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Dosimetric Comparison of 3-Dimensional Conformal Radiotherapy (3DCRT), Intensity Modulated Radiotherapy (IMRT) and Volumetric-Arc Radiotherapy (VMAT) in Cervical Cancer Treatment

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Abstract

Background: Cervical cancer being the fourth most frequently diagnosed cancer, concurrent chemoradiation forms the mainstay of the treatment from stage IB3 to IVA. As we witnessed advancement in radiotherapy technologies, attempts had been taken to reduce the dose to the OARs without compromising the tumor coverage. In this study we will compare the PTV coverage, conformity index and doses received by the OARs (urinary bladder, rectum, bowel bag, bilateral head of femur) by all the three techniques namely 3DCRT, IMRT and VMAT for carcinoma cervix patients undergoing concurrent Chemoradiotherapy (CRT) at our institution and further implement the results in our clinical practice.

Material and Methods: Forty-five of biopsy-proven carcinoma cervix in stage IIA to IIIB were taken up for the study. Following imaging, contouring was carried out using the principal clinical findings and conventional RTOG recommendations. Dose prescription to the cervix was 50 Gy in 25 fraction and planned with all three modalities, 3DCRT, IMRT and VMAT. The patient was treated with the 3DCRT plan and the IMRT and VMAT plans were made for dosimetric purpose only.

Results: Quantitative dose evaluation performed of three techniques V40, V45, V50, Dmean for Bladder and Rectum, Dmean and D100 for Femur, V30, V40, D195 CC, Dmean for Bowel. Results show that VMAT plan is preferable than IMRT for sparing Bladder and rectum.

Conclusion: IMRT and VMAT both could be advocated for practice was tumor coverage was almost similar in both of them and decision could be made on patient specific logistics.

Keywords: Concurrent Chemoradiotherapy; Cancer; Radiotherapy

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Introduction

Cervical cancer is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women, with an estimated 604,000 new cases and 342,000 deaths worldwide in 2020 [1]. In India, cancer of cervix uteri ranks third among the new cases diagnosed with cancer (123,907 cases, 9.4%, cumulative risk 2.01) but ranks second for mortality by cancer site (77,348 cases, 9.1%, cumulative risk 1.30). The 5-year prevalence for all ages is 42.82 per 100,000 [2].

For treatment of cervical cancers, surgery is typically reserved for early-stage disease (stage IA, IB1, IB2 and selected cases of stage IIA1) [3]. Concurrent chemoradiation forms the mainstay of the treatment from stage IB3 to IVA [4,5]. A recent meta-analysis suggested a 6% improvement in 5-year survival (Hazard Ratio [HR] 0.81; P<0.001) [6]. For patients without nodal disease or with disease limited to the pelvis only, treatment consists of pelvic EBRT with concurrent platinum-containing chemotherapy and brachytherapy [4,5,7,8].

As we walked through different ages of radiotherapy we developed better and better techniques with much greater precision and conformity and eventually also decreasing the treatment related side effects experienced by the patients. Conventionally, radiotherapy was given through a 2 field (AP-PA) approach or a 4-field approach (AP-PA and 2 lateral fields) to cover the gross disease with coverage to the bilateral parametria also [9]. Delivering 45 Gy to 50 Gy results in significant morbidity, especially hematological, genitourinary and gastrointestinal. So, attempts had been taken to reduce the dose to the OARs without compromising the tumor coverage [10,11].

3-Dimensional Conformal Radiotherapy (3DCRT), Intensity Modulated Radiotherapy (IMRT) and Volumetric-arc radiotherapy (VMAT) are the three major techniques that are widely used depending upon the availability at the respective centers. The dosimetric analysis in terms of Planning Target Volume (PTV) coverage and doses received by the Organs at Risk (OARs) has shown similar coverage of PTV but much lesser doses to the OARs with advancing technique from 3DCRT to IMRT/VMAT [12]. So, in dosimetric terms, VMAT is superior to 3D-CRT for EBRT of locally advanced cervical cancers [13]. There are very few studies comparing head-to-head dosimetry in cervical cancer cases for 3DCRT, IMRT and VMAT. In this study we will compare the PTV coverage, conformity index and doses received by the OARs (urinary bladder, rectum, bowel bag, bilateral head of femur) by all the three techniques namely 3DCRT, IMRT and VMAT for carcinoma cervix patients undergoing Concurrent Chemoradiotherapy (CRT) at our institution and further implement the results in our clinical practice.

Material and Methods

Forty-five of biopsy-proven carcinoma cervix in stage IIA to IIIB were taken up for the study. All patients were simulated in supine position without thermoplastic mold but with knee rest for immobilization. IV contrast was given with dose calculated at 1 ml/Kg up to a maximum of 60 ml. Scans were taken in a slice thickness of 2.5 mm from T12 vertebral level to mid-thigh. Fiducials were placed at the expected isocenter, approximately halfway between the umbilicus and the symphysis pubis in the midplane.

Following imaging, contouring was carried out using the principal clinical findings and conventional RTOG recommendations. To create the final PTV, the primary and nodal CTVs were united and given extensions of 0.7 cm in all directions.

Dose prescription to the cervix was 50 Gy in 25 fraction and planned with all three modalities, 3DCRT, IMRT and VMAT. The patient was treated with the 3DCRT plan and the IMRT and VMAT plans were made for dosimetric purpose only. Angle (0, 90, 180 and 270 in 3DCRT and 0, 51, 102, 153, 204, 255, 306 in IMRT) is used to evenly separate coplanar beam and Further more full arcs (clockwise and anticlockwise) used in VMAT. Energy used in IMRT, VMAT 6X and in 3DCRT lateral 15X and AP and PA according to depth 10X and 6X respectively.

The planning goal was 95% of Prescription Dose (PD) to cover 98% of the PTV and not exceed 105% of maximum dose. OARs dose analyzed according to both QUANTEC and EMAMI.

Maximum control points per arc VMAT 180 IMRT 30, minimum segment width (cm) VMAT 0.5 & IMRT 0.5, fluence smoothing medium for both VMART & IMRT, grid spacing 0.3 for Vmat and Imrt both and for 3D it was 0.5. Algorithm Monte Carlo was used for VMAT and IMRT & collapsed cone in 3D version- monaco 6.00.01.

Analyses (including the mean and standard deviation of aforementioned parameter as mentioned in the Table 1, averaged nearly the 20 selected cases) were carried out with the use of Microsoft Excel 2016. Furthermore, the Histogram and 2D scatter plot were obtained using ORIGIN Pro 2019b.

Results

Out of the total 45 patients included in the study, five patients of IIA stage, twenty patients with IIB stage, five patients with IIIA stage and fifteen patients with IIIB stage of cervical cancer were selected along with median age of 54 years.

The detailed dosimetry comparisons between 3DCRT, IMRT AND VMAT are shown in Table 1. As compared to IMRT, VMAT shows similar target dose coverage in addition to less HI and more CI.

The Conformity Index (CI) and Homogeneity Index (HI) were 0.88 and 1.05 respectively for IMRT, and 0.84 and 1.06 respectively for VMAT.

Quantitative dose evaluation performed of three techniques V40, V45, V50, Dmean for Bladder and Rectum, Dmean and D100 for Femur, V30, V40, D195 CC, Dmean for Bowel. Results show that VMAT plan is preferable than IMRT for sparing Bladder and rectum.

For the bilateral femurs and small bowel, results were comparable between IMRT and VMAT, but superior to 3DCRT. 95% dose to PTV coverage was comparable in all the three plans with no significant difference.

Discussion

3DCRT remains the mainstay of radiation therapy to carcinoma cervix treatment in most of the center today, even after the advent of newer modalities like IMRT & VMAT. But due to very limited studies comparing the dose coverage and OAR sparing, the shift from 3DCRT to IMRT or VMAT has not been attempted so widely. Although now radiotherapy centers are taking a step forward to this road and focus on more and more conformity, sparing the OARs so that we can have a margin of dose constraints for the brachytherapy, ultimately leading

Table 1: Dosimetry comparisons between 3DCRT, IMRT and VMAT.

	3DCRT	IMRT	VMAT
Dmean (PTV)	50.61 ± 0.63	50.53 ± 0.70	50.52 ± 0.67
Dmax (PTV)	52.82 ± 1.50	54.14 ± 0.48	54.72 ± 0.53
Dmean (Bladder)	48.90 ± 2.36	44.89 ± 3.87	44.90 ± 3.17
V40 (Bladder)	91.53 ± 9.64	79.18 ± 11.96	79.40 ± 11.99
V45 (Bladder)	90.83 ± 9.59	71.93 ± 17.33	75.52 ± 10.73
V50 (Bladder)	81.11 ± 14.91	56.31 ± 17.96	49.77 ± 13.82
D100 (Bladder)	37.25 ± 5.94	20.79 ± 9.59	22.51 ± 11.13
Dmean (Rectum)	49.23 ± 2.03	49.31 ± 1.27	48.41 ± 2.16
V40 (Rectum)	96.55 ± 4.97	97.11 ± 2.43	95.50 ± 5.15
V45 (Rectum)	93.30 ± 6.54	95.51 ± 3.99	90.19 ± 9.04
V50 (Rectum)	80.74 ± 15.83	73.82 ± 18.04	68.43 ± 16.72
D100 Gy (Rectum)	29.33 ± 15.05	29.66 ± 14.81	27.61 ± 15.73
Dmean (Left Femur)	24.00 ± 2.76	16.73 ± 3.93	15.99 ± 3.53
D100 Gy (Left Femur)	9.65 ± 7.13	3.04 ± 1.74	4.06 ± 2.61
Dmean (Right Femur)	23.01 ± 3.74	15.25 ± 3.38	15.12 ± 3.18
D100 Gy (Right Femur)	9.47 ± 6.74	2.98 ± 1.70	3.88 ± 2.28
Dmean (Small Bowel)	25.48 ± 4.27	23.15 ± 2.59	24.74 ± 3.20
V30 (Small Bowel)	36.92 ± 7.53	33.18 ± 5.76	32.02 ± 7.61
V40 (Small Bowel)	20.53 ± 6.42	17.82 ± 5.75	17.65 ± 4.75
195 cc Gy (Small Bowel)	46.69 ± 4.19	43.83 ± 4.95	44.63 ± 4.34
H.I.	1.09 ± 0.08	1.05 ± 0.02	1.05 ± 0.02
C.I.	0	0.87 ± 0.04	0.84 ± 0.07
PTV COV 95%	99 ± 1%	99 ± 1%	99 ± 1%

D100: Dose received by 100 percent volume; V45: Volume receiving 45 Gy

to patients with fewer genitourinary and gastrointestinal toxicities.

Previously was a paradigm shift from 2D-box field method to 3DCRT with three-dimensional conformal radiotherapy gives significantly better PTV coverage, which may translate into better local control and survival [14]. Geographically missing the pelvic lymph nodes can have catastrophic effects, especially when the illness is well advanced. The majority (66%) of pelvic nodal failures were marginal, according to research by Beadle et al. [15,16]; 71 out of 119 patients had recurrences above the treatment area, 2 had inguinal nodal failures, and 2 additional patients had recurrences both above the treatment field and in the inguinal lymph nodes. This was one of the earliest studies to link the treatment portals and the place of regional recurrence. So, more studies are now done by which we can spare the organs at risk more and more without actually compromising the tumor and lymph nodal drainage areas coverage.

In our study we compared the three modalities, 3DCRT, IMRT, VMAT for 45 patients, where IMRT and VMAT significantly improved V40 and mean dose for rectum, bladder and small bowel. The PTV coverage and CI were also better with IMRT and VMAT, therefore alleviating our fear of any target miss. This was in agreement to some studies which were done in past few years [16]. Upon comparing IMRT with VMAT, coverage was similar in addition to less HI and more CI.

Previous studies comparing their modalities, the normal dose constraints were evaluated using QUANTEC analysis mostly, but we compared them on both scales of QUANTEC & EMAMI and found that VMAT was superior to both IMRT and 3DCRT.

These practice changing parameters could be incorporated in clinical practice and long-term analysis are warranted that could reflect changes in progression free survival or overall survivals. We had a moderately limited sample size but our results were promising, so it could be carried out on larger sample size and paves way for further research in this regard.

Conclusion

In terms of PTV Coverage, H.I., C.I., and OARs sparing, VMAT was superior to IMRT and 3DCRT. Although IMRT and VMAT both could be advocated for practice was tumor coverage was almost similar in both of them and decision could be made on patient specific logistics.

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Dr. Pritanjali Singh conceived the idea. Mr. Rajhans Kumar done the planning and experiment and carried out the data analysis. Dr. Amrita Rakesh drafted the manuscript. All the authors contributed to the editing and reviewing of paper.

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