder & Bladder Wall (Paired t- test)

Variables	Mean	SD	t-value	p-value	Significance
Rectum Mean	39.59	5.256	-7.248	0.000	S
Rectum Wall Mean	41.45	5.338			
Rectum Max	75.47	3.608	-1.260	0.213	NS
Rectum Wall Max	76.52	7.234			
Bladder Mean	47.45	8.991	-10.248	0.000	S
Bladder Wall Mean	51.38	9.301			
Bladder Max	77.55	7.464	-1.363	0.179	NS
Bladder Wall Max	78.67	9.730			

($p \leq 0.05$ – Significant, CI = 95 %)

Table II Comparison between Rectum and Rectum Wall at between different doses (Paired t- test)

RECTUM		Mean	SD	t-value	p-value	Significance
V30	Rectum	64.10	12.03	-1.759	0.085	NS
	Rectum Wall	65.08	11.28			
V50	Rectum	34.69	8.330	-8.941	0.000	S
	Rectum Wall	39.41	7.800			
V60	Rectum	23.57	8.161	-9.765	0.000	S
	Rectum Wall	30.19	7.012			
V65	Rectum	16.66	6.509	-13.564	0.000	S
	Rectum Wall	24.30	8.040			
V70	Rectum	8.40	5.635	-13.170	0.000	S
	Rectum Wall	15.24	8.212			
V75	Rectum	1.57	2.996	-3.733	0.000	S
	Rectum Wall	2.75	4.846			

($p \leq 0.05$ – Significant, CI = 95 %)

Table III Comparison between Bladder and Bladder Wall at between different doses (Paired t- test)

BLADDER		Mean	SD	t-value	p-value	Significance
V65	Bladder	29.10	10.29	-10.834	0.000	S
	Bladder Wall	37.16	11.60			
V70	Bladder	22.24	8.802	-10.626	0.000	S
	Bladder Wall	29.60	10.08			
V75	Bladder	13.10	7.146	-11.261	0.000	S
	Bladder Wall	20.30	7.918			

($p \leq 0.05$ – Significant, CI = 95 %)

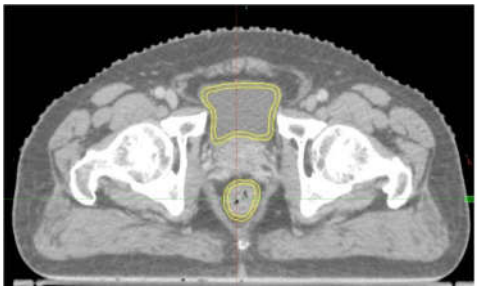

Fig 1(a)

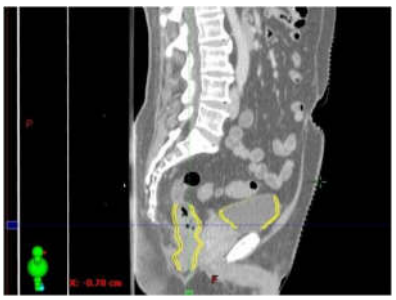

Fig I (b)

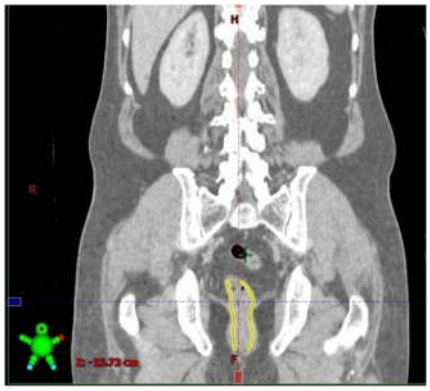

Fig I (c)

Fig I (a, b, c) showing axial, sagittal and coronal sections of CECT Lower Abdomen representing bladder and rectal wall contouring

Fig II Graph showing comparative analysis of dose volume parameters of bladder and rectum with bladder and rectal walls respectively

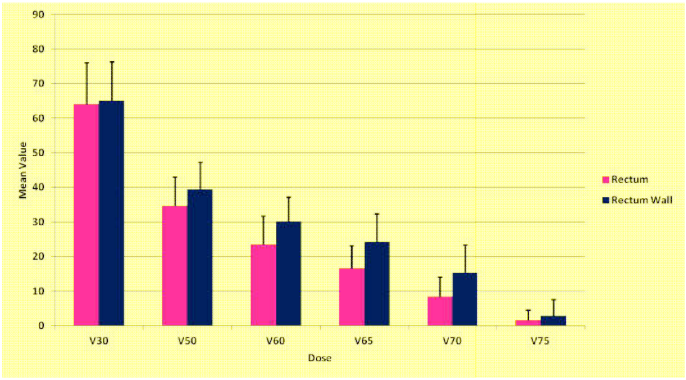

Fig III Comparison of dose volume parameters of rectum and rectal wall

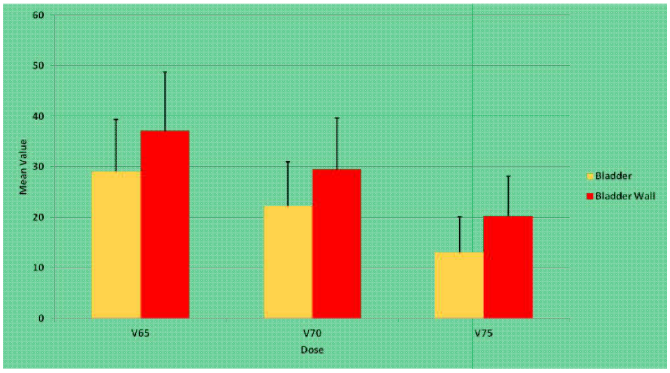

Fig IV Comparison of dose volume parameters of bladder and bladder wall

RESULTS

The mean age of the patients was 70.4 (44-87 years).
The dose volume parameters of rectum and bladder versus their respective walls are as follows

Rectum and rectal wall

The average of mean doses to rectum was 39.59 Gy and that received by rectal wall was 41.45 Gy. The average of maximum doses to rectum and rectal wall were found to be almost similar and were 75.47 and 76.52 respectively, the difference being statistically insignificant (Table I and Fig II).
For rectum drawn as solid organ, mean dose rectal dose volume for endpoints V30, V50, V60, V65, V70, V75 were 64.1%, 34.69%, 23.57%, 16.66%, 8.4%, 1.57% respectively. For rectal wall, mean rectal dose volume for V30, V50, V60, V65, V70, V75 were 65.08%, 39.41%, 30.19%, 24.3%, 15.24% and 2.75% respectively (Table II and Fig III). V50, V60, V65, V70, V75 mean outcomes were significantly higher for rectal wall but the difference of V30 was not statistically significant.

Bladder and bladder wall

The mean dose to bladder was 47.45Gy and that to the bladder wall was 51.38 Gy. The maximum dose to bladder and bladder wall was almost identical, that is, 77.5 Gy and 78.67 Gy respectively (Table I and Fig II).

Outcomes of mean bladder dose volume for end points V65, V70, V75 were 29.1%, 22.24% and 13.1% respectively. Utilizing the bladder wall delineation method, the mean V65, V70 and V75 Gy were 37.16%, 29.6% and 20.3% respectively. V65, V70 and V75 mean outcomes were significantly higher with bladder wall contouring method (Table III and Fig IV).

DISCUSSION

Over the past few decades, the evolution of radiotherapy techniques and dose escalation has translated into better treatment outcomes in carcinoma prostate. However, increased dose to the prostate can result in higher doses to the surrounding normal structures like bladder and rectum and thereby increasing the chances of acute and late side effects. For solid organs like liver, parotid and lungs, DVH (Dose Volume Histogram) is used to represent dose volume distribution. However, this concept could not be as such extrapolated to hollow organs[3]. For an accurate estimation of the doses delivered to the bladder and rectum, it is essential to delineate the walls because the use of solid organs generated from the outer surface contours will include the dose to urine and faeces in the DVH, thus obscuring the dose to bladder wall and rectal wall tissue. Harsolia et al reported that an analysis of the bladder wall volume correlates more accurately with the chronic genitourinary toxicity than the absolute solid volume of the bladder[4]. It is a challenging task to delineate only the functional tissue between outer and inner surface as the inner walls of these hollow organs is not clearly visualized on CT scans. Two methods have been suggested for delineating the walls- one is the uniform contraction of 3 mm from the outer surface and other is manual delineation of the inner and outer wall. Guckenberger et al demonstrated that method of delineation significantly influences the dose representation in DVH and the delineation of the walls results in superior sparing of the hollow organs[5]. Different methods of contouring may modify dosimetric results and in turn leading to misinterpretation of chronic toxicities. Rasmussen et al demonstrated that the thickness of rectal wall as measured by ultrasound was found to have a median of 2.6 mm[6]. In our study, we delineated bladder and rectum as solid organs as well as using a uniform contraction of 3 mm from the outer wall. Wang et al also studied the effect of rectal volume delineation methods on dose constraints end points in the treatment of prostate cancer treated with IMRT. They identified clear differences in rectal DVH while using two methods i.e. ERV (Entire Rectal Volume) or rectal wall. They also found that these differences are also dependent upon prescribed dose and rectal volume and/or rectal length[7].

Peterson et al identified potential dose constraints for anterior rectal wall which further help in minimizing the risk of rectal adverse events. Anterior rectal wall is at greatest risk of injury as it lies closest to the target volume and receives the highest dose of radiation[8]. The effect of bladder and rectum delineation methods on DVH has also been studied by Gomez

et al. Their analysis showed statistically significant differences in the main parameters used to assess the risk of late toxicity of these structures and this difference was found to be more important in case of inverse planning. Higher doses were received by the walls as compared to the solid organs. They found that at mid dose levels (40Gy in rectum and 45Gy in bladder), the volume percentage of the organ receiving a particular dose is higher in cases of walls than in solid organs[9]. In our study also, we found that the mean doses received by the walls of these organs was significantly higher than the solid organs. Also, the volume percentages receiving important doses are also significantly higher for the organs when they were drawn as walls as compared to solid organs. The maximum doses received were same for the walls as well as solid organs, and this finding corroborated with that of Gomez et al. The reason is attributed to the fact that higher doses are close to the PTV which is near to the anterior wall of the rectum and posterior wall of bladder. Increase in the relative volume irradiated at a dose level of 60Gy is 28% for the rectal wall and 27.6% for the bladder wall as compared to the solid organs. At 70 Gy, it was 81.4% for the rectal wall and 33% for the bladder wall and it was 75.15% for rectal wall and 54.9% for the bladder wall at dose of 75Gy. These values carry dosimetric implication in the sense that volume of bladder and rectum receiving doses between 50 and 80 Gy is a remarkable interpreter of chronic cystitis and proctitis. In the low dose area, the difference between rectum and rectal wall was found to be insignificant.

Although, radiation cystitis and proctitis are infrequent but if they occur, they deteriorate the quality of life of the patients. A variety of factors have been studied to identify the high risk group of patients such as diabetes, previous surgery, age, preexisting anorectal dysfunction [10,11,12] androgen deprivation therapy etc. Apart from these non modifiable risk factors, a clear relationship exists between irradiated volumes (higher values of V50, V60, V65, V70) and risk of late rectal toxicity [13]. Several authors have also reported correlations between moderate dose region and late rectal toxicity. Jackson et al reported a correlation between late bleeding and the volume irradiated at moderate dose (40-50Gy)[14]. Fiorino et al also reported a correlation between intermediate dose region (50-60Gy) and rectal toxicity[10]. Ishiwaka et al reported a relationship between V10-72 and grade 1 toxicity and a significant correlation between late bleeding and volume irradiated at moderate dose (40-50 Gy)[15].

All the above mentioned studies emphasized the significance of irradiated volumes and late genitourinary toxicity. To reduce the burden of long term morbidity and to improve the quality of life of the patients, in addition of respecting the dose constraints, we need to do precise evaluation of the dose volume parameters.

This study was done to evaluate the differences in the dose volume parameters of the solid organs and their walls in irradiation of prostate carcinoma and a significant statistical difference have been found between the same. Some prospective studies including larger number of patients will further authenticate this study.

Acknowledgements

We appreciate the support of Radiation Physics and technologists team in this work and would like to thank Dr Geetika Arora for assisting in the statistical analysis.

References

1. **Al-Mamgani A**, van Putten WL, **Heemsbergen WD**, Van Leenders, Slot A, Dielwart MF, Incrocci L et al. Update of Dutch multicenter dose escalation trial of radiotherapy for localized prostate cancer. Int J Radiat Oncol Biol Physics, 2008; 72 (2): 980-8.
2. International Commission on Radiation Units and Measurements. ICRU report 83: prescribing, recording and reporting intensity modulated photon beam therapy (IMRT). J ICRU 2010: 10 (1).
3. Susan L Tucker, Lei Dong, Rex Cheung, Jennifer Johnson, Radhe Mohan, Eugene H Huang et al. Comparison of Rectal Dose Wall Histogram versus Dose Volume Histogram for modeling the incidence of Late rectal bleeding after Radiotherapy. Int J Radiat Oncol Biol Physics; 60(5): 1589-1601.
4. Harsolia A, Vargas C, Yan D, Brabbins D, Lockman D, Liang J et al. Predictors for chronic urinary toxicity after the treatment of prostate cancer with adaptive three-dimensional conformal radiotherapy: dose-volume analysis of a phase II dose-escalation study. *Int J Radiat Oncol Biol Phys*. 2007;69(4):1100–1109.
5. Matthias Guckenberger, Jurgen Meyer, Kurt Baier, Dirk Vordermark, Michael Flentje. Distinct effects of rectum delineation method sin 3D conformal vs IMRT treatment planning of prostate caner. Radit Oncol 2006; 1:34.
6. Rasmussen SN, Riis P: Rectal wall thickness measured by ultrasound in chronic inflammatory diseases of the colon. *Scand J* Gastroenterol 1985, 20(1):109-114.
7. Tony J C Wang, Chi Zhang, Ying Wei, David P Horowitz, Eileen P. Connolly, Simon K Chang et al. Comparison of effect of rectal volume delineation methods on dose constraint endpoints in the treatment of prostate cancer with intensity modulated radiotherapy. J Radiat Oncol 2013; 2: 303-308.
8. Jennifer L. Peterson, Steven J. Buskirk, Michael G. Heckman, Nancy N.Diehl, Johnny R.Bernard Jr, Katherine S.Tzou. Image-guided intensity-modulated radiotherapy for prostate cancer: Dose constraints for the anterior rectal wall to minimize rectal toxicity. Medical Dosimetry; 2014: 12-17.
9. Laura Gomez, Carlos Andres, Antonio Ruiz. Dosimetric impact in the dose-volume histograms of rectal and vesical wall contouring in prostate cancer IMRT treatments. Reports of Practical Oncology and Radiotherapy, 2017; 22: 223-230.
10. Fiorino C., Fellin G., Rancati T., Vavassori V., Bianchi C., Casanoca Borca V. Clinical and dosimetric predictors of late rectal syndrome after 3D-CRT for localized prostate cancer: preliminary results of a multicenter prospective study. Int J Radiat Oncol Biol Phys. 2008; 70(4):1130–1137.
11. Herold D.M., Hanlon A.L., Hanks G.E. Diabetes mellitus: a predictor for late radiation radiation morbidity. Int J Radiat Oncol Biol Phys. 1999; 43:475–479.

12. O'Brien P.C. Radiation injury of the rectum. Radiother Oncol. 2001; 60:1–14.
13. Fellin G., Fiorino C., Rancati T., Vavassori V., Baccolini M., Bianchi C. Clinical and dosimetric predictors of late rectal toxicity after conformal radiation for localized prostate cancer: results of large multicenter observational study. Radiother Oncol. 2009;93:197–202.
14. *Jackson A, Skwarchuk MW, Zelefsky MJ, Cowen DM, Venkatraman ES, Levegrun S, Burman CM et al. Late rectal bleeding after conformal radiotherapy of prostate cancer. II. Volume effects and dose-volume histograms. Int J Radiat Oncol Biol Phys. 2001; 49: 685-698.*
15. Ishikawa Y, Kadoya N, Matsushita H, Sugawara T, Kubozono M, Rei Umezawa et al. (2014) Dose–Volume Constraints in Rectum in Patients with Prostate Cancer after 74-Gy 3-Dimensional Conformal Radiotherapy. J Radiol Radiat Ther 2(2): 1032

How to cite this article:

Prekshi Chaudhary *et al* (2020) 'A Study of Impact of Methods of Delineation of Hollow Organs on Dose Volume Parameters in Prostate Cancer Intensity Modulated Radiation Therapy', *International Journal of Current Advanced Research,* 09(01), pp. 20949-20953. DOI: http://dx.doi.org/10.24327/ijcar.2020. 20953.4105

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