Comparative Study of Conventional Planning and MRI Based Volume Optimized Planning of Intracavitary Brachytherapy of Cervical Cancer

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ABSTRACT

BACKGROUND

Cervical cancer is one of the commonest malignancies among women in India. The main stay of treatment is the combination of External Beam Radiation Therapy (EBRT) and Intracavitary Brachytherapy (ICBT) in these patients. We compared conventional point A based treatment planning and MRI based volume optimized planning in ICBT of cervical carcinoma along with doses to organs at risk in both plans. We also compared the radiation doses to organs at risk in both the plans by International Committee on Radiation Units (ICRU) recommended points and dose volume histograms.

METHODS

Eighteen Patients with cancer cervix (72.22% with stage IIB) received EBRT on linear accelerator by four field technique using 15 MV energy for a dose of 46 Gray (Gy) – 50 Gy in 23-25 fractions 2.0 Gy per fraction, five days per week, for 5 weeks to whole pelvis. Most of the patients received at least three doses of chemotherapy. A total of 50 high-dose rate intracavitary brachytherapy (HDR-ICBT) applications done in 18 patients were used for analysis in the study. Clinical history, gynaecology examination and punch biopsy were undertaken. The patients were assessed during EBRT after 2 weeks, for ICBT application and suitable patients were selected for the procedure. CT based point A planning and MRI based volume optimised planning were done for each ICBT application before intracavity brachytherapy. Contouring of rectum, bladder, right and left femoral heads, and small bowel were done.

RESULTS

The median age of patients in this study was 50.4 ± 03.25 years. 72.22% (13/18) of the patients were of stage IIB. The mean dose delivered to 90% high-risk clinical target volume (D90- HR-CTV) for all 50 applications by volume optimized planning was 06.87 ± 0.942 Gy. The mean D90-HR-CTV by point A based conventional planning was 13.69 ± 1.06 GY. The mean D100-HR-CTV by volume optimized planning was 05.30 Gy (± 0.20). The mean D100-HR-CTV by point A based conventional planning was 08.91 ± 0.74 Gy. Maximum doses in the bladder and rectum were significantly lower ($p<0.05$) for MRI planning than for the conventional approach (06.49 GY Vs. 07.45 GY) for bladder; (04.57 GY vs. 05.06 GY) for rectum respectively. Both bladder (D2cc) and rectum (D2cc) doses could be reduced significantly by volume optimization.

CONCLUSIONS

D90-HR-CTV adequately covered by MRI based volume optimized planning was superior to conventional point A based planning in terms of both conformity of target coverage and evaluation of Organ at Risk (OARs), including the rectum and bladder. Both bladder and rectum doses in the most irradiated 2cc volume are significantly reduced in volume optimized planning. Hence, volume optimized planning would be more beneficial in large volume diseases to get better target coverage at the same time sparing the organs in small volume diseases. Hence, the use of MRI-based volume optimization brachytherapy for patients with large volume tumours with parametrial invasion is beneficial.

KEYWORDS

Cancer, Cervix, Woman, Radiotherapy, Brachytherapy, EBRT, ICBT, Prognosis

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BACKGROUND

Cervical cancers in India contribute to 6 to 29% of cancers occurring in women.[1] The combination of EBRT and ICBT forms the main stay of treatment.[2,3] In most centers prescribing dose to point 'A', an empiric point which does not reflect the radiating dose to the tumour is practiced in Intracavitary Brachytherapy and the tumour itself is not imaged. But the doses should be specified in terms of total reference air Kinetic Energy Released in Matter ("Kerma") and by a reference isodose surface, 60 Gy).[4] But this method is used only minimally in Gynaecological Intracavitary Brachytherapy.[1, 5, 6] Whereas 3-dimensional (3D) treatment planning systems helps the radiation oncologists to plan and calculate the spatial dose distribution to the target volume. It also reduces the dose to normal tissues and decreases the chances of toxicity and at the same time enhances the dose to the tumour to produce greater rates of local control.[7]

The true maximum doses to the ICRU defined bladder and rectum on the CT-based 3D Brachytherapy are in fact underestimated.[8, 9] There is a wide range of difference between the maximum dose of radiation reaching the rectum and bladder from the CT planning and to that obtained from radiograph base planning.[10, 11, 12] Instead calculating Dose volume histogram (DVH) using 3-D based volumetric planning provides a better evaluation of the radiation dose to the target volume and organs at risk (OAR). So improved imaging of the target and OAR allows a more precise demarcation of the target volume and OAR. Consequently, a better assessment of the dose delivered to these structures can be predicted.[4] With this background the present study was undertaken to document, validate and compare volume-based planning with conventional point A based planning.

METHODS

This study was conducted from November 2011 to May 2013 at Vydehi Institute of Medical Sciences and Research Centre, Bangalore. The present study was a prospective dosimetric comparative study of point A based conventional planning and MRI guided volume optimized planning in intracavitary brachytherapy of cervical cancer. All consecutive patients who met the eligibility criteria were included in till the required sample size was attained.

Sample Size

Based on the previous year records the sample size was calculated as 50 by using Sample size formula

$N = 4pq/d^2$

$N=4 \times 86.1 \times 13.9 / (9.7)^2 = 50.87$

Hence 50 applications were included in the study.

Inclusion Criteria

1. Patients with cervical cancer fit for curative treatment of radiation and chemotherapy.
2. Patients with proven histopathology of squamous-cell carcinoma
3. Patients with stage IB-IVA cervical cancer according to intrnational Federation of Gynaecology and Obstetrics (FIGO)-2008.
4. Patients aged 18 to 70 years.
5. Patients with Eastern Cooperative Oncology Group (ECOG) performance status 0- 1.

Exclusion Criteria

1. Patients with Metastatic disease of carcinoma cervix.
2. Patients with previous total or partial hysterectomy.
3. Patients with contraindications to anaesthesia.
4. Patients with previous Radiation therapy to pelvis.

Data Collection Method

Eighteen Patients received EBRT on Linear accelerator by four field technique using 15 MV energy for a dose of 46 Gy – 50 Gy in 23-25 fractions as 01.8 Gy - 02.0 Gy per fraction, five days per week, for 5 weeks to whole pelvis. Most of the patients received at least three doses of chemotherapy. A total of 50 HDR-ICBT applications done in 18 patients were used for analysis in the study. Clinical history, gynaecology examination and punch biopsy were undertaken. Patients were staged according to International Federation of Gynaecological Oncology (FIGO) 2008.[1] The patients were assessed during EBRT for brachy application after 15 fractions. CT simulation and MRI were done before brachy treatment. The patients were assessed during EBRT for brachy application after 15 fractions. CT simulation and MRI were done before brachy treatment. Contouring of rectum, bladder, right and left femoral heads, and small bowel were done.

Statistical Analysis

Data were entered in Microsoft excel and analyzed using appropriate statistical software. The methods used were percentages, mean values, standard deviation and T-Test calculator for 2 independent means. P value was taken as significant at <0.05.

RESULTS

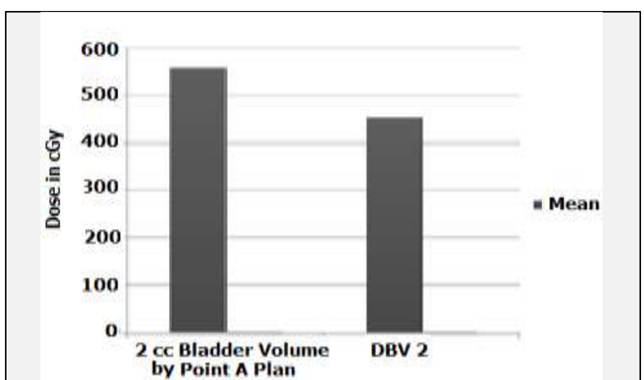

Figure 1. Mean Dose to 2 cc of Bladder Wall by Both Plans

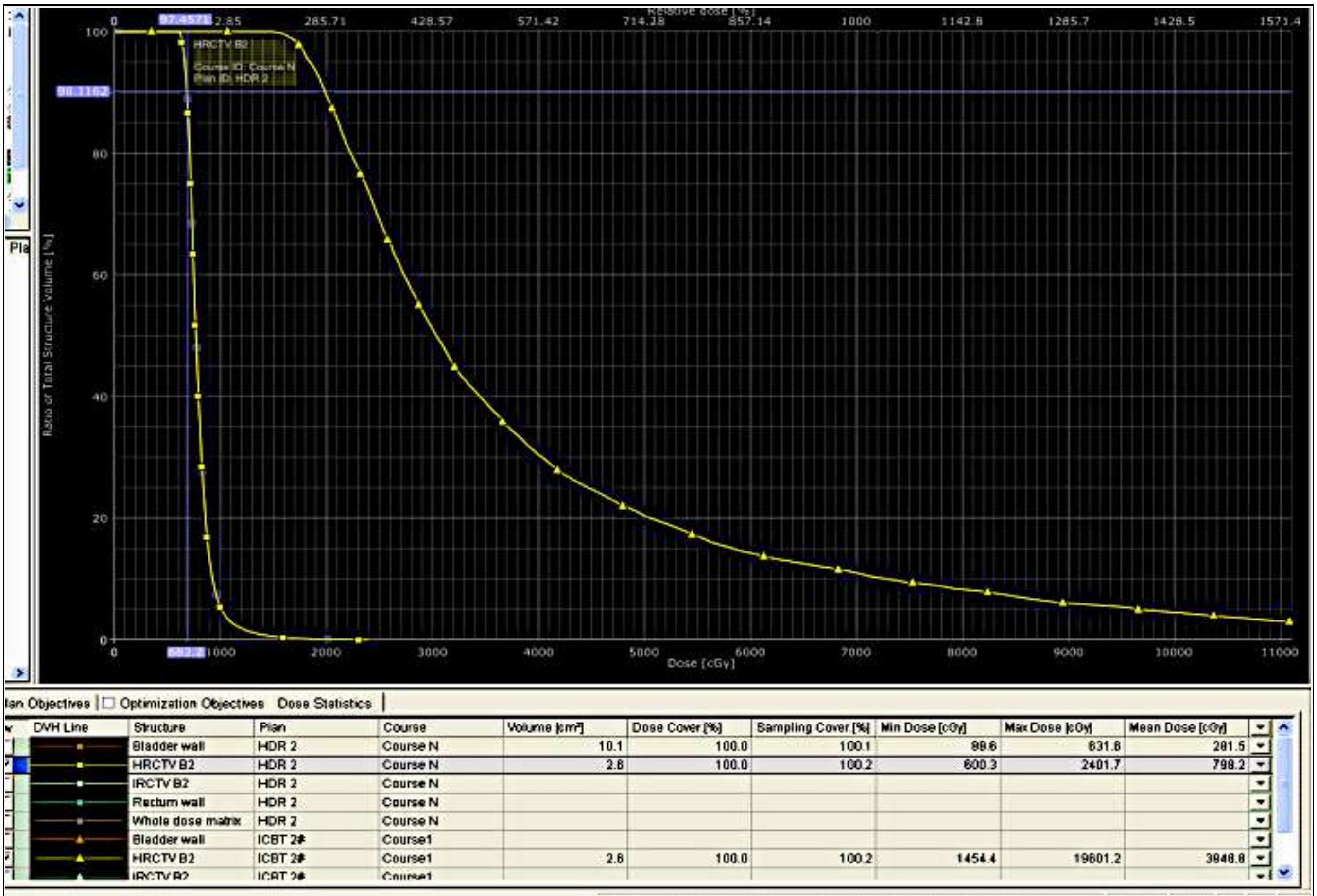

Figure 2. HR-CTV Doses: DVH Showing Mean D90-HCTV by Volume Optimized Plan WWS Shown in the Graph

	D90HRCTV Mean Dose ± SD (Gy)	D90IRCTV Mean Dose ± SD (Gy)	Bladder Dose (D2cc) Mean Dose ± SD (Gy)	Rectal Dose (D2cc) Mean Dose ± SD (Gy)
Point A	13.69 ± 3.76	4.79 ± 1.77	5.56 ± 1.80	5.12 ± 10.05
Volume optimised plan	6.87 ± 0.33	3.79 ± 1.03	4.53 ± 1.44	4.50 ± 1.08
P value	0.532	0.564	0.215	0.635

Table 1. (Means of Mean Doses of D90HRCTV, D90-IR-CTV, D2cc Bladder Doses and D2cc Rectal Doses with SD in Gy) ± 1 Standard Deviation (SD) by Point A Based Plan and Volume Optimised Plan Using 3DDVH Parameters (n = 50)

	Rectal Dose Mean Dose ± SD (Gy)	Maximum Rectal Dose. Means of Mean Dose ± SD (Gy)	Bladder Dose Mean Dose ± SD (Gy)	Maximum Bladder Dose Means of Mean Dose ± SD (Gy)
Point A (ICRU pt.)	4.92 ± 1.10	10.75 ± 407	4.70 ± 160	13.79 ± 6.63
Volume optimised	4.50 ± 1.08	9.76 ± 68	4.53 ± 1.44	9.61 ± 7.68
P value	0.085 Not significant	0.384 Not significant	0.522 Not significant	0.001 Significant

Table 2. {Mean Dose (GY) and Maximum Dose (GY)} ± 1 Standard Deviation (SD) to Rectum and Bladder by Point A and Volume Optimized Plan Using 3DDVH Parameters.

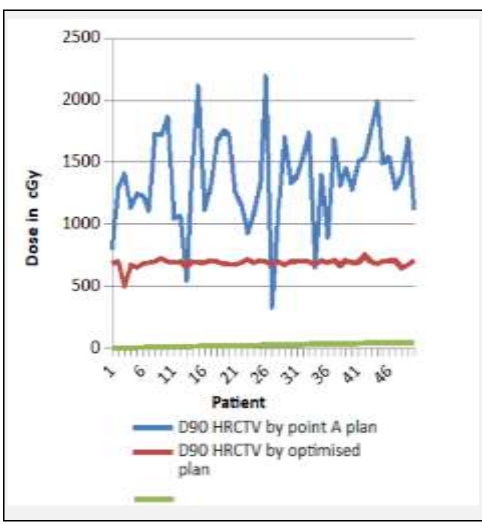

Figure 3. Graph of Mean D90HRCTV by Both Plans

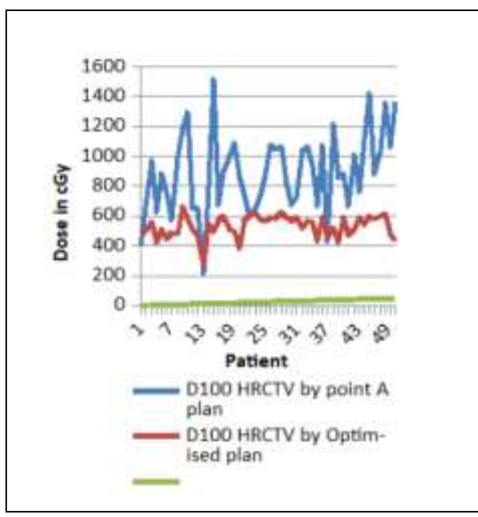

Figure 4. The Mean D100HRCTV by Both Plans

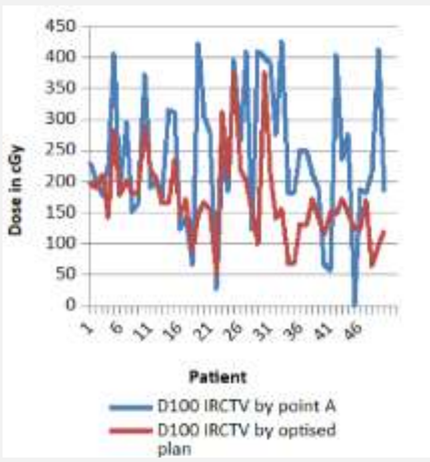

Figure 5. The Mean D90IRCTV by Both Plans

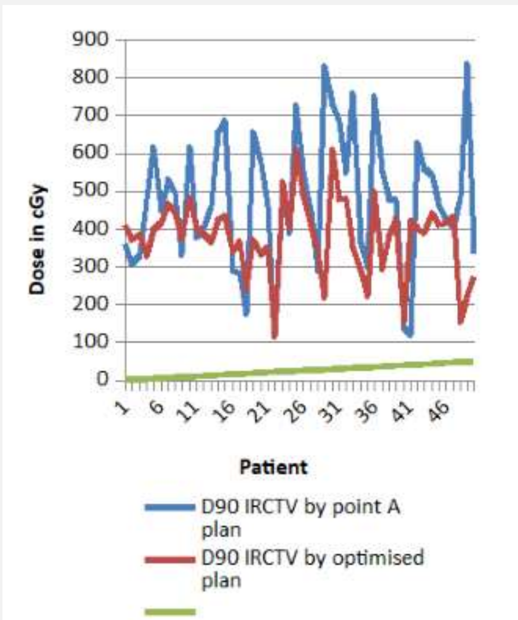

Figure 6. The Mean D90IRCTV by Both Plans

18 patients with cervical cancer were included in this study. The median age of patients in this study was 50.4 ± 3.25 years (range of 26 to 65 years). Among the 18 patients 09(50 %) belonged to rural background and the 50 % to urban areas. 72 % of the patients were multipara and the remaining 28 % were unipara. 38.8 % of women were of low socioeconomic group, 33.33 % belonged to middle income group and the remaining 27.87 % belonged to high income group. Most of the patients 72 % were in stage IIB, followed by 22 % in stage IIIB and 06 % were in stage IIIA. Among the HR-CTV doses, D90 the mean D90-HR-CTV for all 50 applications by volume optimized planning was 06.87 ± 0.94 Gy, the mean D90-HR-CTV by point A based conventional planning was 13.69 ± 01.06 Gy, (Figure 1 and 2). And the, D100 the mean high risk clinical target volume D100-HR-CTV by volume optimized planning was 5.30 ± 0.20 Gy. The mean D100-HR-CTV by point A based conventional planning was 08.91 ± 0.74 Gy, (Figure 3). Among the IRCTV doses, the D90 the mean dose to 90% intermediate risk clinical target volume IR-CTV- (D90-IR-CTV) by volume optimised planning was 03.79 Gy and by point A based conventional planning was 04.79 Gy and D100 the mean dose to 100 % IRCTV-(D100-IR-CTV) by volume optimised planning was 01.71 Gy and by point A planning was 02.42 Gy (Figure 4 and 5).

The summary of Mean dose (Gy) and maximum dose (Gy) ± 1 standard deviation (SD) to rectum and bladder by point A and volume optimized plan using 3D dose volume Histogram (DVH) parameters for all 50 applications was tabulated in Table 2. There was a significant statistical correlation between Maximum Bladder dose by conventional point A based radiation and volume optimised planning with p value at 0.001 (p significant at < 0.05), (Table 2).

Bladder Doses

The mean dose for 2cc of bladder volume by point A based planning was 5.56 Gy and by Volume optimised planning (DBV2) was 04.53 Gy. Standard deviation between these two was 01.84 ± 0.52 Gy. The mean difference of 1.03 Gy was less for 2cc bladder by volume optimised planning compared to point A based planning. The results were not significant statistically as p was >0.05 (Fig. 1).The mean ICRU bladder point dose in conventional plan was 04.70Gy and by volume optimised planning it was 04.53 Gy. The mean DBV2 of 02.1 Gy is less when compared to ICRU bladder point dose (BICRU), with Standard deviation of 02.32 ± 0.64 Gy. The results were not significant statistically as p value was > 0.05.

Rectal Doses

The mean 2cc of rectal volume dose by "point A" based planning was 05.12 Gy and by volume optimized planning; minimal doses delivered to the 2 cm^3 of bladder and rectum receiving the highest dose (DBV2 and DRV2), (DRV2) was 04.50 Gy. The mean difference between these two was 0.62 Gy with standard deviation of 0.37 Gy, the results were significant as the p value was < 0.05. All the data was shown as graphs below.

HRCTV Doses

DVH showing mean D90HRCTV by volume optimized plan was shown in the graph in Fig 2. Both the D90HRCTV for all 50 applications by volume optimized planning and DVH showing mean D90HRCTV by point A based planning was depicted in Fig 3.D100 the mean D100HRCTV by volume optimized planning was 05.30 ± 0.20 Gy. The mean D100HRCTV by point A based conventional planning was 08.91 ± 0.74 Gy, Mean V100 for HRCTV evaluated in our study was 05.56 cc Fig 4.

IRCTV Doses

D90 the mean dose to 90% IR-CTV (D90-IR-CTV) by volume optimised planning was 03.79 Gy and by point A based conventional planning was 04.79 Gy and D100 the mean dose to 100 % IR-CTV (D100-IR-CTV) by volume optimised planning was 01.71 Gy and by point A planning was 02.42 Gy Fig. 5, 6.

The mean International Commission on Radiation Units (ICRU) rectal point dose in conventional plan was 04.92 Gy and by volume optimised planning was 04.50 Gy. The mean difference between ICRU rectal point and DRV2 was 04.17 Gy, with standard deviation of 01.67 ± 0.46 Gy which was not significant with p value > 0.05 (Table 1).

DISCUSSION

Earlier the Intracavitary Brachytherapy treatment for carcinoma cervix was relied upon orthogonal radiographs but they only provided spatial information of the applicator with respect to bony structures, hence its use was limited in terms to calculate the radiation doses received by the volumes of critical structures and tumours. Advanced imaging and 3D Conformal Radiotherapy treatment planning is being used now in EBRT. CT scan-based planning for Intracavitary Brachytherapy evaluates doses to critical structures using DVH but are still based on point A prescription. But organ delineation is better on MRI compared to CT scan; fusion of CT scan and MRI data in cancer cervix patients would help in delineating the target volumes of interest in Brachytherapy.Viswanathanetal.[13] opined from their study that the CT scan of tumours showing the contours definitely overestimated width of the tumour. It resulted in differences in the D90. D100 and volume treated to the actual prescribed dose, which was greater for HR CTV compared with that using MRI. In this study MRI for tumour volume delineation was used. The mean D90-HR-CTV by volume optimized planning was 06.87 Gy (± 0.94). In volume optimized plan, dose will be confined only to the volume of interest which is HRCTV. In all the patients, the response to EBRT and chemotherapy was near complete with minimal indurations at cervix. Hence in all the cases HR-CTV included the entire cervix, lower uterine segment and upper 1/3rd vagina. In conventional planning, dose is prescribed to point A which is 2 cms from central axis, whereas in volume optimized planning dose was optimized to HR-CTV with lateral margin being 1 cm from central axis. This resulted in high dose region in HR-CTV in point A based planning and ultimately in higher mean D90 and D100 doses for HR-CTV and IR-CTV. Since the prescription of dose and target volume differed in conventional and volume optimized plans, D90 and D100 are not comparable in both the plans.

In case of bulky disease where the entire volume cannot be covered by point A, volume optimized planning will help in adequate coverage. In this study such a situation did not arise. Tanderup K et al.[14] after evaluating the radiation dose with MRI image guided adaptive Brachytherapy (IGABT) found that HR-CTV dose (D90) was varying with standard plans with point A dose prescription; with tumours < 31 cc the HR-CTV was well covered in 94% of patients, while OAR constraints were exceeded in 72% of patients. Whereas optimization reduced the violation of OAR constraints to only 6% of patients while maintaining excellent target coverage. With tumours >31 cc, optimization improved the HR-CTV (D90) by a mean of 07 GY resulting in full coverage in 72% of patients as compared to 25 % for standard plans at the same time reducing violation of OAR constraints. In this study the mean dose to D90-IR-CTV by point A based planning was 04.79 Gy and by volume optimised planning was 03.79 Gy. By doing volume optimisation, we could achieve adequate dose coverage of HR-CTV and reduce high dose volume which helped in reducing post RT complications like cervical stenosis. There was a significant statistical correlation between Maximum Bladder dose by conventional point A based radiation and volume optimised planning with p value at 0.001 (p significant at <0.05), (Table 2). ICRU recommended point doses for bladder and rectum significantly underestimate the maximum doses received by them.[10]

As demonstrated in various other similar studies, in this study also the rectum and bladder doses were found to be greater (Table 3) than the corresponding ICRU reference point doses.[9,10,12,15,16,17,18,19,20,21,22]Jamema S, V et al[23] found that mean D2 of rectum and bladder was found to be 01.11 (± 0.2) Gy and 01.56 (± 0.6) Gy times the mean ICRU reference points respectively. In this study ICRU rectal point dose correlated well with maximum bladder dose, while ICRU bladder point underestimated the maximum bladder dose. Hence for evaluating the maximum doses to OARs, the dose to a clinically significant volume was used. Long term follow-up is required for assessment of the tumour response and also the side effects. There were limitations infusing CT with MRI due to variation in the curvature of coach (flat couch for CT scan and curved couched for MRI). It was found that the position of the tandem was affected by the amount of bladder filling, but it was difficult to maintain the same bladder volume during the entire treatment. Though patients could be treated with empty bladder, this would result in more bladder volume exposure to radiation.

Observation	Present Study	Potter R &-Demopoulos J et al[13]	Datta N.R et al[14]	Onal C & Arslan G[15]
Mean D2cc for Bladder (cGY)	9.61 ± 768	8.60 ± 170	4.54 ± 93.7	5.0 ± 08
Mean D2cc for Rectum (cGY)	9.76 ± 685	6.40 ± 90	5.99 ± 0.3	4.9 ± 06

Table 3. Comparison of Mean D2cc for Bladder (cGY) Rectum and Bladder Doses in Various Studies

CONCLUSIONS

D90-HR-CTV adequately covered by MRI based volume optimized planning was superior to conventional point A based planning in terms of both conformity of target coverage and evaluation of OARs, including the rectum and bladder. Both bladder (D2cc) and rectum (D2cc) could be reduced significantly by volume optimization. Hence, volume optimized planning would be more beneficial in large volume diseases to get better target coverage at the same time sparing the organs in small volume diseases. Hence the use of MRI-based volume optimization brachytherapy for patients with large volume tumours with parametrial invasion is beneficial.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Bengaluru: National Centre for Disease Informatics and Research National Cancer Registry Program (ICMR): 2016. Incidence, distribution, trends in incidence rates and projections of burden of cancer. Three-Year Report of Population Based Cancer Registries 2012-2014.

[2] Perez CA, Camel HM, Kuske RR, et al. Radiation therapy alone in the treatment of carcinoma of the uterine cervix: a 20year experience. Gynecol Oncol 1986;23(2):127-140.

[3] Thompson S, Delaney G, Gabriel GS, et al. Estimation of the optimal Brachytherapy utilization rate in the treatment of carcinoma of the uterine cervix: review of clinical practice guidelines and primary evidence. Cancer 2006;107(12):2932-2941.

[4] Nag S, Cardenes, Chang S, et al. Proposed guidelines for image-based intra-cavitarybrachy therapy for cervical carcinoma: report from image-guided brachytherapy working group. Int J Radiation Oncology Biol Phys 2004;60(4):1160-1172.

[5] Grigsby PW, Williamson JF, Chao CKS, et al. Cervical tumor control evaluated with ICRU 38 reference volumes and integrated reference air kerma. Radiother Oncol 2001;58(1):19-23.

[6] Potter R, Van Limbergen E, Gerstner N, et al. Survey of the use of the ICRU 38 in recording and reporting cervical cancer brachytherapy. Radiother Oncol 2001;58(1):11-18.

[7] Paton AM, Chalmers KE, Coomber H, et al. Dose escalation in brachytherapy for cervical cancer: impact on (or increased need for) MRI-guided plan optimization. Br J Radiol 2012;85(1020):e1249-e1255.

[8] Ling CC, Schell MC, Working KR. CT-assisted assessment of bladder and rectum dose in gynecological implants. Int J Radiat Oncol Biol Phys 1987;13(10):1577-1582.

[9] Schoeppel SL, LaVigne ML, Martel MK, et al. Three-dimensional treatment planning of intracavitary gynecologic implants: analysis of ten cases and implications for dose specification. Int J Radiat Oncol Biol Phys 1994;28(1):277-283.

[10] Kim RY, Pareek P. Radiography based treatment planning compared with computed tomography (CT) based treatment planning for Intracavitary Brachytherapy in cancer of the cervix: analysis of dose volume histograms. Brachytherapy 2003;2(4):200-206.

[11] Fellner C, Potter R, Knocke TH, et al. Comparison of radiography and computed tomography based treatment planning in cervix cancer in Brachytherapy with specific attention to some quality assurance aspects. Radiother Oncol 2001;58(1):53-62.

[12] Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix and endometrium. FIGO Committee on Gynecologic Oncology. International Journal of Gynecology and Obstetrics 2009;105(2):103-104.

[13] Pelloski CE, Palmer M, Chronowski GM, et al. Comparison between CT-based volumetric calculations and ICRU reference point estimates of radiation doses delivered to bladder and rectum during intracavitary radiotherapy for cervical cancer. Int J Radiat Oncol Biol Phys 2005;62(1):131-137.

[14] Cibula D, Potter R, Planchamp F, et al. The European Society of Gynaecological Oncology / European Society for Radiotherapy and Oncology/European Society of Pathology Guidelines for the Management of Patients with Cervical Cancer. International Journal of Gynecological Cancer 2018;28(4):641-655.

[15] Report 83. The International Commission on Radiation Units and Measurements. Journal of the ICRU 2010;10(1):90-95.

[16] Jamema SV, Saju S, Mahantshetty U, et al. Dosimetric evaluation of rectum and bladder using image-based CT planning and orthogonal radiographs with ICRU 38 recommendations in intracavitary Brachytherapy. J Med Phys 2008;33(1):3-8.

[17] Potter R, Dimopoulos J, Georg P, et al. Clinical impact of MRI assisted dose volume adaptation and dose escalation in brachytherapy of locally advanced cervix cancer. J Radonc 2007;83(2):148-155.

[18] Datta NR, Srivastava A, Das MKJ, et al. Comparative assessment of doses to tumor, rectum and bladder as evaluated by orthogonal radiographs vs. computer enhanced computed tomography-based intracavitary brachytherapy in cervical cancer. J Brachy 2006;5(4):223-229.

[19] Onal C, Arslan G, Topkan E, et al. Comparison of conventional and CT-based planning for intracavitary brachytherapy for cervical cancer: target volume coverage and organs at risk doses. Journal of Experimental & Clinical Cancer Research 2009;28(1):95.

[20] Lang S, Nulens A, Briot E, et al. Inter-comparison of treatment concepts for MR image assisted brachytherapy of cervical carcinoma based on GYN GEC-ESTRO recommendations. Radiotherapy and Oncology 2006;78(2):185-193.

[21] Sun LM, Huang EY, Ko SF, et al. Computer tomography-assisted three-dimensional technique to assess rectal and bladder wall dose in intracavitary Brachytherapy for uterine cervical cancer. Radiother Oncol 2004;71(3):333-337.

[22] Brooks S, Bownes P, Lowe G, et al. Cervical brachytherapy utilizing ring applicator: comparison of standard and conformal loading. Int J Radiat Oncol Biol Phys 2005;63(3):934-939.

[23] Jamema SV, Saju S, Mahantshetty U, et al. Dosimetric evaluation of rectum and bladder using image-based CT planning and orthogonal radiographs with ICRU 38 recommendations in Intracavitary Brachytherapy. J Med Phys 2008;33(1):3-8.