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Research Article

A Case Series of Dosimetric Comparison-VMAT (RapidArc), IMRT, 3DCRT for Extended Field Radiotherapy in Cervical Cancer

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Abstract

Purpose: To compare plans of 3DCRT, IMRT and VMAT (RapidArc) and evaluate them in different dosimetric aspects along with dose to organs at risk with each technique to determine the best treatment technique for Extended field RT in cervical cancer patients

Material & Methods: We evaluated External Beam radiotherapy plans of 10 patients of FIGO 2018 stage rIIIC2 who received Extended Field Radiotherapy (EFRT) to primary site along with regional nodes-bilateral external, internal iliac lymph nodes, presacral and para-aortic lymph nodes. The dose prescribed for all patients was 50.4Gy/28 fractions at 180cGy/fraction. Few patients had received gross nodal boost following this, but for better comparison only the initial phase of 50.4Gy/28 fractions was considered. All patients were planned with 3DCRT, IMRT and RapidArc. We evaluated and compared these plans dosimetrically in terms of Homogeneity Index, Conformity Index, Target Volume Coverage, Gradient Index, Unified Dosimetry Index, Integral dose, Monitor units and Doses to Organs at risk such as Anorectum, Bladder, Bowel Bag, Bilateral Femoral Heads, Bilateral Kidneys and Bone Marrow.

Results: Intensity modulated techniques RapidArc and IMRT significantly spared critical organs compared to 3DCRT. Between RapidArc and IMRT, the critical organ sparing was comparable, but RapidArc had better target coverage, lesser MU and lesser treatment time. All techniques had acceptable HI, CI, GI, UDI and whole body Integral dose.

Conclusion: Intensity modulated techniques should be the standard for EFRT in cervical cancer. Both RapidArc and IMRT are acceptable techniques of treatment delivery although the former may be preferred if and when available.

Keywords: Extended field radiotherapy; Cervical cancer radiotherapy; VMAT cervical cancer; RapidArc; EFRT; Dosimetry; Para-aortic radiotherapy

Abbreviations

3DCRT: Three-Dimensional Conformal Radiotherapy; IMRT: Intensity Modulated Radiotherapy; VMAT: Volumetric Modulated Arc Therapy; FIGO: International Federation of Gynecologists and Obstetricians; EBRT: External Beam Radiotherapy; EFRT: Extended Field Radiotherapy; EPID: Electronic Portal Imaging Device; CTV: Clinical Target Volume; PTV: Planning Target Volume; PALN: Para-Aortic Lymph Node; HI: Homogeneity Index; CI: Conformity Index; GI: Gradient Index; UDI: Unified Dosimetry Index; ICRU: International Commission for Radiation Units and Measurements; ID: Integral Dose; LINAC: Linear Accelerator; MU: Monitor Units; OAR: Organ at Risk; Gy: Gray

Introduction

Cervical cancer is the most common gynecological cancer and second most common cancer amongst women in India. It is also the second most common cause for cancer related mortality in women in India [1]. Concurrent chemo radiation has been the standard of care for locally advanced cervical cancer ever since the National cancer Institute alert in 1999 and the benefits of the same has been subsequently well evaluated and documented in several meta-analyses [2-4].

3DCRT has been widely accepted and practiced as the standard modality of Extended Field Radiotherapy (EBRT) in many centers across the world for treatment of cervical cancer. For Extended Field RT (EFRT) in cervical cancer, few studies have demonstrated the favorable toxicity profile of Extended Field-Intensity Modulated Radiation Therapy (EF-IMRT), especially with Bone marrow sparing [5,6]. Volumetric Modulated Arc Therapy (VMAT) is an advanced form of IMRT which delivers precise 3D dose distribution in a single or multiple arc treatment with the gantry rotating about 360 degrees. In VMAT by RapidArc (Varian Inc., Palo Alto, California, USA), the treatment time is usually only a few minutes.

In this study, we evaluate and compare 3DCRT, IMRT and RapidArc plans of patients who were planned for Extended Field RT.

Material and Methods

Selection criteria

Biopsy proven cervical squamous cell carcinoma patients who

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had FIGO 2018 stage rIIIC2 disease who received extended field RT till para-aortic lymph nodes. FIGO 2018 stage rIIIC2 cervical cancer is defined as tumor involvement of para-aortic lymph nodes, irrespective of size and extent; the prefix "r" denotes that the involvement was diagnosed radiologically.

Immobilization and simulation

We followed a bladder protocol for all 10 patients in which, after voiding, each patient consumed around 300ml of water over a duration of 20 minutes following which they were taken for immobilization procedure. Pelvicthermoplastic cast was done with patients' hands above the head or over the chest based on their preference. Then, the patients were asked to void and follow the same bladder protocol to prepare for CT simulation.

During simulation, with the patient in treatment position, CT Abdomen and Pelvis with Intravenous Contrast was taken from T10 vertebral level till midthigh with a slice thickness of 3mm and the images were transferred to our Treatment planning system.

Contouring and treatment planning

We use Eclipse Treatment planning system version 13.7.39 for contouring and treatment planning. GTV was contoured by identifying the gross tumor on Contrast CT scans. CTV- primary (CTV-P) included entire uterus including cervix with gross tumor, entire parametrium on both sides and vagina. For vaginal inclusion in CTV-P, if there was involvement of upper half of vagina, 2/3 of the vagina was contoured and if there was more than half of vaginal involvement, entire vagina was contoured tillintroitus.

CTV-Pelvic Lymph Nodes (CTV-PELVICLN) comprised of bilateral internal & external iliac, presacral, obturator lymph nodes which were contoured in accordance with Taylor et al. guidelines for Pelvic lymph node contouring [7] as follows:

The common iliac, external and internal iliac vessels were contoured. For the common iliac lymph node contouring, a 7mm circumferential margin was given and the posterolateral borders were extended along psoas muscle and vertebral body. For the external iliac lymph node contouring, the 7mm circumferential margin was extended 10mm anterolaterally along the iliopsoas muscle to include the lateral external iliac nodes and for the internal iliac lymph nodes, the 7mm circumferential margin from the respective vessel was extended to pelvic side wall. The external and internal iliac nodal contours were joined with a 17mm wide strip along the pelvic side wall for the obturator lymph node delineation. Pre-sacral lymph nodes were delineated using a 10mm strip over the anterior sacrum and entire mesorectal space was covered for inclusion of mesorectal nodes.

For delineation of CTV-PALN for the Para-Aortic lymph nodes, first the Aorta and Inferior vena cava were contoured. Then, a 10mm circumferential expansion was given from the aorta except 15mm laterally. From the IVC, 8mm anteromedial and 6mm posterolateral expansion were given [8]. The cranial limit for CTV-PALN was the emerging of left renal vein from the IVC and the caudal limit was till aortic bifurcation.

The final CTV-N comprised of the merged contours of CTV-PELVICLN and CTV-PALN. PTV was given as per our Institutional protocol which is:

For the PTV primary (PTV-P), 10mm circumferential expansion on all aspects except the posterior, where a 5mm margin was given from the CTV-P.

For the PTV nodes (PTV-N), 5mm circumferential margin was given from the CTV-N. Both PTV-P and PTV-N were then merged to create the final target volume PTV50.4/28.

The organs at risk delineated were bladder, anorectum, bilateral femoral heads, bowel bag, bilateral kidneys and bone marrow, in accordance with the RTOG guidelines for female pelvic normal tissue contouring consensus recommendations.

EBRT plans were generated for all patients using 3DCRT, IMRT and RapidArc. Dose prescribed was 50.4Gy/28 fractions at 1.8Gy per fraction, five fractions a week over five and a half weeks.

Plan specifications:

3DCRT: 4 field fixed beam angles (AP, PA, 2 lateral fields - Box Technique)

IMRT: 7 fields, Step and Shoot IMRT, Collimator angle 10º (Sliding Window Technique)

RapidArc: Two complete arcs- Clockwise (181º-179º) and Counter-clockwise (179º-181º), Collimator angle 10º

Other relevant data:

LINAC-Varian® Unique Performance (6MV)

Contoured Mean Bladder Volume-197.5cc (Range 170-227.3cc) Contoured Mean Rectal Volume-49.5cc (Range 28.1-63.9cc).

After generation of plans, they were compared to assess their quality in terms of various variables like Homogeneity Index, Conformity Index, Target Volume Coverage, Gradient Index, Unified Dosimetry Index, Integral dose, Monitor units and Doses to Organs at risk such as Rectum, Bladder, Bowel Bag, Bilateral Femoral Heads, Bilateral Kidneys and Bone Marrow.

Dosimetryindices

Dose homogeneity index: Dose Homogeneity Index (HI) helps to scale the hotspots in and around the planning target volume. We calculated HI based on the formula:

$HI=D_{max}/D_p$

Where

D_{max} is the maximum point dose

D_p is the prescribed dose to the target volume i.e., the prescription isodose line chosen to cover the margin of the tumor, which in this case, is 95%

According to the above formula which was initially proposed by the RTOG, an ideal HI value is 1 [9].

Conformity Index

Conformity Index (CI) provides a reliable method for quantifying the degree of conformity based on isodose surfaces and volumes. It was calculated based on the formula:

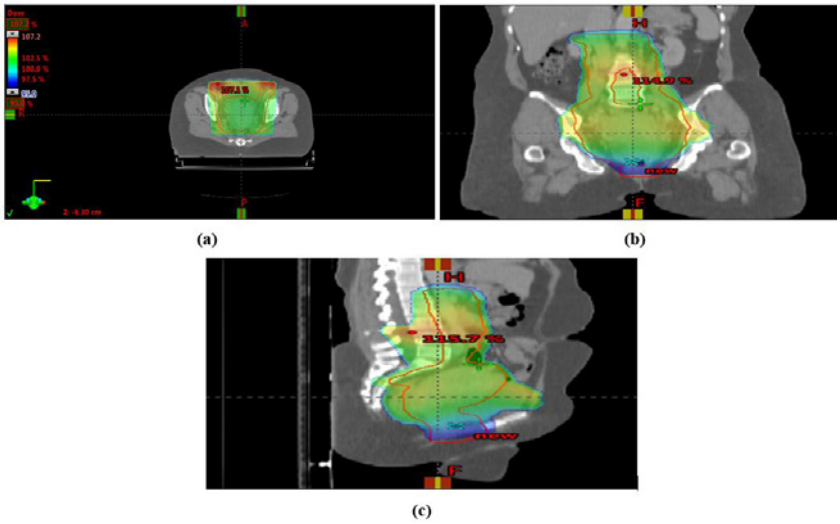

Figure 1: a: Showing 95% dose color wash for 3DCRT in transverse view. **b:** Showing 95% dose color wash for 3DCRT infrontal view. **c:** Showing 95% dose color wash for 3DCRT in sagittal view.

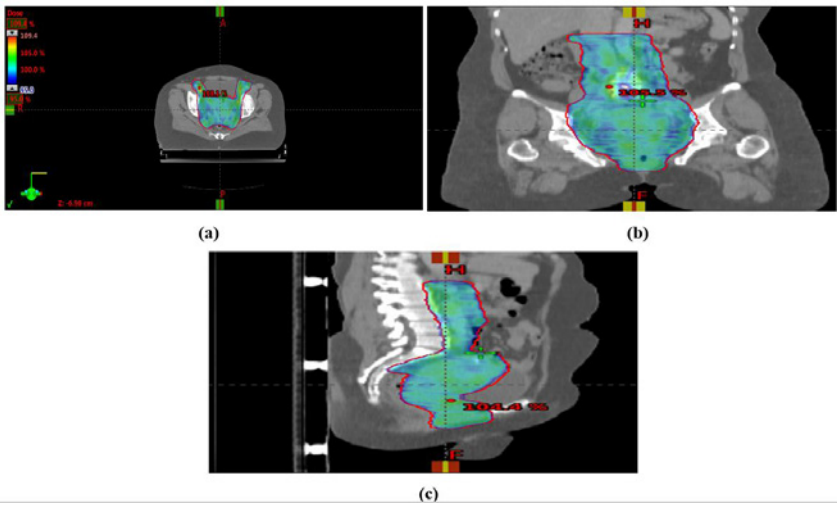

Figure 2: a: Showing 95% dose color wash for IMRT in transverse view. **b:** Showing 95% dose color wash for IMRT in frontal view. **c:** Showing 95% dose color wash for IMRT in sagittal view.

CI = TV/PTV

where,

TV= Treated volume (i.e. The volume that is encompassed by 95% isodose) PTV= Planning target volume

According to the above formula proposed by ICRU 62 report, ideal CI value is 1.

Dose gradient index: Dose gradient index (GI) helps to assess the degree of steepness/ shallowness of dose fall-off in the tumor volume. Lower GI implies steeper dose fall-off and better plan conformity [10].

GI = PTVPD/PTVPD50%

where,

PTVPD50% represents planning target volume coverage at 50% of PD

Target volume coverage: The dose coverage was defined as the ratio of minimum dose within target volume to the prescription dose. The plan is considered acceptable if target volume completely covers 90% of prescription isodose. If target is covered by 80-89 % of prescribed dose, it is regarded as a minor deviation. A major deviation is when <80% of prescribed dose is encompassed by target volume. But, in most clinical scenarios, a ±10% deviation is accepted [11].

Coverage = D_{min}/PD

Unified dosimetry index formula: Unified Dosimetry Index (UDI) combines the above four dosimetry objectives of dose homogeneity index, conformity index, dose gradient index and target volume coverage into one single and simple equation that is utilized for calculating a figure of merit. This figure of merit helps to quantify the overall quality of a dosimetry plan. An ideal UDI value is 1. Low

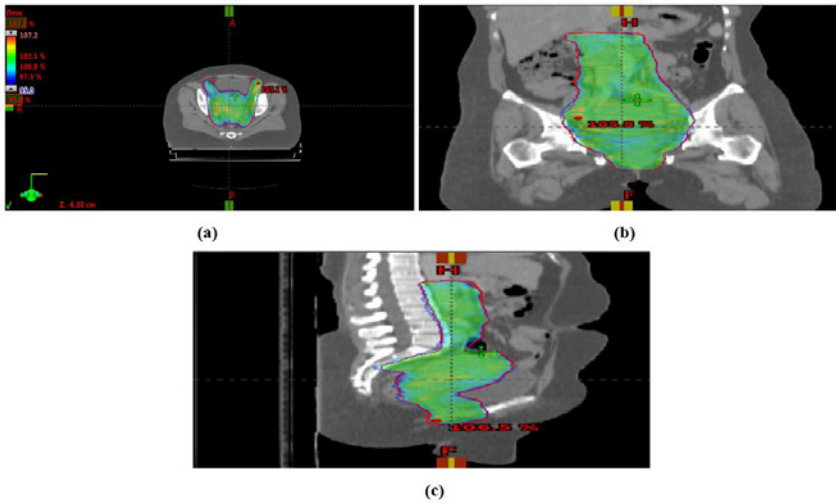

Figure 3: a: Showing 95% dose color wash for RapidArc in transverse view. **b:** Showing 95% dose color wash for RapidArc in frontal view. **c:** Showing 95% dose color wash for RapidArc in sagittal view.

Table 1: Comparison of mean bladder doses across the study group (N=10).

Bladder	3DCRT (Mean ± SD)	IMRT (Mean ± SD)	RapidArc (Mean ± SD)	p value		
				3DCRT *vs* IMRT	3DCRT *vs* RapidArc	IMRT *vs* RapidArc
V5	100 ± 0.0	100 ± 0.0	100 ± 0.0	-	-	-
V10	100 ± 0.0	100 ± 0.0	99.97 ± 0.09	1	0.231	0.231
V20	100 ± 0.00	78.19 ± 14.74	74.75 ± 20.14	0.002	0.001	0.598
V30	99.61 ± 1.23	44.58 ± 15.74	40.57 ± 13.28	<0.001	<0.001	0.458
V40	93.94 ± 4.65	15.85 ± 10.17	15.77 ± 7.66	<0.001	<0.001	0.981
V50	79.91 ± 14.48	0.03 ± 0.09	0.23 ± 0.64	<0.001	<0.001	0.958
Min(Gy)	33.80 ± 5.39	13.40 ± 2.11	13.05 ± 3.81	<0.001	<0.001	0.849
Mean	49.79 ± 1.59	28.79 ± 3.95	27.93 ± 4.26	<0.001	<0.001	0.585
Max(Gy)	52.91 ± 1.09	49.64 ± 1.98	50.52 ± 1.65	0.003	<0.001	0.233

UDI value corresponds to a good plan, whereas a high value (>1) indicates a relatively poor plan.

Analysis is simplified by considering equal weightage of all four indices of UDI [12].

UDI = Coverage × CI × HI × GI.

Integral dose: ID is equal to the product of mean dose received by organ, volume receiving that dose, and the density of that volume as represented by the equation.

$ID\ (GyL) = D_{mean} \times V \times \rho$

Where,

D_{mean} = Mean dose received by the organ

V= Volume of the organ that receives the dose, ρ= Density of the volume of that organ.

Complex calculation is warranted for the accurate determination of ID with variable tissue densities. Uncertain tie sexist with the assumption of uniform density of the patients body volume.

Therefore, in our study, we calculated Integral dose of the body by creating a structure set "Body-PTV" and assessed the same during plan evaluation. Although no ideal threshold value for ID is recommended, it is necessary to maintain it as low as possible without significantly compromising target coverage [11].

For evaluation of Organs at risk such as Anorectum, Bladder, Bowel Bag, Bilateral Femoral Heads, Bilateral Kidneys and Bone Marrow, the following were taken into consideration- Minimum dose, mean dose, maximum dose, Volume of the organ receiving 5Gy, 10Gy, 20Gy, 30Gy, 40Gy and 50Gy represented as V5, V10, V20, V30, V40 and V50 respectively.

Statistical analyses

Statistical analyses were done using SPSS version 23 for windows. The statistical test used was One Way Anova with post hoc analysis to find the significance of difference between the three study groups. Significant difference was defined as "p"value<0.05.

Results

Interpretation of bladder dosimetry (Table 1, Figure 4):

- No significant difference was found in terms of V5 and V10

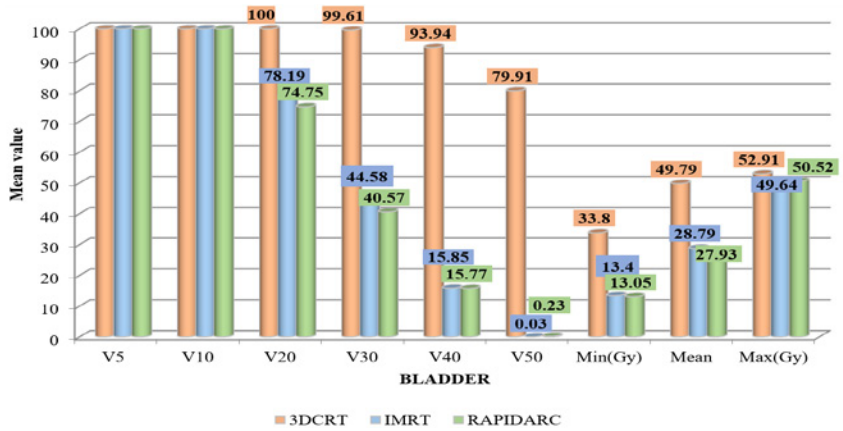

Figure 4: Bar chart of Comparison of mean bladder doses across the study group.

Table 2: Comparison of mean Anorectum doses across the study group (N=10).

Rectum	3DCRT (Mean ± SD)	IMRT (Mean ± SD)	RapidArc (Mean ± SD)	p value		
				3DCRT *vs* IMRT	3DCRT *vs* RapidArc	IMRT *vs* RapidArc
V5	100 ± 0.0	100 ± 0.0	99.94 ± 0.19	1	0.231	0.231
V10	100 ± 0.0	99.82 ± 0.58	98.15 ± 2.91	0.812	0.023	0.039
V20	99.49 ± 1.09	88.13 ± 15.87	86.06 ± 17.64	0.075	0.037	0.738
V30	98.08 ± 3.37	62.04 ± 29.73	55.43 ± 20.56	0.001	<0.001	0.487
V40	82.06 ± 11.58	20.94 ± 19.81	18.2 ± 10.89	<0.001	<0.001	0.76
V50	59.07 ± 16.30	0.12 ± 0.27	0.64 ± 1.12	<0.001	<0.001	0.902
Min	30.97 ± 2.52	14.85 ± 6.24	12.93 ± 7.01	<0.001	<0.001	0.45
Mean	46.88 ± 2.44	31.85 ± 5.83	31.09 ± 4.86	<0.001	<0.001	0.716
Max	52.64 ± 1.01	49.18 ± 2.41	50.49 ± 2.78	0.002	0.038	0.194

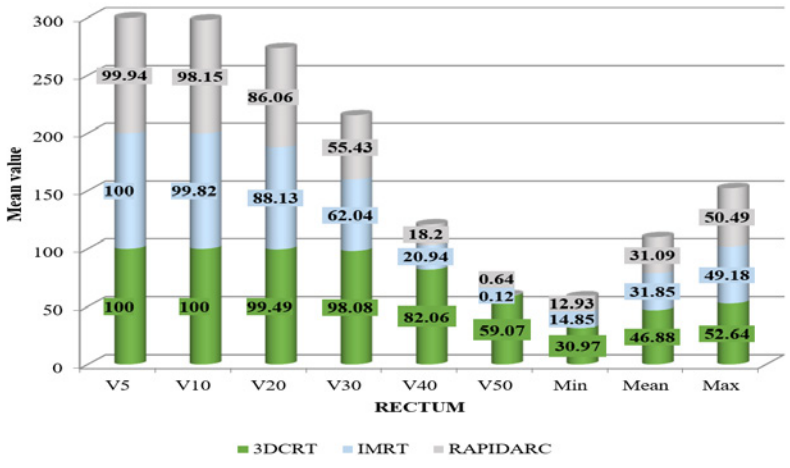

Figure 5: Stacked bar chart of Comparison of mean Anorectum doses across the study group (N=10).

between all the treatment techniques.

- Between 3DCRT and IMRT, significant difference was observed in terms of V20, V30, V40, V50, minimum dose, maximum dose and mean dose in favor of IMRT.
- Between 3DCRT and RapidArc, significant difference was observed in terms of V20, V30, V40, V50, minimum dose, maximum dose and mean dose in favor of RapidArc.
- There were no significant differences between IMRT and RapidArc with any of the parameters.

Interpretation for Anorectum dosimetry (Table 2, Figure 5):

Table 3: Comparison of mean bilateral kidneys across the study group.

Bilateral Kidneys	3DCRT (Mean ± SD)	IMRT (Mean ± SD)	RapidArc (Mean ± SD)	p value		
				3DCRT *vs* IMRT	3DCRT *vs* RapidArc	IMRT *vs* RapidArc
V5	83.90 ± 9.06	96.14 ± 4.93	95.51 ± 4.90	<0.001	<0.001	0.834
V10	59.37 ± 9.33	76.69 ± 9.66	70.73 ± 11.08	0.001	0.018	0.196
V20	44.02 ± 12.06	27.97 ± 7.31	24.02 ± 5.06	<0.001	<0.001	0.316
V30	26.41 ± 11.13	6.24 ± 2.70	6.60 ± 1.169	<0.001	<0.001	0.906
V40	7.81 ± 4.48	1.33 ± 1.92	0.83 ±0.63	<0.001	<0.001	0.697
V50	-	0 ± 0	0 ± 0	-	-	-
Min	2.54 ± 1.18	3.55 ± 2.45	3.11 ± 1.50	0.218	0.483	0.587
Mean	17.08 ± 6.86	15.37 ± 6.24	15.25 ± 1.52	0.486	0.458	0.964
Max	51.90 ± 1.89	43.21 ± 14.38	47.50 ± 1.43	0.029	0.252	0.264

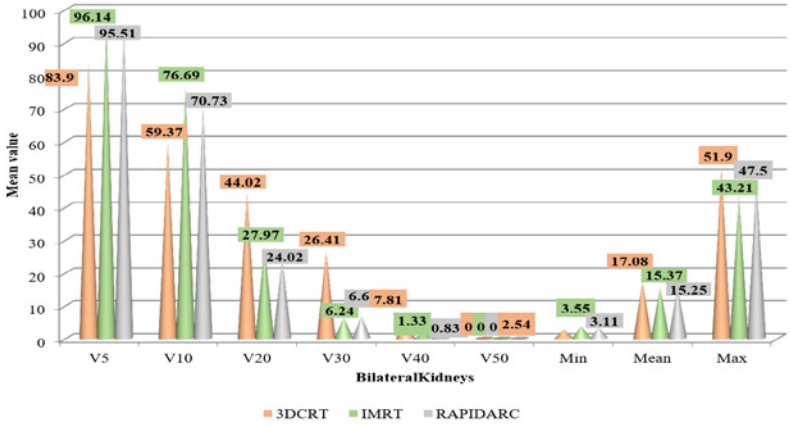

Figure 6: Bar chart of Comparison of mean bilateral kidneys across the study group.

- No significant difference was found for V5 between all the treatment techniques.
- Between 3DCRT and IMRT, significant difference was found in terms of V30, V40, V50, Minimum, Mean and Maximum dose in favor of IMRT.
- Between 3DCRT and RapidArc, there was significant difference amongst all variables except V5 in favor of RapidArc.
- Between IMRT and RapidArc, there was significant difference only for V10 in favor of RapidArc.

Interpretation of Bilateral kidneys dosimetry (Table 3, Figure 6):

- Between 3DCRT and IMRT, significant differences were observed in terms of V5 and V10 in favor of 3DCRT.
- Between 3DCRT and IMRT, Significant differences were observed with V20, V30, V40 and maximum dose in favor of IMRT.
- Between 3DCRT and RapidArc, significant differences were observed in terms of V5 and V10 in favor of 3DCRT.
- Between 3DCRT and RapidArc, Significant differences were observed with V20,V30, V40 and maximum dose in favor of RapidArc.
- There were no significant differences between IMRT and RapidArc with any of the parameters.

Interpretation of bowel bag dosimetry (Table 4, Figure 7):

- No significant differences were found for V5 and V10 between the study groups.
- Between 3DCRT and IMRT, there were significant differences in terms of V20, V30, V40, V50, Dose to 65cc, 120 cc &195cc of bowel bag volume and maximum dose in favor of IMRT.
- Between 3DCRT and RapidArc, there were significant differences in terms of V20, V30, V40, V50, Dose to 65cc, 120 cc &195cc of bowel bag volume and maximum dose in favor of IMRT.
- Between 3DCRT and RapidArc, there was a significant difference observed in terms of minimum dose in favor of 3DCRT.
- There were no significant differences between IMRT and RapidArc with any of the parameters.

Interpretation of Bilateral femoral heads dosimetry (Table 5, Figure 8):

- No significant difference was found for V5 between the study groups.
- Between 3DCRT and IMRT, there were significant

Table 4: Comparison of mean bowel bag dose across the study group.

Bowel	3DCRT (Mean ± SD)	IMRT (Mean ± SD)	RapidArc (Mean ± SD)	p value		
				3DCRT *vs* IMRT	3DCRT *vs* RapidArc	IMRT *vs* RapidArc
V5	96.66 ± 3.72	93.82 ± 19.25	99.79 ± 0.46	0.587	0.559	0.27
V10	89.76 ± 5.75	89.15 ± 20.16	95.09 ± 8.18	0.917	0.386	0.334
V20	81.72 ± 7.33	63.19 ± 18.20	63.49 ± 14.16	0.006	0.009	0.963
V30	46.38 ± 14.87	26.49 ± 10.47	27.94 ± 9.04	0.001	0.002	0.791
V40	14.81 ± 7.53	7.15 ± 4.71	8.81 ± 4.34	0.006	0.032	0.537
V50	7.76 ± 5.49	0.01± 0.02	0.11 ± 0.17	<0.001	<0.001	0.944
65cc	50.61 ± 1.90	41.32 ± 2.90	42.18 ± 3.49	<0.001	<0.001	0.502
120cc	47.46 ± 4.70	38.66 ± 4.11	39.14 ± 4.44	<0.001	<0.001	0.809
195cc	41.94 ± 6.90	35.15 ± 4.67	35.69 ± 5.12	0.012	0.02	0.831
Min	3.70 ± 0.90	4.82 ± 1.60	6.32 ± 2.70	0.193	0.004	0.086
Mean	27.93 ± 6.23	23.32 ± 5.40	23.05 ± 5.53	0.084	0.068	0.916
Max	53.57 ± 0.92	50.80 ± 1.15	51.47 ± 2.03	<0.001	0.003	0.312

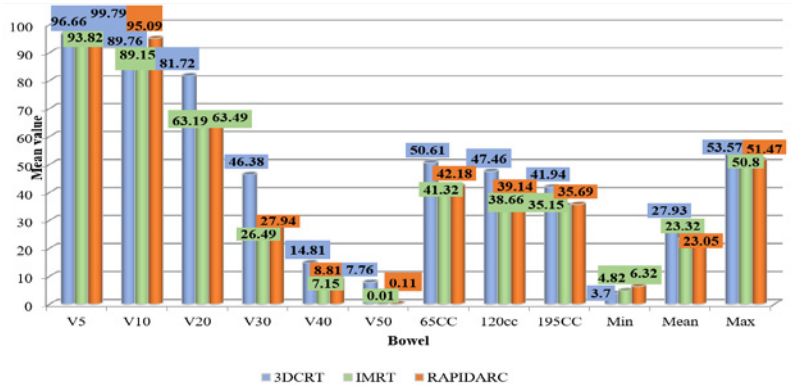

Figure 7: Bar chart of Comparison of mean bowel across the study group.

Table 5: Comparison of mean bilateral femoral heads across the study group.

Bilateral Femoral Heads	3DCRT (Mean ± SD)	IMRT (Mean ± SD)	RapidArc (Mean ± SD)	p value		
				3DCRT *vs* IMRT	3DCRT *vs* RapidArc	IMRT *vs* RapidArc
V5	97.50 ± 5.12	94.37 ± 6.30	96.33 ± 5.98	0.239	0.655	0.459
V10	95.01 ± 7.54	69.80 ± 13.91	75.58 ± 13.10	<0.001	0.001	0.299
V20	88.15 ± 14.90	30.92 ± 8.05	33.32 ± 8.46	<0.001	<0.001	0.628
V30	49.27 ± 26.49	8.16 ± 2.69	12.12 ± 3.24	<0.001	<0.001	0.572
V40	10.38 ± 2.64	1.39 ± 0.87	2.80 ± 1.24	<0.001	<0.001	0.085
V50	3.59 ± 1.98	0 ± 0	0.02± 0.06	<0.001	<0.001	0.947
Min	5.62 ± 2.40	2.88 ± 1.21	3.39 ± 1.25	0.001	0.007	0.509
Mean	27.75 ± 6.20	16.12 ± 2.41	17.19 ± 2.57	<0.001	<0.001	0.568
Max	52.29 ± 1.09	48.89 ± 2.55	49.42 ± 1.96	0.001	0.003	0.551

differences in terms of V10, V20, V30, V40, V50, minimum dose, mean dose and maximum dose in favor of IMRT.

- Between 3DCRT and RapidArc, there were significant differences in terms of V10, V20, V30, V40, V50, minimum dose, mean dose and maximum dose in favor of RapidArc.
- There were no significant differences between IMRT and RapidArc with any of the parameters.

Interpretation of bone marrow dosimetry (Table 6, Figure 9):

- No significant differences were found for V5 and V10

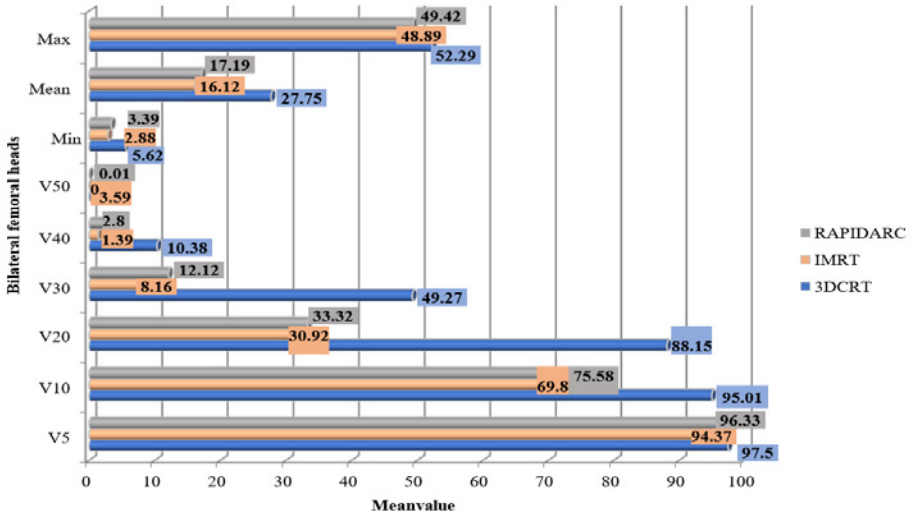

Figure 8: Bar chart of Comparison of mean bilateral femoral heads across the study group.

Table 6: Comparison of mean bone marrow across the study group.

Bone Marrow	3DCRT	IMRT	RapidArc	p value		
				3DCRT *vs* IMRT	3DCRT *vs* RapidArc	IMRT *vs* RapidArc
V5 (Mean ± SD)	97.70 ± 6.40	97.22 ± 6.83	97.22 ± 6.87	0.874	0.873	0.999
V10 (Mean ± SD)	96.29 ± 7.06	94.21 ± 7.166	95.67 ± 7.38	0.524	0.85	0.653
V20 (Mean ± SD)	93.60 ± 7.68	79.95 ± 5.24	75.10 ± 7.65	<0.001	<0.001	0.131
V30 (Mean ± SD)	81.53 ± 8.34	48.21 ± 6.68	45.53 ± 14.26	<0.001	<0.001	0.566
V40 (Mean ± SD)	46.58 ± 4.19	15.22 ± 4.53	17.94 ± 9.59	<0.001	<0.001	0.365
V50 (Mean ± SD)	28.95 ± 5.69	0.08 ± 0.19	0.19 ± 0.50	<0.001	<0.001	0.943
Min (Mean ± SD)	4.87 ± 1.85	4.21 ± 2.13	5.33 ± 3.14	0.548	0.676	0.311
Mean (Mean ± SD)	38.76 ± 2.96	28.71 ± 1.52	27.29 ± 1.60	<0.001	<0.001	0.149
Max (Mean ± SD)	53.68 ± 0.87	51.78 ± 1.39	51.36 ± 2.41	0.18	0.005	0.576

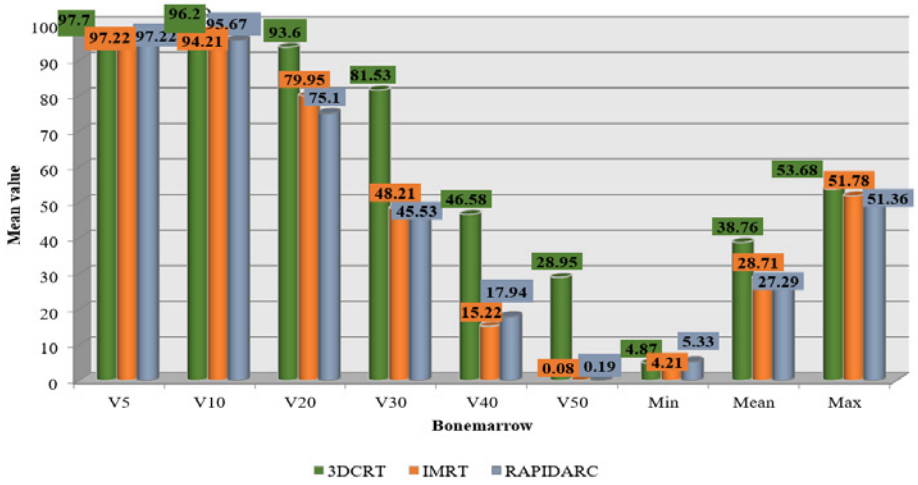

Figure 9: Bar chart of Comparison of mean bone marrow across the study group.

Table 7: Comparison of mean dose and index across the study group (n=10).

Parameter	RapidArc	IMRT	3DCRT	p value		
				IMRT *vs* RapidArc	3DCRT *vs* RapidArc	3DCRT *vs* IMRT
Integral dose	25.94 ± 4.08	26.67 ± 4.32	31.64 ± 5.90	0.738	0.014	0.029
Homogeneity index	1.08 ± 0.02	1.08 ± 0.02	1.07 ± 0.02	0.648	0.339	0.162
Conformity index	0.98 ± 0.02	0.97 ± 0.02	0.99 ± 0.01	0.155	0.091	0.003
Target volume coverage	0.81 ± 0.03	0.73 ± 0.03	0.82 ± 0.07	0.001	0.567	<0.001
Gradient index	1.01 ± 0.01	1 ± 0	0.93 ± 0.02	0.169	<0.001	<0.001
Unified dosimetry index	0.86 ± 0.04	0.76 ± 0.05	0.81 ± 0.08	0.001	0.062	0.1

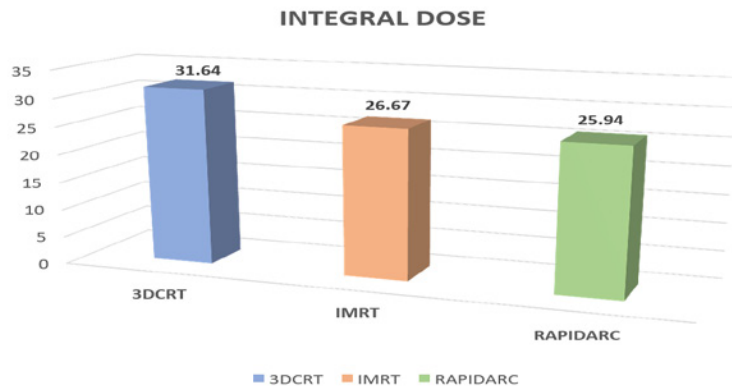

Figure 10: Bar chart of Comparison of mean integral dose across the study group (n=10).

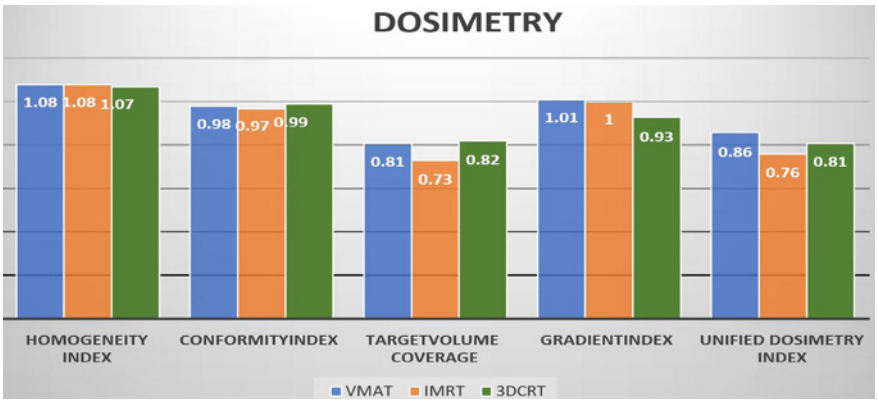

Figure 11: Bar Histogram comparison of various dosimetry indices across the study group (n=10).

between the study groups.

- Between 3DCRT and IMRT, there were significant differences in terms of V20, V30, V40, V50 and Mean dose in favor of IMRT whereas maximum dose was not significant.
- Between 3DCRT and RapidArc, there were significant differences in terms of V20, V30, V40, V50, Mean dose and Maximum dose in favor of RapidArc.
- There were no significant differences between IMRT and RapidArc with any of the parameters.

Dosimetry (Table 7, Figure 10, Figure 11):

Interpretation integral dose:

- Between 3DCRT and IMRT, significant difference was found in favor of IMRT with p=0.029.
- Between 3DCRT and RapidArc, significant difference was found in favor of RapidArc with p=0.014.
- Between IMRT and RapidArc, there was no significant difference with p=0.738.

Homogeneity index: No significant differences were found between the study groups.

Conformity Index:

- Between 3DCRT and IMRT, significant difference was found in favor of 3DCRT (p=0.003).

Table 8: Comparison of mean monitor units across the study group (N=10).

Parameter	RapidArc	IMRT	3DCRT	p value		
				RapidArc *vs* IMRT	RapidArc *vs* 3DCRT	IMRT *vs* 3DCRT
Monitor units	628.90 ± 106.62	1551.10 ± 197.45	255.30 ± 19.17	<0.001	<0.001	<0.001

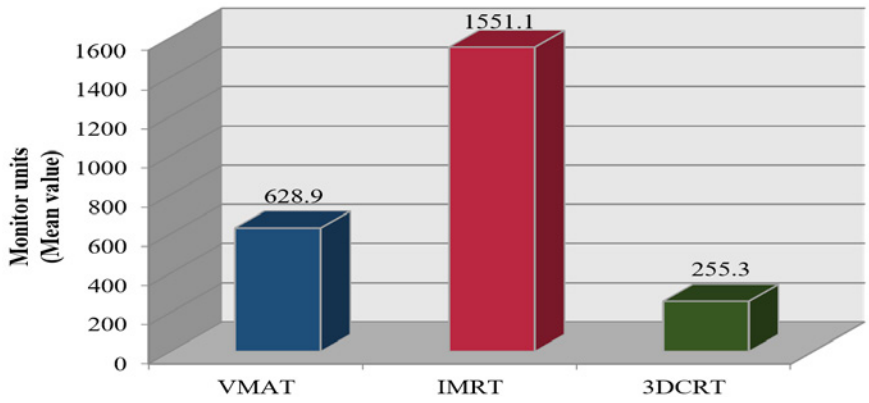

Figure 12: Bar chart of Comparison of mean monitor units across the study group (N=10).

- No significant differences were found between 3DCRT and RapidArc or IMRT and RapidArc.

Target volume coverage:

- Between 3DCRTand IMRT, significant difference was found in favor of 3DCRT with p<0.001.
- Between 3DCRT and RapidArc, no significant difference was found (p=0.567).
- Between IMRT and RapidArc, there was significant difference in favor of RapidArc with p=0.001.

Gradient Index:

- Between 3DCRT and IMRT, significant difference was found in favor of IMRT with p<0.001.
- Between 3DCRT and RapidArc, significant difference was found in favor of IMRT with p<0.001.
- Between IMRT and RapidArc, there was no significant difference with p=0.169.

Unified dosimetry index:

- No statistically significant difference was found between 3DCRT and IMRT with p=0.1
- Between 3DCRT and RapidArc, there was no statistically significant significant difference with p=0.06
- Between IMRT and RapidArc, there was statistically significant difference with p=0.001 in favor of IMRT

Interpretation (Table 8, Figure 12):

- Significant difference was found between 3DCRT and IMRT in favor of 3DCRT (p<0.001).
- Significant difference was found between 3DCRT and RapidArc in favor of 3DCRT (p<0.001).
- Significant difference was found between IMRT and RapidArc in favor of RapidArc (p<0.001).

Discussion

While planning Radical External Beam Radiotherapy for a patient of Carcinoma cervix FIGO 2018 stage IIIC2, the oncologist has to take various factors into consideration. These are the patient related factors such as Age, Performance status, Comorbidities, Renal function, Baseline Hemoglobin and treatment related factors such as Total dose, Dose per fraction, Treatment volume/field, Technique, dose to organs at risk and administration of concurrent chemotherapy.

Atiq et al. compared RapidArc and IMRT in terms of plan quality of Pelvic RT for cervical cancer and concluded that RapidArc was better in terms of homogeneity, conformity, coverage, high gradient index and better normal tissue sparing with comparable integral dose [11]. Literature for comparison of techniques for extended field RT in cervical cancer are lacking.

In terms of integral dose to the whole body, whereas no significant difference was found between IMRT and RapidArc, we found that 3DCRT did worse when compared to IMRT and RapidArc. While there was no significant difference in terms of homogeneity index, 3DCRT was doing significantly better with respect to conformity index than the other two study groups.

3DCRT and RapidArc did significantly better having target volume coverage of 82% and 81% respectively compared to 73% of IMRT. Though the ideal target coverage is >90%, a coverage of 80% or more is acceptable as a minor deviation as stated by ICRU. It is also not uncommon for oncologists accept a lower target coverage for protection of an OAR [13].

All the study groups had acceptable dose gradient index and UDI values. As regards to the monitor units, 3DCRT (255.3) did

significantly better compared to RapidArc (628.9) and IMRT (1551.1). This translates to a daily treatment time from a few minutes in 3DCRT and RapidArc to nearly 20 minutes with IMRT including time taken for patient positioning and image verification using EPID. Longer treatment times mean more variation in bladder filling during radiotherapy delivery, apart from patient inconvenience especially for those who find it difficult to hold their bladder for a longer time.

Both bladder and rectal filling can be variable throughout the duration of radiotherapy for cervical cancer despite protocol. A bladder volume variation of >130cc from planning can potentially lead to CTV lying outside the PTV. Eminowicz et al proposed that the bladder filling be in the range of 150-300cc accounting for pelvic organ motion during radiotherapy [14]. In our study, the average bladder volume contoured was 197.5cc (Range 170-227.3cc).

Guy et al. in their study showed the dosimetric superiority of IMRT and VMAT compared to 3DCRT for pelvic radiotherapy of cervical cancer in terms of better OAR sparing [15]. On extrapolating these findings and comparing to our study, we did observe better OAR sparing of bladder, anorectum, bilateral kidneys, bowel bag, bilateral femoral heads and bone marrow with the two intensity modulated techniques compared to 3DCRT. 3DCRT fared better with respect to V5 and V10 for the kidneys compared to the intensity modulated techniques.

Cozzi et al. demonstrated superiority of RapidArc over IMRT for pelvic RT in cervical cancer in terms of better homogeneity, conformity, better sparing of bladder, rectum and less integral dose [16].

In our study, we did not find any significant difference in critical organ sparing between RapidArc and IMRT. RapidArc had lower volume doses to bladder, anorectum and bilateral kidneys compared to IMRT whereas IMRT had lower volume doses to bowel bag, bilateral femoral heads and bone marrow. But none of these differences were significant. In some cases like bowel bag, though IMRT had lower volume doses compared to RapidArc, their mean doses were almost equivalent.

The superior target coverage, significantly reduced MU and treatment time with VMAT compared to fixed field IMRT in pelvic RT for cervical cancer was observed by Guo et al. [17], which our study corresponds with.

Limitations

Ours was a retrospective study done in a sample size of 10 patients. Therefore, the clinical toxicity profile with each technique cannot be understood adequately. For this, we need prospective studies with larger sample size and long term follow up.

Conclusion

Loco-regional control after EFRT for cervical cancer is good, the predominant pattern of failure being outside the treatment field. The acute toxicities of concern that occur in these patients are usually bone marrow and bowel related. Intensity modulated techniques outscore 3DCRT in terms of critical organ sparing. Among these, RapidArc might have an advantage over IMRT in terms of better target coverage, significantly less treatment time, lower integral dose to the body while having comparable critical organ sparing if not better.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer J Clinicians. 2018; 68: 394-424.
2. Green JA, Kirwan JM, Tierney JF, et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. The Lancet. 2001; 358: 781-786.
3. Wang N, Guan QL, Wang K, et al. Radio chemotherapy versus radiotherapy in locally advanced cervical cancer: a meta-analysis. Archives of Gyn and Obst. 2011; 283: 103-108.
4. Chemo radiotherapy for Cervical Cancer Meta-Analysis Collaboration. Reducing uncertainties about the effects of chemo radiotherapy for cervical cancer: a systematic review and meta-analysis of individual patient data from 18 randomized trials. J Clini Onc. 2008; 26: 5802.
5. Salama JK, Mundt AJ, Roeske J, Mehta N. Preliminary outcome and toxicity report of extended-field, intensity-modulated radiation therapy for gynecologic malignancies. Int J Radiation Onc Bio Phy. 2006; 65: 1170-1176.
6. Beriwal S, Gan GN, Heron DE, et al. Early clinical outcome with concurrent chemotherapy and extended-field, intensity-modulated radiotherapy for cervical cancer. Int J Radiation Onc Bio Phy. 2007; 68: 166-171.
7. Taylor A, Rockall AG, Powell ME. An atlas of the pelvic lymph node regions to aid radiotherapy target volume definition. Clini Onc. 2007; 19: 542-550.
8. Keenan LG, Rock K, Azmi A, et al. An atlas to aid delineation of para-aortic lymph node region in cervical cancer: Design and validation of contouring guidelines. Radiotherapy and Onc. 2018; 127: 417-422.
9. Kataria T, Sharma K, Subramani V, et al. Homogeneity Index: An objective tool for assessment of conformal radiation treatments. J Med Phy/Association of Medi Phy of India. 2012; 37: 207.
10. Pyakuryal A, Myint WK, Gopalakrishnan M, et al. A computational tool for the efficient analysis of dose volume histograms for radiation therapy treatment plans. J Appl Clini Med Phy. 2010; 11: 137-157.
11. Atiq A, Atiq M, Iqbal K, et al. A comparative study of RapidArc and intensity-modulated radiotherapy plan quality for cervical cancer treatment.
12. Akpati H, Kim C, Kim B, et al. Unified dosimetry index (UDI): a figure of merit for ranking treatment plans. Journal of Applied Clini Med Phy. 2008; 9: 99-108.
13. DasIJ,Cheng CW,Chopra KL, et al. Intensity-modulatedradiationtherapydose prescription, recording, and delivery: Patterns of variability among institutions and treatment planning systems. J Natl Cancer Inst. 2008; 100: 300-307.
14. Eminowicz G, Motlib J, Khan S, et al. Pelvic organ motion during radiotherapy for cervical cancer: understanding patterns and recommended patient preparation. Clini Onc. 2016; 28: e85-e91.
15. Guy JB, Falk AT, Auberdiac P, et al. Dosimetric study of volumetric arc modulation with RapidArc and intensity-modulated radiotherapy in patients with cervical cancer and comparison with 3-dimensional conformal technique for definitive radiotherapy in patients with cervical cancer. Med Dosim. 2016; 41: 9-14.
16. Cozzi L, Dinshaw KA, Shrivastava SK, et al. A treatment planning study comparing volumetric arc modulation with RapidArc and fixed field IMRT for cervix uteri radiotherapy. Radiother Onc. 2008; 89: 180-191.
17. Guo M, Huang E, Liu X, Tang Y. Volumetric modulated arc therapy versus fixed-field intensity-modulated radiotherapy in radical irradiation for cervical cancer without lymphadenectasis: dosimetric and clinical results. Oncol Res Treat. 2018; 41: 105-109.