ORIGINAL ARTICLE

Study of Variation of dose Due to Interfraction Organ Movement in Interstitial Brachytherapy: A Single Institute Experience

Shikha Dhal, Sumit Goyal, Harshvardhan Reddy, Ankita Parikh, Sonal Patel Shah, U. Suryanarayana
Department of Radiation oncology, Gujarat Cancer and Research Institute, Ahmadabad, Gujrat, India

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Shikha Dhal

ABSTRACT

Introduction: Concurrent chemo-radiation is the main treatment in locally advanced cervical cancer. The change of bladder and rectum volume may lead to change in the positions of these structures and target volume during MUPIT implant which may lead to variation in dose to the organ at risk and target.

Materials and Methods: Ten patients of gynecological malignancy were included. MUPIT template was positioned under anesthesia. CT scan was done for the contouring of bladder, rectum, and target and for planning purpose which generates plan (P1). CT scan was repeated before the third fraction of the treatment (CT2). The resultant plan (P2) was analyzed qualitatively and quantitatively.

Results: Bladder volume variations of 88.18% to -68.15% were noted. This change in volume lead to differences in the maximum dose in bladder between fractions. The maximum dose variation ranged from 62.53% to -21.49%. The rectal volume variation ranges 11.71% to -46.20% due to the rectal filling. High variation in maximum dose to the rectum were observed which might be due to rectal filling. CTV volume is increased by 19.48% while in other by 19.05% and in all other patients the volume is decreased. CTV volume maximum decreased by 30.54% which might be due to decrease in edema developed during procedure. The volume variation in CTV is in range of19.48% to -30.54%.

Conclusion: It is proposed that re-planning using repeat CT scan is required before third fraction implementation.

INTRODUCTION

In India, cervical cancer is the most common female related cancer followed by cancer breast. The current estimates indicate approximately 132,000 new cases diagnosed and 74,000 deaths annually in India, accounting to nearly 1/3rd of the global cervical cancer deaths.[1] Locally advanced disease are usually treated by concurrent chemo-radiation.[2,3]

External beam radiotherapy is administered either by two or four field's techniques to deliver a homogeneous dose to primary tumor and to potential sites of regional spread. Further doses of radiotherapy is delivered using brachytherapy. Two types of brachytherapy techniques used in carcinoma cervix are Intra-cavitary brachytherapy (ICBT) and interstitial brachytherapy (ISBT).[4]

Interstitial brachytherapy is usually performed in those patient in whom ICBT is not possible or distribution of dose is not proper. The templates used in interstitial brachytherapy are Martinez Universal Perineal Interstitial Template (MUPIT), Nori-Hilaris Anderson template and Syed Neblett template.[5,6,7,8]

The change of bladder and rectum volume leads to change in the positions of these structures and target volume during the treatment which may lead to variation in dose to the organ at risk (bladder and rectum) and target. Due to this variation doses to the organ at risk may increase and to the target decreases. This gave us the impetus for an inter-fraction repeat CT scan for assessment of movement of organ at risk

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Corresponding Author:
Dr. Shikha Dhal, Assistant Professor, Department Of Radiation Oncology, Gujarat Cancer and Research Institute, Asarwa, Ahmedabad B-803 Spectrum Tower, Shahibhaug, Near Police Stadium, Ahmedabad, Gujarat - 380004, India. Email: shikha_dhal08@yahoo.co.in

and target for prevention of under dose to the target and overdose to the critical structures.

MUPIT was designed for treatment of bulky disease, paravaginal or distal vaginal involvement, recurrent or residual disease, cervical vault disease, ano-rectal cancer, prostatic carcinoma and perineal tumors.[9,10,11] MUPIT consists of one acrylic template (with straight and angled holes), two acrylic cylinders and cover plate.[6]

MATERIALS AND METHODS

Ten sequential patients of gynecological malignancy were included in this study from January to December 2015, after conclusion of external beam radiation therapy, patients were examined for the feasibility of brachytherapy (ICBT or Interstitial brachytherapy). Patients which were adequate for ICBT were not included while in those ICBT couldn't be possible or there was bulky parametrial, paravaginal disease, vault disease residual after external beam radiotherapy not likely to be adequately covered by ICBT, or there was distorted anatomy due to per se disease or a conical vagina where application of central tandem and ovoid's was not possible were taken for interstitial brachytherapy using MUPIT. All the patients were examined under anesthesia after completion of external beam radiotherapy to assess for the above criteria for the patient to be suitable for implant.

External beam radiotherapy up to 50Gy in 25 fractions was given to patients of carcinoma cervix. Dose for interstitial brachytherapy was 4 Gray per fraction for four fraction in all the cases. All fractions were delivered with the plan created using the initial CT scan. Bowel and rectal preparation was done prior to the application of MUPIT by giving enema and polyethylene glycol with electrolyte preparation for gastrointestinal lavage and keeping patient nil per oral for 12 hours.

Spinal and Epidural anesthesia was used for the implantation of the MUPIT. Catherization of bladder using dilute contrast for inflating Folly's bulb. Contrast was used for delineation of the bladder wall and for dosimetry purpose. MUPIT template was positioned and sutured to the skin for fixation of template. The depth of needle insertion is determined by doing per-vaginal, per-rectal examination and assessment of disease using clinic-radiological findings. After assessment of length of needles, they were placed inside holes according to the disease status. Care was taken for avoiding insertion of needles in the posterior wall of bladder and anterior rectal wall. After application of the template, patients were instructed for being in recumbent position and to avoid minimal of the movements as the assembly was in place for two days. They were kept nil per oral for one day and next day they were allowed for clear liquid diet only and during this patient was kept on intravenous fluids for hydration and nutrition. After the removal of the implant patients were allowed for semisolid and solid diet.

CT scan was done with slice thickness of 5mm after implantation of MUPIT for the contouring of bladder, rectum, and target and for planning purpose. (Figure 1) Target (CTV) includes the needles which were implanted in the disease. The disease extent and length prescribed is assessed by examination under anesthesia prior to implant.

Day one CT scan images were imported to treatment planning system. Then delineation of clinical target volume (CTV), rectum, and bladder was done on that imported CT images by the radiation oncologist. Oncentra brachytherapy planning system was used for planning. CTV was contoured covering the needles. The Catheters were reconstructed and active loading of all needles was done by physicist according to the institutional protocol. Geometric and graphical optimization was utilized and reach to a final plan (P1). (Figure 2)

The next day before giving the third fraction repeat CT scan was done and imported to the treatment planning system. CT2 scan was taken with taking into account the initial parameters. To avoid the contouring errors same radiation

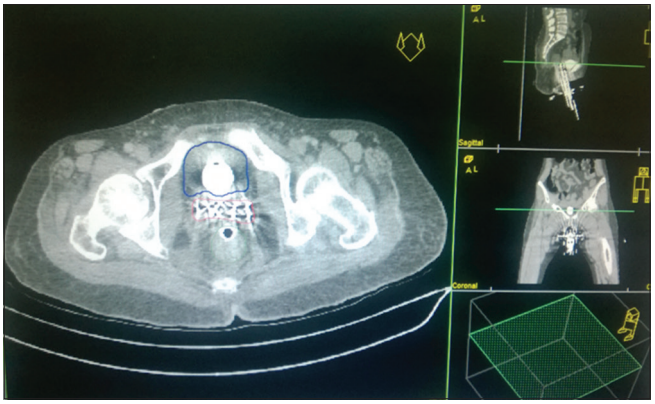

Figure 1: Cross sectional image of CT scan along with reconstructed images with contouring of target and organ at risk

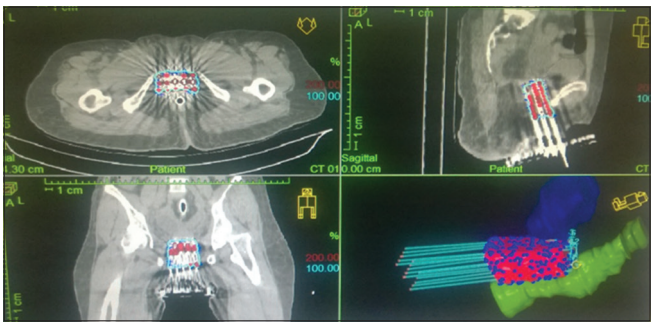

Figure 2: CT scan images with reconstructed needles and plan generated

oncologist contour the target and organ at risk (bladder and rectum) in second CT scan. Intention behind the day 2nd CT scan was to evaluate any shrinkage in the target volume which may be due to resolution of some edema due to the implant procedure or change in the volume of the bladder or rectum that will ultimately affect the doses to the target, bladder and rectum.

The activity of source, dwell positions and times were replicated manually as in the initial plan of day one. This second plan (P2) was also evaluated qualitatively and quantitatively.

The evaluation parameters were the volume and dose variation of the target and organ at risk in the second CT scan images with respect to the day one CT scan images.

RESULTS

Total ten patient were included in the study all were of cervical cancer patient in whom intracavitary brachytherapy was not possible. All the patients were in age group of 30-45 years.

Bladder was catheterized so as to circumvent the bladder volume due to filling. Comparing with initial plan dose, 4/10 patients showed increase in bladder volume and 6/10 showed decrease in bladder volume. Bladder volume variations up to the tune of 88.18% to -68.15% were noted. This change in volume lead to differences in the dose maximum of the bladder between first and third fraction. The maximum dose decreased in 4 patients and increased in 6 patients. It can be understood that the drift in bladder volume is proportional to dose maximum of bladder. As bladder volume can reduce or increase in any direction so we cannot make any correlation of increase in maximum dose to bladder and its volume. Dose maximum of bladder ranged from 62.53% to -21.49%. (Table 1) Mean bladder dose was found to decrease in 6 patients and increase in rest 4 patients. Again there is no association obtained between the two. (Figures 3, 4, 5, 6) Dose to 2cc of volume of bladder increased in five patients as well as decreased in five patient in second plan as compared to 2cc dose of bladder in initial plan. Again this shows that we should replan before third fraction in order to avoid excess of dose to bladder as it can lead to long term complication in the patients. (Table 1)

The rectal volume variation ranges 11.71% to -46.20% due to the rectal filling and it was found to increase in one patient and decreased in rest of all patients. High variation in dose maximum of rectum was found. The dose maximum reduced to 22.33% in one patient and rest 4 patients

Table 1: Bladder dose distribution

Number of patient	Bladder (%)			
	Minimun	Maximum	Mean	Volume
1	−5.13	31.62	−2.35	18.81
2	−9.52	10.66	−6.29	−14.31
3	−17.54	62.53	−16.77	88.18
4	−34.69	−7.69	−23.33	15.92
5	−2.70	1.03	3.77	−15.23
6	66.66	−17.56	52.05	−68.15
7	−13.04	13.95	−7.14	42.76
8	7.69	−21.49	11.63	−64.80
9	24	−15.33	6.09	−4.13
10	−9.48	10.10	−5.70	−13.29

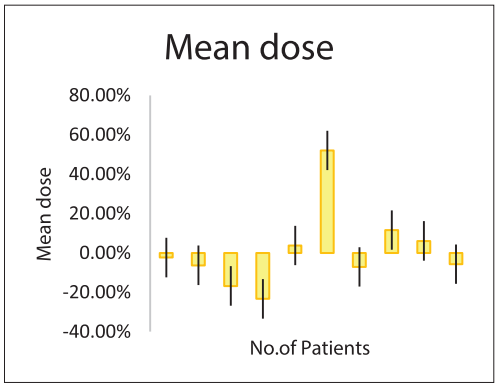

Figure 3: Mean dose distribution of bladder

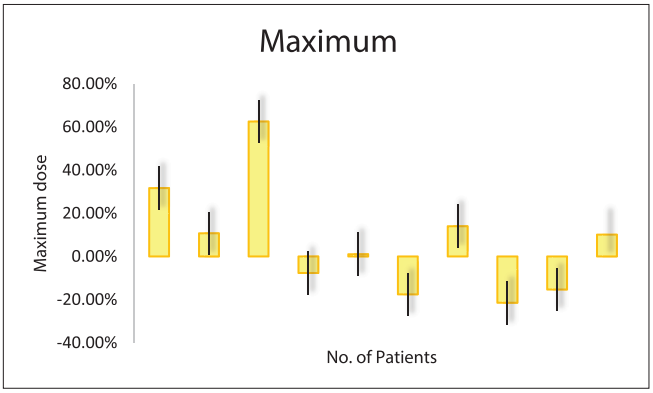

Figure 4: Maximum dose distribution of bladder

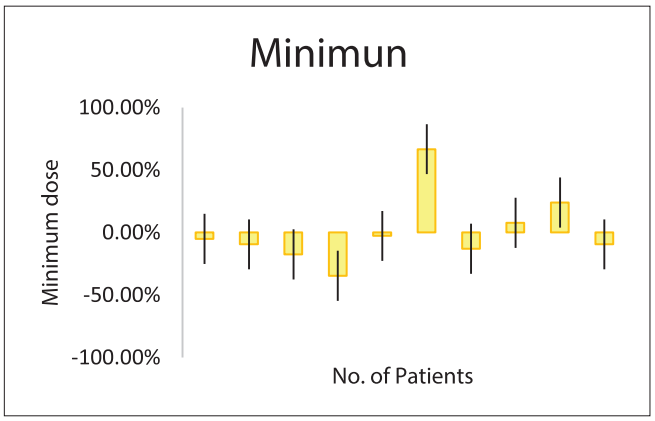

Figure 5: Minimum dose distribution of bladder

decreased in the range of 3.5% to 1.6% while increased in rest up to 108% which might be due to rectal filling variation.

The mean dose increased in 9 patients and a marginal decrease is observed in 1 patient. The range of mean dose varied from 27.82% to- 5.97%. (Table 2) No relationship could be found between the rectal volume and doses. (Figures 7, 8, 9, 10) Dose to 2cc of volume of rectum increased in four patient and decreased six patient in second plan as compared to 2cc dose of rectum in initial plan. Again this shows that we should replan before third fraction in order to avoid excess of dose to rectum as it can lead to long term as well as early reaction complication in the patient due to overdose. (Table 2)

Clinical target volume is increased by 19.48%, 19.05% and in all other patients the volume is decreased. Clinical target volume maximum decreased by 30.54% which might be due to decrease in edema developed during procedure. The volume variation in CTV is in range of19.48% to -30.54%. (Table 3) No variation in the maximum dose as the needles were in the target. The minimum dose in CTV ranges between 24.04% to -21.24%. There was increase in the minimum dose in 3/10 patients, and decrease in rest of the

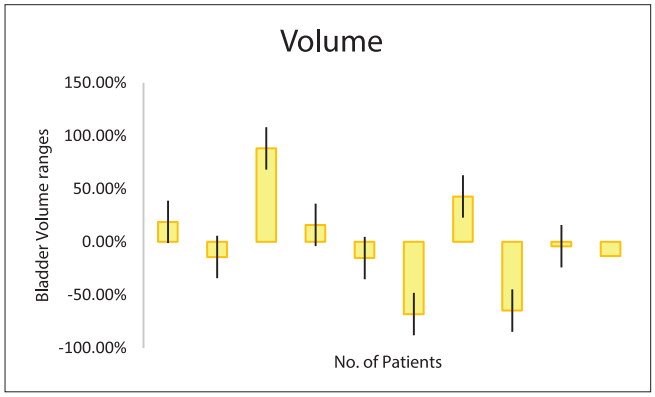

Figure 6: Bladder Volume distribution

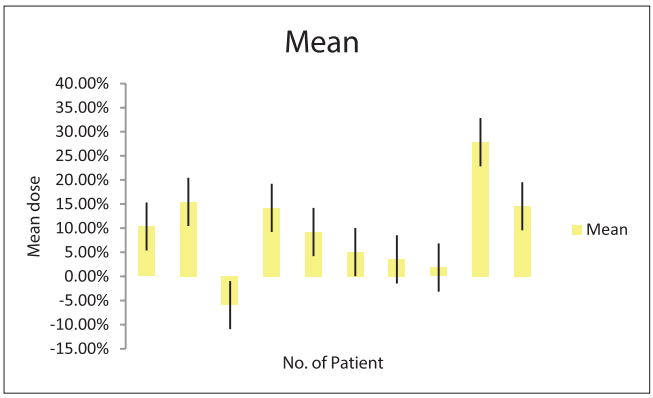

Figure 7: Mean dose distribution of rectum

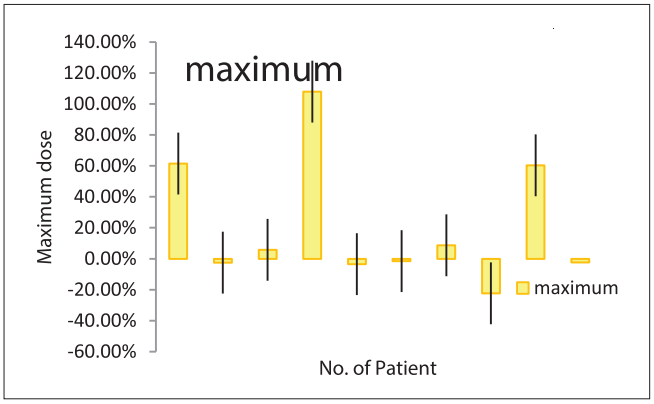

Figure 8: Maximum dose distribution of rectum

Table 2: Rectum dose distribution

Number of patient	Rectum			
	Minimum	Maximum	Mean	Volume
1	1.38	61.50	10.34	−40.35
2	11.76	−2.50	15.44	−4.57
3	−13.70	5.77	−5.97	−34.27
4	1.69	108.00	14.20	−23.14
5	2.82	−3.50	9.19	−46.20
6	1.16	−1.60	5.03	−7.20
7	18.31	8.68	3.54	−23.89
8	8.54	−22.33	1.81	−40.81
9	93.94	60.36	27.82	11.71
10	10.67	−2.33	14.54	−4.75

Table 3: CTV dose distribution

Number	CTV			
	Minimum	Maximum	Mean	Volume
1	−1.84	0.00	0.33	−9.77
2	−21.24	0.00	0.46	−18.53
3	−6.74	0.00	−9.85	−17.72
4	−8.16	0.00	−0.94	−7.16
5	−5.65	0.00	−4.50	19.05
6	−11.41	0.00	−0.35	−14.14
7	24.04	0.00	−11.17	−6.17
8	2.21	0.00	−13.74	−30.54
9	20.51	0.00	−0.17	19.48
10	−20.19	0.00	0.64	−19.03

Table 4: Comparison of doses of all patients

Patient number	Plan 1			Plan 2		
	D90 (dose) (%)	D2cc Bladder	D2cc Rectum	D90 (%)	D2cc Bladder	D2cc Rectum
1	106.74	2.98 Gy	2.76 Gy	105.04	3.17 Gy	3.01 Gy
2	107.37	3.24 Gy	3.20 Gy	107.83	3.07 Gy	3.43 Gy
3	109.01	2.98 Gy	3.26 Gy	106.52	3.15 Gy	3.16 Gy
4	108.69	3.33 Gy	3.24 Gy	109.42	2.81 Gy	3.56 Gy
5	105.60	2.73 Gy	3.28 Gy	104.03	2.82 Gy	3.25 Gy
6	106.45	2.60 Gy	2.90 Gy	104.4	2.34 Gy	3.01 Gy
7	104.40	2.30 Gy	3.31 Gy	105.18	2.43 Gy	3.15 Gy
8	106.1	2.71 Gy	2.45 Gy	105.45	1.95 Gy	2.29 Gy
9	108.15	2.08 Gy	3.26 Gy	102.56	2.14 Gy	2.64 Gy
10	108.77	2.55 Gy	2.94 Gy	106.33	2.45 Gy	2.82 Gy

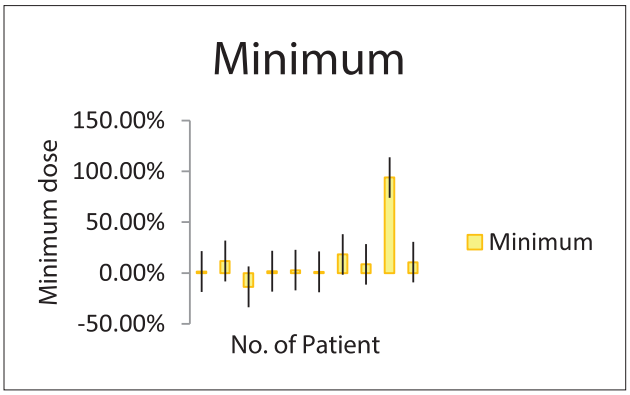

Figure 9: Minimum dose distribution of rectum

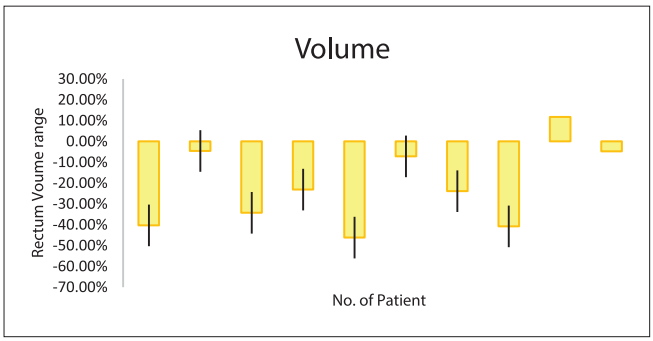

Figure 10: Rectum volume distributionc

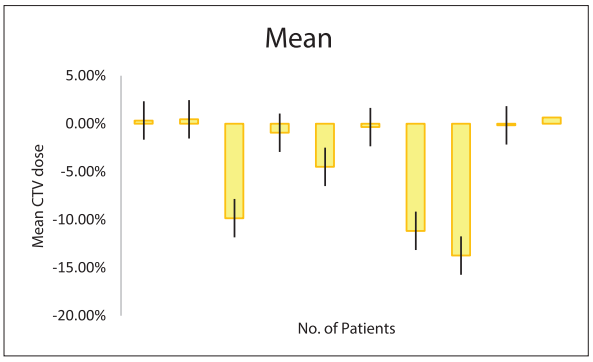

Figure 11: Mean CTV dose distribution

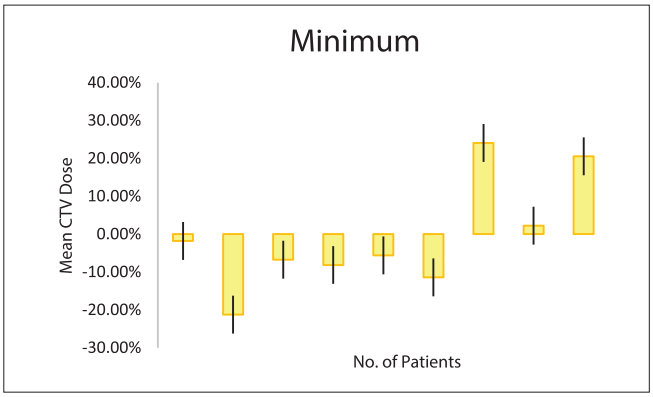

Figure 12: Minimum CTV dose distribution

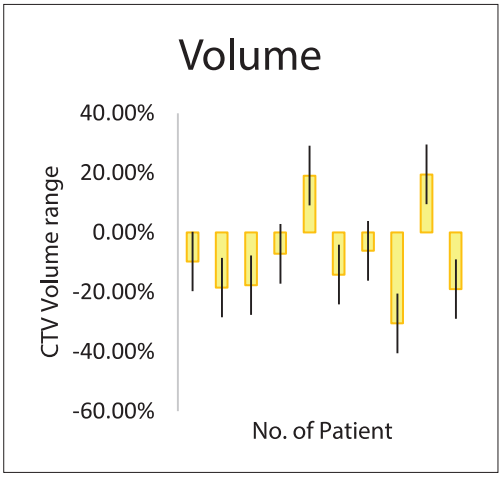

Figure 13: CTV volume distribution

other patients which displays that under dosage of target occurs in the 3rd fraction. The mean dose of CTV ranges between 0.64% to -13.74%. (Figures 11, 12, 13) CTV D90 decreased in 7 patients and increased in 3 patients between the scans, average change in CTV D90 (dose received by 90 percent of volume) is -1.45% of prescription dose and from an average of 107.13 to 105.68%. (Table 4) Volume of target receiving hundred percentage of dose (V100%) is decreased in six patients and increased in four patients in second plan as compared to the initial plan which shows that under dosing or overdosing of target can occur which can lead to decrease/increase in dose to the target which can also effect the control of disease so we should replan if dose to target decreases and there is increase in dose to the organ at risk.

DISCUSSION

As immobilization is not used in brachytherapy, reproducibility is difficult. Also inter fractional errors have been reported frequently in interstitial High Dose Rate (HDR) brachytherapy.[12] There will be tumor volume shrinkage due to resolution of tissue edema developed during the implant procedure. Also there could be needle displacements and deformations. Similarly there are differential bladder and bowel fillings. All the three can lead to overdosing the organs at risk and underdosing the target.[13] Therefore it has been recommended to carry out reimaging before each fraction and replan if the geometric variations of application exceed 5mm.[12]

Volume variation of bladder and rectum has been reported to be from 28.6% to -34.3% and 38.4% to -14.9%by Thanigaimalai et al.[14] In our study bladder and rectal variation were found to range between 88.18 to -68.15% and 11.71 to -46.20%.

Also the same study reports the range of maximum dose in bladder to 17.1% to -66.2%while in our study it is 62.53%

to -21.49%.[14] The maximum dose of rectum in our study was reduced in 5 patient up to 22.33%, increased in 5 patient's maximum up to 108% and; reduced to 12.7% in 1 patient, increased in rest of the patient's maximum up to 410% in the comparison study.

There was reduction in mean doses of bladder for all the 10 patients studied by Thanigaimalai et al. while in our study it decreased in 6 patients and increased in 4 patients.[14] Range of mean doses was 52.5% to -2.35%. Mean dose in rectum was reported to be 14 to -0.8% in the study compared to 27.82% to -5.97% in our study.

The range of D2cc of bladder in 10 patients in plan1 and 2 were reported as 2.4 to 6.4Gy and 1.7 to 6.5Gy in the study by Bhagwat et al. In our study they are 2.08 to 3.33Gy and 1.95 to 3.17Gy respectively. They reported an increase in D2cc of 5 patients, mean D2cc being 0.7Gy (range: 0.3 to 1.8Gy) and decrease in 5 patients, mean D2cc being 0.4 Gy (range: 0-0.5Gy).[15] In our study also it increased in 5 patients, mean D2cc being 0.13Gy (range: 0.06 to 0.19Gy) and decrease in 5 patients, mean D2cc being 0.36 Gy (range: 0.1-0.76Gy).

The range of D2cc of rectum in 10 patients in plan1 and 2 were reported as 1.8 to 5.2Gy and 1.7 to 7.2Gy in the study by Bhagwat et al. In our study they are 2.76 to 3.31Gy and 2.29 to 3.56Gy respectively. They reported an increase in D2cc of 6 patients, mean D2cc being 0.7Gy (range:0.3 to 2Gy) and decrease in 4 patients, mean D2cc being 0.4 Gy(range: 0-0.5Gy).[15] In our study it increased in 4 patients, mean D2cc being 0.23Gy (range: 0.11 to 0.32) and decreased in 6 patients, mean D2cc being 0.2 Gy (range: 0.03-0.62Gy).

Damato et al reported dosimetric changes in D2cc of bladder and rectum of -1.1% and 5.2%.[13] These overall differences in bladder and rectal volume and doses could be due to differences in organ filling and different bowel preparation protocol and different dose per fraction for implant at different centers.

The maximum dose to CTV highest variation was up to 13% in 1 patient and in rest was around 1% in the study by Thanigaimalai et al.[14] There was no variation in maximum dose in our study. The minimum dose to the target in our study ranged from 24.04 to -21.24%and in the comparison study it is in the range of 8.5 to -15.2%.Change in mean dose to CTV ranged from 0.64 to 13.74% in our study while it was 9.8 to 13.3% in the comparison study.

Our CTV D90 decreased in 7 patients and increased in 3 patients between the scans. Average change in CTV D90 between the scans as reported by Damato et al. was -5.1% of the prescription dose from an average of 100% to 95%.[13] In our study the average change in CTV D90 is -1.45% of prescription dose and from an average of 107.13 to 105.68%.

Rey et al also reported CTV D90 reduction from 93.4% to 87.7% from day1 to day 3 scans.[16]

Another study on CTV dosimetry delineated on 3 Magnetic Resonance Imaging (MRI) scans also showed average decrease of 5.7%.[17]

Results in the CTV volumes and doses may vary due to differences in the tumor volume, tumor shrinkage due to resolution of edema or displacement of needles due to patient's motion, or differences in institutional patient's nursing care or during CT scan.

Damato et al. reported <1 cm displacements and deformations in the needle.[13] Although we have not accounted for needle displacement in our study which is one of our limitation which we look forward to assess in future. Another limitation is the small sample size. Similarly long follow up is also not available as yet to assess for any late toxicity. Lastly, it will be more appropriate to using in vivo dosimetry or Thermo luminiscence (TL) material for more relevant dosimetric data.

CONCLUSION

Inter fractional variations obtained in volume and doses are patient specific, needle displacement specific, organ filling specific; however strong volume-dose correlation remains to be established. Hence it is proposed that re-planning using repeat CT scan is mandatory before third fraction implementation. The results can be further accurately quantified if larger study be performed.

REFERENCES

1. WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Summary report on HPV and cervical cancer statistics in India 2007.
2. Sitathanee C, Pairatchvet V, Narkwong L et al. High-dose-rate interstitial brachytherapy in the management of carcinoma of the uterine cervix and other gynecologic malignancies. J Med Assoc Thai. 2005; 88:1045-1050.
3. Jamema SV, Saju S, Shetty UM et al. Dosimetric comparison of inverse optimization with geometric optimization in combination with graphical optimization for HDR prostate implants. J Med Phys. 2006; 31:89-94.
4. Gaddis O, Morrow CP, Klement V et al. Treatment of cervical carcinoma employing a template for transperineal interstitial Ir192 brachytherapy. Int J Radiat Oncol Biol Phys. 1983; 9:819-827.
5. Ampuero F, Doss LL, Khan M et al. The Syed-Neblett interstitial template in locally advanced gynecological malignancies. Int J Radiat Oncol Biol Phys. 1983; 9:1897-1903.
6. Martinez A, Cox RS, Edmunson GK. A multiple-site perineal applicator (MUPIT) for treatment of prostatic, anorectal, and

gynecological malignancies. Int J Radiat Oncol Biol Phys. 1984; 10:297-305.
7. Perez CA, Brady LW, Halperin EC. Principles and practice of radiation oncology. 4th ed. Lippincott Williams and Wilkins: Philadelphia (PA); 2004;576-7.
8. Syed AM, Neblett D, Feder BH. Treatment of extensive carcinoma of cervix with "transperineal parametrial butterfly". Int J Radiat Oncol Biol Phys 1978; 4:735-42.
9. Aristizabal SA, Surwit EA, Hevezi JM, Heusinkveld RS. Treatment of advanced cancer of the cervix with transperineal interstitial irradiation. Int J Radiat Oncol Biol Phys 1983; 9:1013-7.
10. Aristizabal SA, Valencia A, Ocampo G. Interstitial parametrial irradiation in cancer of the cervix stage IIb-IIIb: An analysis of pelvic control and complications. Endocurie Hyperth Oncol 1985; 1:41-8.
11. Nag S, Martinez-Monge R, Ellis R, et al. The use of fluoroscopy to guide needle placement in interstitial gynecological brachytherapy. Int J Radiat Oncol Biol Phys 1998; 40:415-20.
12. S Kandasamy, K.S.Reddy, V Nagarajan, P Vedasoundaram,G Karunanidhi. Inter-fraction variation in interstitial high-dose-rate brachytherapy. Journal of Radiotherapy in Practice 2015;14, 143-151.
13. A.L. Damato, R.A. Cormack, A.N. Viswanathan.Characterization of implant displacement and deformation in gynecologic interstitial brachytherapy. Brachytherapy 2014;13: 100-109.
14. V Thanigaimalai, S Prabakar, K Chokkalingam, B Raghavendiran. Study of dosimetric variation due to interfractionorgan movement in High Dose Rate Interstital (MUPIT) brachytherapy for gynecologic Malignancies Pol J Med Phys Eng 2010; 16(2):85-95.
15. M. Bhagwat, A. Damato, A. Kovacs, K. Townamchai, R. Cormack, A. Viswanathan. OC-86 Inter-Fraction Uncertainties of Oars Metrics in Multifraction Gynecologic Interstitial Brachy-Therapy.World Congress of Brachytherapy 2012.
16. F Rey, C Chang, C Mesina, N Dixit, B.K.Teo, L.L. Lin. Dosimetric impact of inter fraction catheter movement and organ motion on MRI/CT guided HDR interstitial brachytherapy for gynecologic cancer Radiotherapy and Oncology 2013;107: 112–116.
17. Viswanathan AN, Szymonifka J, Tempany- Afdhal CM, et al. A prospective trial of real-time magnetic resonance-guided catheter placement in interstitial gynecologic brachytherapy. Brachytherapy 2013; 12:240-247.

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