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Research Article

Dosimetric Distribution of Vmat Versus 3dcrt in Treatment of Locally Advanced Carcinoma Cervix

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Abstract

Introduction: Cervical Cancer is 4th most common cancer among females. Globally with 604,000 new cases and 342,000 deaths reported annually according to 2020 data. About 90% death occurred in low and Middle-income countries by carcinoma cervix. Concurrent chemoradiation combined with brachytherapy is the standard of care in locally advanced carcinoma cervix.

Method: The aim is to study the dose distribution and advantage of VMAT with conventional radiotherapy. Randomized comparative perspective study in which we have included 60 patients. A total of 60 patients were included and analyzed for disease status at the end of treatment.

Result: No significant differences observed in Dmax, D95, CI, and HI values. VMAT with Rapid Arc plan showed reduced OAR doses, while 3DCRTFIF exhibited higher Bowel V45Gy compared to VMAT with Rapid Arc plan. In our study, Rapid arc shown lower dose to bladder as compart to 3DCRT at D15 49.6 Gy Vs-51.1, D30 48.7 Gy vs 50.7 Gy, D50 46.8 Gy vs 50.4 Gy. Bone marrow toxicity was 10% (9) lesser in VMAT arm as compared to 3D CRT. Some observational studies shown hematological toxicities were higher when used with combination of chemotherapy as compared to EBRT alone (27). 3DCRT patients' median absolute volume was twice received 40 Gy than 3 VMAT. Sometimes it resulted in interruption and delay of treatment time exceeded 52 days causes loss of local treatment and decreases overall survival approximately 1% per day.

Keywords: Volumetric Modulated Arc Therapy; Intensity-Modulated Radiation Therapy; Carcinoma Cervix

Abbreviations

Cervical Cancer is 4th most common cancer among females. Globally with 604,000 new cases and 342,000 deaths reported annually according to 2020 data. About 90% death occurred in low and Middle-income countries by carcinoma cervix [1]. Concurrent chemoradiation combined with brachytherapy is the standard of care in locally advanced carcinoma cervix. With combined modality approach, 5-year disease free survival and overall survival reported 50 to 60% respectively. Local failure rate reported approximately 30% [2]. Concurrent chemo radiotherapy reduced local and distant failure rate and improve [3,4] survival rate with same side effect [5-8]. Recently newer techniques have been introduced in radiation oncology.

Volumetric radiotherapy and [9,10] intensity modulated radiotherapy [7,8]. These techniques were demonstrated favorable outcome by achieving excellent dose distribution and manageable toxicity [9-14].

Early clinical studies shown lower rate of gastrointestinal genitourinary toxicity with volumetric arch therapy than conventional radiotherapy technique. Volumetric arch therapy is a type of intensity modulated radiotherapy with single gantry motion and multileaf collimation have reported improved target coverage with less dose to organ at risk [15]. In addition to dose, patient and target immobilization, tissue conformation and reproducibility are additional factors which limit the OAR toxicity and treatment outcome [16-18]. To minimize the toxicity and improve outcome specialized contouring guidelines have been recommended [19].

Methods

The aim is to study the dose distribution and advantage of VMAT with conventional radiotherapy. Randomized comparative perspective study in which we have included 60 patients. 30 patients in 3D CRT arm and 30 Patients in VMAT arm between Jan 23 to April 23. All cases were histologically proven. Radiological imaging

CECT whole abdomen have been done. All the routine blood investigation has been done.

From stage IIIA -IVA

Staging done according to FIGO, have been included in the study. Patients with distant metastasis have been excluded.

Radiation and chemotherapy

External beam radiotherapy was given with 6MW to 15MW linear accelerator. Histological proven squamous cell carcinoma with stage IIIA to IVA. Carcinoma cervix treated with radiotherapy. The duration was from Jan 2022 to July 2022. Chemotherapy given in all the cases who were newly diagnosed and had not received any treatment under chemotherapy or radiotherapy. All the patients were treated with curative intent. We analyzed the patients who were received EBRT with chemotherapy and patients had karnofsky score >70. We reviewed clinical record of the patient and analyzed following things.

CT simulation

Before simulation patients were instructed to follow bladder and bowel protocols. Patients were immobilized in supine position and thermoplastic mask was kept on their pelvis. Intravenous contrast pushed by auto injector and CT-Simulation was performed by taking 3-5 mm slice thickness on the whole abdomen and pelvis by CT Simulation machine.

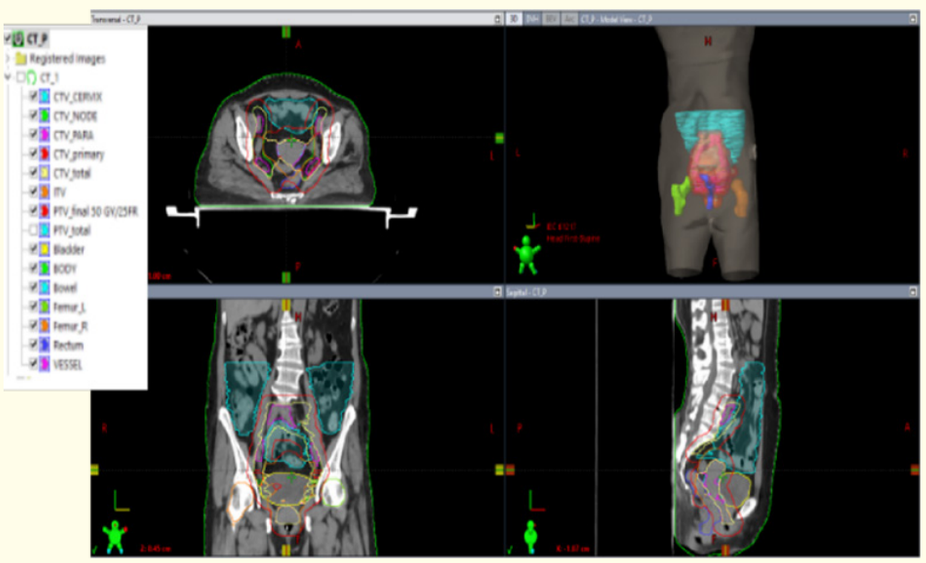

Figure 1: Image of CT Simulation.

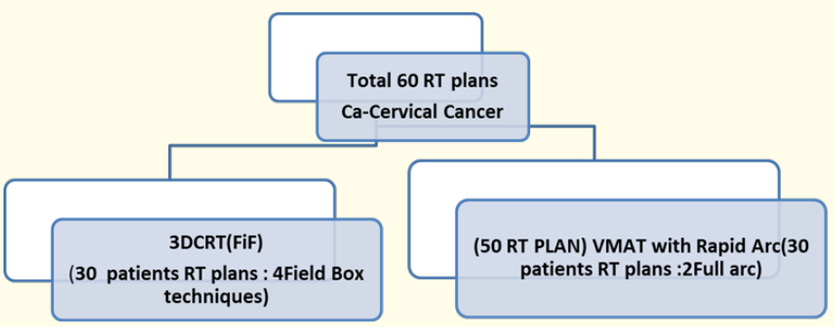

Figure 2

All plans generated using Eclipse Treatment Planning System, Ver. 16.1 with 6MV, Photon optimizer (PO). All Patients received weekly cisplatin 40mg/m^2 during the external radiation. The differences in dosages for the Planned Target Volumes (PTVs), Organs At Risk (OARs) and MU(Monitor Unit) between the two techniques were analyzed with the help of DVH statistics.

Planning goal

- At least 95% of the prescribed dose was delivered to 95% of the PTV in all plans.
- OARs Doses: Femoral heads (Dmax<52Gy, V30Gy<15%), Bladder (Dmax<52.5Gy, V40<60%, V45<55%) and rectum (Dmax<52.5Gy, V40<100%), Bowel volume V45Gy below 195cc

All the plans were compared and evaluated

PTV Target Coverage: The primary goal was to ensure at least 95% of the prescribed dose was delivered to 95% of the PTV in all plans.

The formulas for CI and HI are as follows.

Conformity Index (CI): This measures how well the prescribed isodose volume conforms to the PTV.

Conformity index (CI) =VRI/TV

Where, VRI is the volume of the prescription reference isodose, and TV is the total PTV volume. The closer the values of CI close to 1.0, the better the dose conformity.

Homogeneity Index (HI): This index evaluates the homogeneity of the dose distribution within the PTV.

HI=D5%/D95%

Where, D5%is the dose delivered to 5% of the volume, and D95% is the dose delivered to 95% of the volume. Values of HI closer to 1 indicate greater dose homogeneity within the volume of PTV.

OARs (Organs at Risk) Doses: This includes the evaluation of doses to specific organs, such as the Bladder, Rectum, Femoral Head, and Bowel, at different percentages of their volumes (D15, D35, D50). Limiting doses to OARs is crucial to minimize treatment-related side effects.

Maximum Dose to Bowel Bag at V45Gy of 195cc: This specifies the maximum dose to a specific volume of the bowel. Keeping this dose within acceptable limits is essential to prevent adverse effects.

Results

A total of 60 patients were included and analyzed for disease status at the end of treatment.

- **Patient Characteristics:** Predominantly over 50 years old with squamous cell carcinoma. Most patients staged as IIIA and IIIB according to FIGO.
- **Hemoglobin Levels:** Range: 7.5-9.5 gm%. 17% of patients required blood transfusions during treatment.
- **Treatment Duration:** Median duration: 5 weeks, with intermittent breaks due to low hemoglobin levels and gastrointestinal side effects.
- **Findings:** No significant differences observed in Dmax, D95, CI, and HI values. VMAT with Rapid Arc plan showed reduced OAR doses, while 3DCRTFIF exhibited higher Bowel V45Gy compared to VMAT with Rapid Arc plan.

Patient characteristics

	3DCRT(30)	IMRT(30)
Age		
Mean	4.5+/-10.5	4.9+/-10.9
Median	50	53
Addiction		
Smoking	5/30(16%)	6/30(20%)
Tabacco chewing	3/30(10%)	2/30(6.6%)
Chief complain		
White discharge per vagina	80%	85%
Bleeding per vagina	70%	72%
Pain in abdomen	56%	58%
Backache	26%	32%
Parity		
Nulliparity	2/30(6.6%)	0/30
Multiparity	28/30(93.3%)	30/30(100%)
HPE		
Keratinizing Sq cell cancer	56.6%	53.3%
Non Keratinizing Sq cell cancer	40%	45%
Adeno sqamous	3.3%	1.7%
Stage		
Stage IIIA	12/30(40%)	15/30(50%)
Stage IIIB	16/30(50%)	9/30(30%)
Stage IV A	3/30(10%)	6/30(20%)
Menopause		
Post menopause	25(83.3%)	2.2(73.3%)
Pre menopause	5(16.6%)	8(26.6%)

Table a

PTV Coverage

The PTV Coverage details Dmax, Dmin, D95%, HI and CI of both techniques are shown in Table. Rapid Arc plan lowest minimum dose inside PTV (Dmin) with mean dose of 41.3Gy which significantly increased to 42.4Gy in 3DCRT (FIF). The PTV Coverage, HI and CI non-significant differences was observed in both techniques.

PTV	RAPID ARC			3DCRT FIF			p-value
	Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD	
Dmax	50.8	55.4	53.8 ± 1.00	21.9	55.4	52.2 ± 6.38	0.3175025
Dmin	25.9	50	41.3 ± 5.87	23.5	51.2	42.4 ± 5.11	0.5121245
D95%	88.4	98	96.6 ± 1.90	92.9	99.8	97.3 ± 1.76	0.2330152
HI	1.04	1.14	1.06 ± 0.0190	0.969	1.14	1.07 ± 0.0305	0.1392026
CI	0.75	1	0.970 ± 0.068	0.708	0.999	0.966 ± 0.06	0.8392579

Table b

Organs at risk

The mean value of D15, D35, D50 of urinary bladder were lower in Rapid arc as compared to 3DCRT (FIF) and significant difference was observed. Dose to rectum significant differences was observed in both techniques and D50 dose to rectum is 49.01Gy in Rapid arc is lower than 49.83Gy in 3DCRT(FIF). Both Femoral Heads Dmax was higher in 3DCRT(FIF) as compared to VMAT and showed significant differences.

Difference in Doses to OAR In 3DCRT(FIF) and IMRT Techniques

0ARs		PAPID ARC			3DCRT FIF			p-value
		Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD	
Baldder	D15%(Gy)	45.9	50.8	49.6 ± 0.953	49.4	52.8	51.1 ± 1.10	0.000639
	D35%(Gy)	42.1	50.2	48.7 ± 1.75	49	52.3	50.7 ± 1.03	0.00032
	D50%(Gy)	32.8	49.9	46.8 ± 4.05	48.8	52.2	50.4 ± 0.988	0.00013
Rectum	D35%(Gy)	49.9	50.6	49.61.14	49.6	52.6	50.7 ± 0.861	0.000442
	D50%(Gy)	42.1	50.2	48.7 ± 1.75	49	52.3	50.7 ± 1.03	0.000013
	D15%(Gy)	44.4	49.8	49 ± 1.10	47.8	52.1	49.8 ± 1.01	0.0102817
RT F. H	Dmax(Gy)	45.8	51.2	49.1 ± 1.42	50.2	53.4	51.8 ± 0935	0.000131
LT. F. H	Dmax(Gy)	46.3	56.3	49.7 ± 1.90	49.9	53.3	51.7 ± 0.922	0.0000274
Bowel	195cc=Gy	16.7	556	256 ± 139	11.7	204	65.7 ± 55.7	0.0000274

Table c

DVH analysis

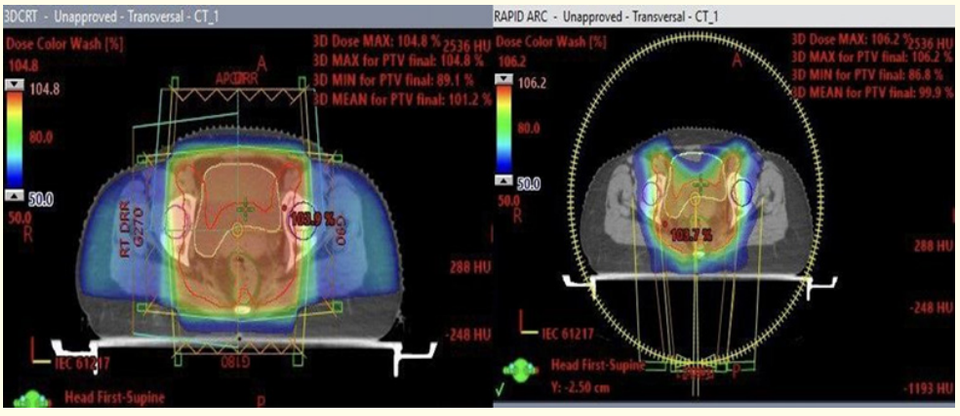

Figure 3: The figure illustrates the Planning Target Volume (PTV) coverage in the axial slice of a patient using both the 3DCRT (Field in Field) technique and VMAT with Rapid Arc planning.

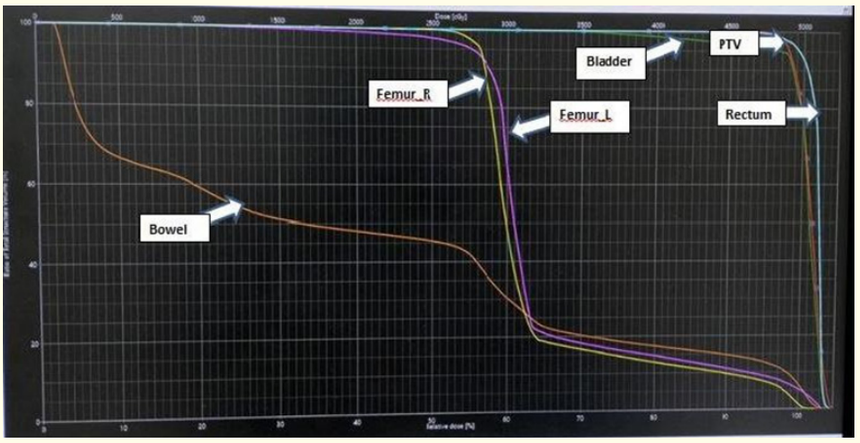

Figure 4: Figure shows PTV, Bladder, Bowel, Rectum, Femoral head of 3DCRT planning technique.

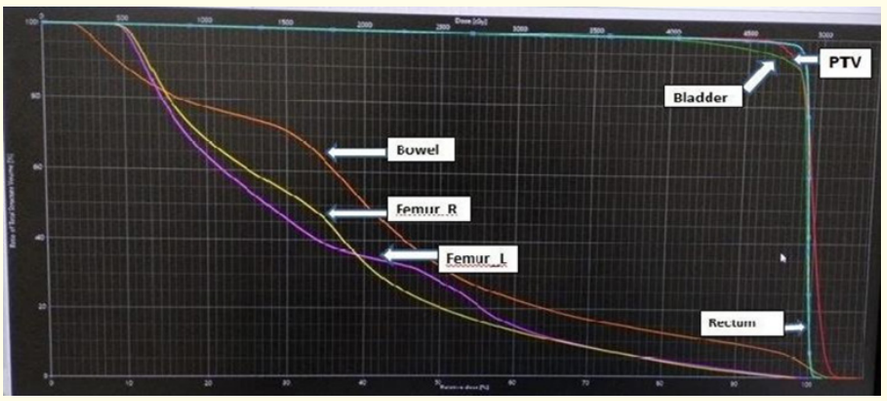

Figure 5: Figure shows PTV, Bladder, Bowel, Rectum, Femoral head coverage of Rapid Arc planning technique.

Toxicity profile of patients

Acute Toxicity		3DCRT	RAPID ARC	P-VALUE
	GRADE	(30)		
Genito urinary	1	10(33.3%)	6(20%)	0.003
	2	3(10%)	1(3.3%)	0.052
	3	0	0	
Gastro intestinal	1	9(30%)	7(23.3%)	0.141
	2	6(20%)	2(6.6%)	0.023
	3	1(3.3%)	0	
Anemia	1	14(46.6%)	11(36.6%)	0.146
	2	8(26.6%)	5(16.6%)	0.256
	3	2(6.6%)	1(3.3%)	0.034
Neutropenia	1	4(13.3%)		0.382
	2	4(13.3%)		
	3	2(6.6%)		
Thrombocytopenia	1	15(6.6%)	3(10%)	0.029
	2	2(6.6%)	0	
	3	0	0	

Table d

Discussion

Both 3D CRT and VMAT showed proper dose coverage to target and planning target volume (PTV), D max and Dmean were in acceptable range according to ICRU guidelines [25]. Cozzi., *et al*. and Sharfo., *et al*. showed similar result of target volume coverage while study done by Renard- D drini found an improved target coverage [13,14,20]. Cozzi., *et al*. found better organ at risk sparring with Sherfo., *et al*. have different observation [13,14]. Study done shown superior statistically significant CI as compared to 3D CRT. Similar results were reported by Gary., *et al*. in locally advanced cervical cancer [15]. Value of conformity closer to 1 suggest more conformal distribution of radiation does. High precision radiotherapy can be delivered by improved conformity and it is essential in tumor does escalation -36 and minimization of high dose exposure to OAR. Major goal of radiotherapy is to conformity delivery of maximum prescribed dose to target volume and thus increase tumor control.

Hi can be defined as uniformal distribution of radiation does to target volume. In our study both C1 and H1 were achieved nearer to 1. Rectal dose D15 received 49.6 Gy vs 50 Gy and D30 48.7 Gy vs 50.7 which D50 was 49 Gy vs 49.9 Gy. Respective trial conducted by Gallagher., *et al*. evaluated various radiotherapy techniques to reduce radiation does to small bowel in a patient undergoing irradiation to pelvic area [21]. Severity of acute effects are related with volume of small bowel irradiated. Acute and late effects are associated with small bowel volume received more than 45 Gy. Cozzi., *et al*. reported greater reduction of radiation does to small bowel volume receiving more than 40 Gy with VMAT [13].

Study done by Droje shown significant reduction of late small toxicity with VMAT. Late small bowel toxicity is associated with the bowel volume received higher dose of radiation >50 Gy [22]. These dosimetric advantage with VMAT technique can resulted into clinical efficiency. Due to reduction of small bowel toxicity long term morbidity can be reduced remarkably. In our study, small bowel about 195cc received radiation dose of VMAT which 256 cm received in 3D CRT. Study done by Rosak., *et al*. interruption of treatment during course of radiation were due to gastrointestinal toxicity [23]. Study done by Pagera reported increased acute genitourinary toxicity. Grade 3 urinary toxicity were reported 3.3% with VMAT. Vandeeatic., *et al*. reported 0% and Gandhi., *et al*. reported 05% with IMRT [12,24]. Gandhi., *et al*. found similar rate of genitourinary toxicity with IMRT and 3D CRT [10]. Some other studies shown 13.6 % grade 3 genitourinary toxicity [12]. Some studies shown about 25% of all patients reported acute urinary toxicities [24,25]. Lin., *et al*. showed lower bladder doses after meta-analysis of cervical cancer treatment by IMRT [26].

In our study, Rapid arc shown lower dose to bladder as compart to 3DCRT at D15 49.6 Gy Vs-51.1 , D30 48.7 Gy vs 50.7 Gy, D50 46.8 Gy vs 50.4 Gy. Bone marrow toxicity was 10% [9] lesser in VMAT arm as compared to 3D CRT. Some observational studies shown hematological toxicities were higher when used with combination of chemotherapy as compared to EBRT alone [27]. 3DCRT patients' median absolute volume was twice received 40 Gy than 3 VMAT. Sometimes it resulted in interruption and delay of treatment time exceeded 52 days causes loss of local treatment and decreases overall survival approximately 1% per day [28].

Various studies suggested that IMRT offers better OAR sparing in gynecological cancer [29]. Similar finding shown by study done by Raseka., *et al*. organ at risk toxicity depend upon maximum does receive by femoral head, bladder, rectum, bowel bag and bone marrow. Well., *et al*. shown correlation with dosimetric value and clinical symptoms resulted acute and chronic symptoms [28]. Rectal dose shown more favorable dosimetric distribution for VMAT resulted decrease in clinical toxicity to rectum. According to RTOG 1203-29 [31].

In our study, dose received (R) and (L) femur was lesser compared to 3D CRT (FIF). (P-0.000131) and (0.000274) respectively.

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