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Dosimetric analysis of 3D-conformal radiotherapy and intensity modulated radiotherapy for treatment of advanced stage cervical cancer: A comparative study

Gangarapu Sri Krishna[1,3], Marella Venkata Ramireddy[1], Komanduri Ayyangar[2], Palreddy Yadagiri Reddy[3]

[1]*Department of Radiotherapy, MNJ Institute of Oncology & Regional Cancer Centre, Hyderabad -500004, Telangana, India.*
[2]*Department of Radiation Oncology, University of Nebraska Medical Center, Omaha, Nebraska, USA*
[3]*Department of Physics, University College of Science, Osmania University, Hyderabad, Telangana-500007, India*

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Original Article

Abstract

Purpose: The purpose of this study is to analyze the dosimetric parameters of three dimensional conformal radiotherapy (3DCRT), intensity modulated radiotherapy (IMRT) with seven and nine fields (7F-IMRT, 9F-IMRT) in selected advanced stage cervical cancer cases. **Methods:** Fifteen cases of cervical cancer (IIB to IIIB) were selected for retrospective analysis. All the cases were previously treated with 3DCRT technique with prescribed dose of 50 Gy in 25 fractions. For this study, plans with seven fields IMRT and nine fields IMRT were generated for all patients following Radiation Therapy Oncology Group (RTOG) guidelines. The plans were compared on the basis of planning target volume (PTV) coverage (dose to 1%, 5%, 95% and 99% of target), maximum dose and mean dose to organs at risk (OARs) and also doses at different volumes of OARs. Apart from this, uniformity index (UI), homogeneity index (HI), conformity index (CI) and dose spillage index (R50%) were also calculated with respect to PTV coverage. **Results:** The average dose value of PTV coverage for all three techniques were comparable and all the DVH indices for 7field IMRT (UI (1.04±0.01), HI (0.07 ±0.02), CI (0.75±0.03) and R50% (4.47±0.36)) were better than 3DCRT and 9F-IMRT techniques. All OAR doses were significantly reduced in 7F- IMRT compared to 3DCRT and 9F- IMRT. The target volumes ranged from 769.2 ml to 1375.6 ml with average target volume of 1071.9 ml (SD: 205.38 ml). **Conclusion:** This study showed that significant dose reduction to OARs could be achieved with seven field IMRT plans by maintaining the PTV coverage compared to 3DCRT or 9F- IMRT for treating cervical cancer in advanced stages particularly from IIB to IIIB.

Keywords: Three dimensional conformal radiotherapy, Intensity modulated radiotherapy, Organs at risk, Uniformity index, Conformity index, Homogeneity index, Dose spillage index.

1. Introduction

The most common cancer in women is carcinoma of cervix.[1] In Worldwide, carcinoma of cervix is the fourth most common for females and the seventh most common cancer overall.[2] The Radiation treatment for cervical cancer includes combination of teletherapy and brachytherapy. There are much more advancements in the radiation treatment planning. In early 1990s, three dimensional conformal radiotherapy using CT images was the standard method to deliver radiation. Subsequently, more advanced technology IMRT was innovated in the late 1990s. In IMRT, the intensity of each beam is modified with the help of multileaf collimators (MLC) using inverse planning algorithms to treat the entire tumor while sparing critical structures. IMRT is the basis for all the new techniques like IGRT, VMAT and other modern techniques(SRS and SRT). A number of studies showed the benefit of IMRT over conventional external beam therapy.[3-5] Apart from

Corresponding author: Gangarapu Sri Krishna; Department of Radiotherapy, MNJ Institute of Oncology & Regional Cancer Centre, Hyderabad-500004, Telangana, India.

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IMRT, cancer of cervix treated with other modern techniques were also reported. Bloemers *et al.*[6] showed that for the treatment of locally advanced vulvar cancer, IMRT was attractive option for dose escalation studies. The IMRT with 6 MV photon beam was a better choice instead of 15 MV photons for treatment of carcinoma of cervix as proposed by Tyagi *et al.*[7] Despite treating larger volume with four field box technique, volumetric arc therapy was showing better PTV coverage with minimum dose to OARs[8]. Erpolat *et al.*[9] showed that IMRT planning reduced irradiated bone marrow volumes compared to 3DCRT planning after receiving concurrent chemotherapy (cisplatin). However, no difference between the two techniques was observed in terms of acute and chronic hematologic toxicity. Avinash *et al.*[10] also reported reduction in bone marrow dose while treating with IMRT with concurrent chemotherapy (platinum based) compared to 3DCRT. Mounessi *et al.*[11] reported better conformity around PTV and sparing of OARs with IMRT compared to 3DCRT. Khosla *et al.*[12] concluded that IMRT showed superior plans with respect to target coverage, homogeneity, conformity with sparing of OARs. In addition, they conclude that IMRT reduces NTCP while maintaining TCP. Chang *et al.*[13]showed the dosimetric advantage of IMRT in the context of IGRT where internal movement of tumor was monitored during fractionated radiotherapy. Pathak *et al.*[14] concluded that each IMRT plan must be evaluated and compared by using the S-index score because, S-index is directly related to the biological effects (equivalent uniform dose). Mahmoud *et al.*[15] compared 5 field conformal technique with 8 field IMRT and concluded that IMRT showed better results with respect to sparing of OARs at different volumes, while the PTV was adequately covered. Cozzi *et al.*[16] showed advantage of rapid arc over IMRT: "For rectum the mean dose was reduced by about 6 Gy (10 Gy for the rectum fraction not included in the PTV). Similar trends were observed for the various dose levels with reductions ranging from approximately 3 to 14.4 Gy. For the bladder, Rapid Arc allowed a reduction of mean dose ranging from approximately 4 to 6 Gy and a reduction from approximately 3 to 9 Gy with respect to IMRT. Similar trends but with smaller absolute differences were observed for the small bowel and left and right femoral heads." Like this, many authors[17-20]also, showed advantages of IMRT for cervix as well as other sites also.

In the present study, as we have a database of treated advanced cases of cervical cancer, an independent retrospective investigation of the benefit of IMRT[31] was attempted. Specifically our goal was to compare the 7F-IMRT with 9F-IMRT and show their relative merits with respect to the 3DCRT techniques that was used to treat these patients. The dose coverage to target and the dose spillage to different organs at risk were evaluated using DVH analysis. The results were compared with those reported by other investigators.[11, 12]

2. Methods and Materials

A 6 MV linear accelerator, Clinac 600C (Varian Medical Systems, Palo Alto, CA) having 40 pair MLC, each pair projecting 1cm width at isocenter was used for the delivery of radiation treatments. Fifteen cases of cervical cancer (previously treated with 3DCRT technique) were taken for a retrospective study by re-planning with 7 Fields and 9 Fields IMRT. For all the cases, prescribed dose of 50 Gy was given in 25 fractions (2 Gy/fraction). Thermoplastic sheet (Orfit Industries n.v., Vosveld 9A, 2110 Wijnegem, Belgium) was used for immobilizing the patients. A Philips (16 slice, 85cm diameter, big bore) CT scanner was utilized for imaging of the patients and the CT images of 3 mm slice thickness were acquired in supine position. The CT scans were transferred to the Eclipse treatment panning system (TPS), version 13.6 (Varian Medical Systems, Palo Alto, CA). The gross target volume (GTV), clinical target volume (CTV), planning target volume (PTV) and organs at risk (OARs) were contoured on the CT images by qualified radiation oncologist following the guidelines of International Commission on Radiation Units and Measurements (ICRU) report 83.[21] All the OARs were overlapped with PTV and were not cropped from the PTV. So, large volumes of OARs were included with PTV. As these cases were in advanced stage; the sizes of volumes of PTV were found to vary from 769. 2 ml to 1375.6 ml with a mean value of 1071.93 ml. Initially, the 3DCRT (gantry angles 0^0,90^0, 180^0 and 270^0) was done for all 15 patients. The beam energy of 6MV, beam weightings and MLC leaf positions were optimized by forward planning to reduce the doses to critical organs and better homogeneous dose distribution in the PTV. Following the 3DCRT plan, dynamic 7F- IMRT and 9F- IMRT plans were created using the beam energy of 6MV at gantry angles of 0^0, 35^0, 70^0, 130^0, 230^0, 290^0 & 325^0 for 7F-IMRT and at gantry angles of 0^0, 35^0, 75^0, 110^0, 145^0, 215^0, 230^0, 250^0 & 290^0 for 9F-IMRT. For dose calculation, AAA algorithm was used with a grid size of 2.5 mm. An annular ring was drawn around the PTV with 5 mm and 3 cm margins and a dose constraint for IMRT was defined such that 10% dose fall off per cm. This type of template was created and applied to all the 15 patient plans. In addition, the achievable constraints were changed to obtain possible minimum dose to critical organs without compromising the PTV coverage of at least 95% of dose to 95% of PTV volume. Comparison of dose distribution in PTV and organs at risk were evaluated for all the three techniques.

2.1 Plan analysis based on DVH parameters:

The 3DCRT, 7F-IMRT and 9F-IMRT plans were evaluated and compared based on following dosimetric parameters.

(a) The Conformity Index (CI) was evaluated by the formula[22] below as defined by other investigators.[22, 23]

$$CI = \{TV_{95}/TV\}\{TV_{95}/V_{95}\}$$

where TV_{95} is the volume of target covered by 95% isodose line, TV is the total target volume and V_{95} is the volume of tissue covered by the 95% isodose line. The value of CI varies between 0 to 1 and value close to unity is indicative of better conformity of dose to the PTV.

(b) The Uniformity Index (UI) was evaluated[24] as defined in the literature[24,25] by

$$UI = D_5/D_{95}$$

where D_5 and D_{95} are the minimum doses to 5% and 95% volume of PTV.
The value of UI close to 1 signifies better uniformity of PTV dose.

(c) The Homogeneity Index (HI) was evaluated[26] as defined previously by many authors.[26-28]

$$HI = (D_1-D_{99})/\text{ Prescribed Dose}$$

where D_1 and D_{99} are doses to 1% and 99% of PTV

The smaller the value of HI more is the homogeneous distribution in PTV.

(d) The Dose Spillage Index (R50%) was evaluated[29] as defined by investigators[29, 30]by

$$R50\% = 50\% \text{ Isodose Volume/ PTV volume.}$$

The lower the R50% ratio indicates greater dose fall off and better dose conformity around the PTV.

Statistical analyses of the data sets were done between the three techniques. The p-values were calculated using t-test. When p value is less than 0.05, the difference between the any two treatment techniques was considered as significant. The value of p closer to zero implies that the statistical significance is more between two compared techniques.

3. Results and Discussion

The comparison of detailed results for three techniques (3DCRT, 7F-IMRT and 9F-IMRT) are given in Table1 for PTV coverage and in Table 2 for OAR doses. Percent difference among the three techniques is shown in Table 3. Table 4 shows the average values of DVH indices for the three techniques. Figure1 shows the comparison of typical colour wash dose display between 3DCRT and 7F-IMRT fields for a representative patient. The DVH comparison of PTV coverage and OAR doses for three techniques are given in Figures (2-4).

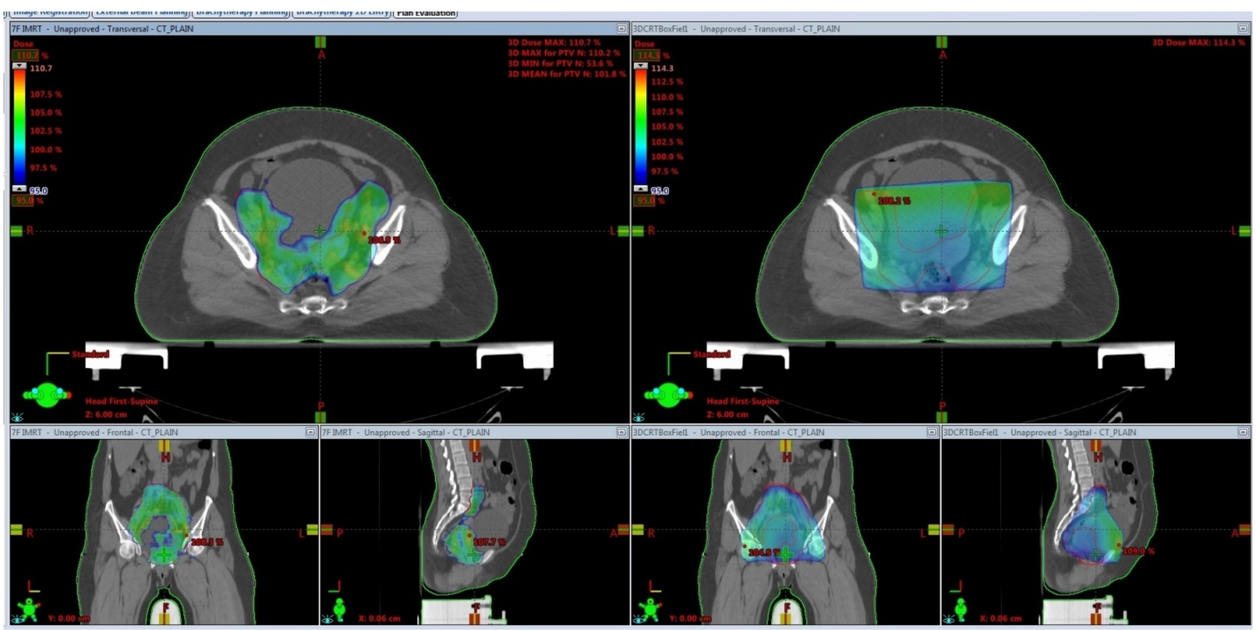

Figure 1: Typical comparison of color wash display for 3DCRT and 7F-IMRT techniques.

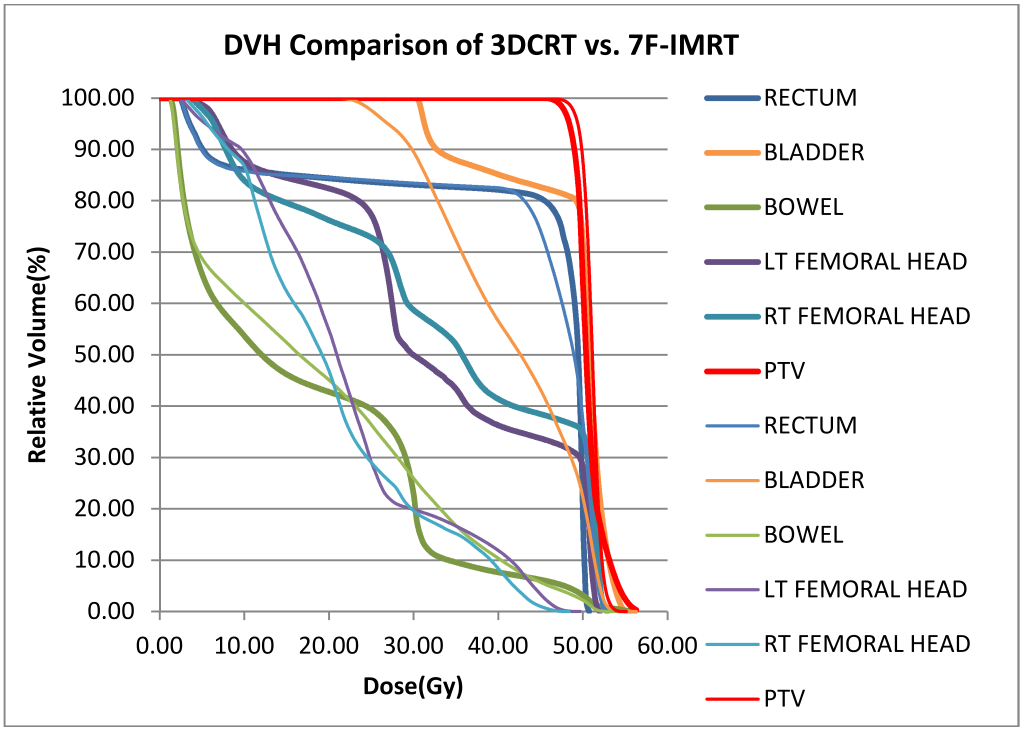

Figure 2: DVH comparison of 3DCRT(Thick lines) and 7F-IMRT(Thin lines) techniques for all structures.

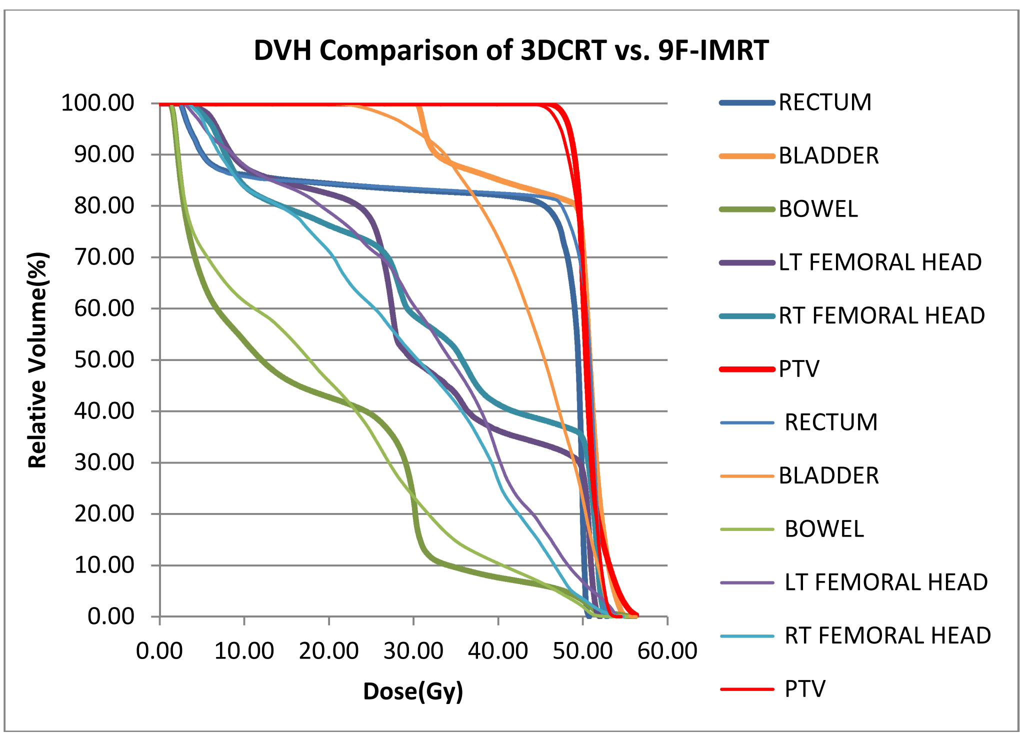

Figure 3: DVH comparison of 3DCRT(Thick lines) and 9F-IMRT(Thin lines) techniques for all structures.

Table 1: Summary of average values for PTV coverage for 3 techniques (3DCRT, 7F-IMRT & 9F-IMRT).

	3D-CRT		7F-IMRT		9F-IMRT		p-value		
PTV	Mean (%)	SD	Mean (%)	SD	Mean (%)	SD	3D vs.7F	3D vs. 9F	7F vs. 9F
D1%	106.0	0.7	105.0	1.4	105.3	1.0	0.02	0.05	0.42
D5%	105.1	0.5	104.1	1.3	104.0	1.0	0.01	0	0.96
D95%	99.3	1.1	99.4	1.3	97.9	1.6	0.8	0.01	0.01
D99%	96.3	2.1	97.4	1.8	95.2	2.2	0.14	0.14	0
TV (95%)	99.4	0.6	99.8	0.4	98.7	1.1	0.05	0.05	0
TV95(ml)	1065.9	211.7	1069.0	209.2	1055.5	202.4	0.97	0.89	0.86
V95(ml)	2625.1	473.8	1407.5	254.9	1421.5	238.0	0	0	0.88
Dmean%	102.4	0.7	102.0	1.2	101.4	1.2	0.23	0.01	0.17
Dmax%	106.9	0.9	107.8	1.8	108.3	1.0	0.09	0	0.35
Dmin%	82.9	7.3	86.0	7.7	79.1	8.3	0.27	0.19	0.03

Table 2: Summary of OAR doses for three techniques (3DCRT, 7F-IMRT, and 9F-IMRT).

OAR	3D		7F		9F		p-value		
	Mean(Gy)	SD	Mean(Gy)	SD	Mean(Gy)	SD	3D vs. 7F	3D vs. 9F	7F vs. 9F
Bladder(max)	53.1	0.8	53.1	1.2	54.4	1.4	0.9	0	0.01
Bladder(mean)	49.3	1.3	44.6	4.7	45.6	3.6	0	0	0.53
Bladder (D50%)	51.2	0.6	46.7	3.0	47.9	2.7	0	0	0.24
Rectum(max)	51.2	0.2	52.8	0.6	53.5	0.2	0	0	0
Rectum(mean)	46.6	2.9	43.8	5.9	44.4	5.2	0.11	0.17	0.75
Rectum (D35%)	50.9	0.4	49.6	1.3	50.4	1.5	0	0.25	0.13
Bowel (max)	53.2	0.2	53.6	1.2	53.8	1.5	0.22	0.14	0.68
Bowel (mean)	25.8	5.7	22.6	4.4	22.9	4.3	0.1	0.12	0.89
Bowel(D100%)	5.1	9.0	4.9	7.5	4.9	6.4	0.94	0.93	1
Bowel(D75%)	17.9	16.2	13.7	13.3	15.0	12.7	0.44	0.59	0.79
Bowel (D50%)	33.6	11.5	27.0	9.5	28.6	9.0	0.1	0.2	0.64
Bowel(D25%)	44.3	8.7	39.2	8.7	41.9	8.2	0.11	0.44	0.37
RT Femoral (max)	51.9	0.7	47.0	2.1	50.1	3.8	0	0.09	0.01
RT Femoral (mean)	29.4	9.9	16.2	3.5	21.2	6.6	0	0.01	0.02
RT. Femoral (D10%)	49.7	2.8	40.6	4.4	42.3	4.7	0	0	0.32
RT Femoral (D50%)	30.9	8.1	18.1	9.1	21.0	8.4	0	0	0.37
RT Femoral (D100%)	7.8	7.9	4.0	5.1	5.3	6.3	0.13	0.35	0.53
Lt.Femoral (max)	51.3	0.1	50.4	0.6	51.5	2.6	0	0.81	0.14
Lt.Femoral (mean)	29.1	4.8	18.4	2.8	23.8	5.9	0	0.01	0
Lt.Femoral (D10%)	45.8	10.2	40.0	5.6	42.1	4.4	0.07	0.22	0.26
Lt.Femoral (D50%)	29.4	4.2	18.7	9.4	21.2	7.0	0	0	0.42
Lt.Femoral (D100%)	8.6	8.5	3.7	4.3	4.8	5.5	0.06	0.15	0.55

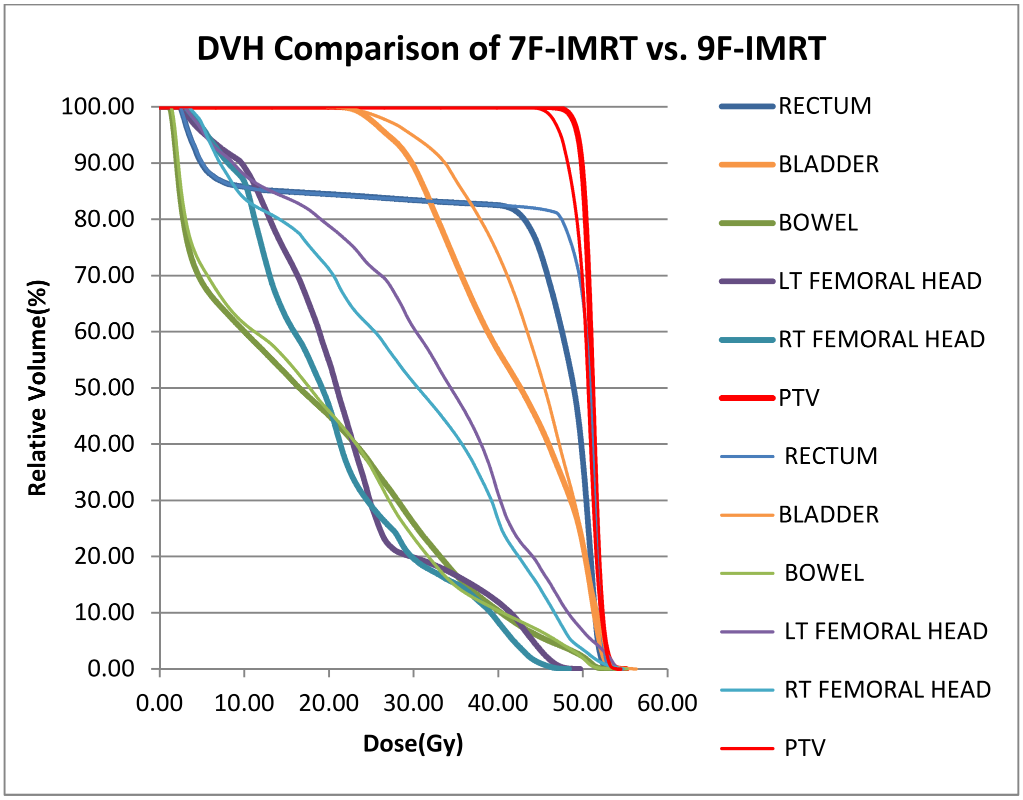

Figure 4: DVH comparison of 7F-IMRT(Thick line) and 9F-IMRT(Thin Line) techniques for PTV coverage and OAR doses

Table 3: Percentage of variation of OAR doses for three techniques.

OAR	3DCRT (Gy)	7F (Gy)	9F (Gy)	Difference (%) 3D vs. 7F	3D vs. 9F	7F vs. 9F
Bladder (max)	53.1	53.1	54.4	-0.1	-2.5	-2.5
Bladder (mean)	49.3	44.6	45.6	9.6	7.6	-2.2
Bladder (D50%)	51.2	46.7	47.9	8.8	6.3	-2.7
Rectum(max)	51.2	52.8	53.5	-3.0	-4.4	-1.3
Rectum(mean)	46.6	43.8	44.4	6.1	4.7	-1.5
Rectum (D35%)	50.9	49.6	50.4	2.6	1.0	-1.7
Bowel (max)	53.2	53.6	53.8	-0.8	-1.1	-0.4
Bowel(mean)	25.8	22.6	22.9	12.3	11.4	-1.0
Bowel (D100%)	5.1	4.9	4.9	4.9	5.1	0.2
Bowel (D75%)	17.9	13.7	15.0	23.5	16.3	-9.5
Bowel (D50%)	33.6	27.0	28.6	19.6	14.8	-5.9
Bowel (D25%)	44.3	39.2	41.9	11.7	5.4	-7.1
RT Femoral Head(max)	51.9	47.0	50.1	9.3	3.5	-6.4
RT Femoral Head(mean)	29.4	16.2	21.2	44.9	28.0	-30.7
RT Femoral Head (D10%)	49.7	40.6	42.3	18.3	14.9	-4.1
RT Femoral Head (D50%)	30.9	18.1	21.0	41.5	32.1	-16.0
RT Femoral Head (D100%)	7.8	4.0	5.3	48.9	31.9	-33.3
LT.Femoral Head(max)	51.3	50.4	51.5	1.7	-0.3	-2.1
LT.Femoral Head(mean)	29.1	18.4	23.8	37.0	18.2	-29.8
LT.Femoral Head (D10%)	45.8	40.0	42.1	12.7	8.0	-5.3
LT.Femoral Head (D50%)	29.4	18.7	21.2	36.4	27.9	-13.4
LT.Femoral Head (D100%)	8.6	3.7	4.8	57.3	44.9	-29.1

Table 4: Average values of calculated DVH indices for three techniques.

DVH Index for PTV	3D-CRT		7F-IMRT		9F-IMRT		p-value		
	Mean value	SD	Mean value	SD	Mean value	SD	3D vs. 7F	3D vs. 9F	7F vs. 9F
UI	1.06	0.01	1.04	0.01	1.06	0.02	0.00	0.00	0.84
HI	0.10	0.02	0.07	0.02	0.09	0.02	0.00	0.00	0.61
CI	0.41	0.06	0.75	0.03	0.72	0.08	0.00	0.23	0.00
R50%	6.46	0.80	4.47	0.36	4.70	0.44	0.00	0.13	0.00

In the present study, as can be seen from Table 4, it was found that the PTV coverage with 3DCRT, 7F-IMRT was better compared to 9F-IMRT. This is also evident by comparing DVH graphs for PTV and OARs shown in Figures (2-4). All the DVH indices are showing the favorable results for 7F-IMRT (p-value 0.00) over 3DCRT technique. Again, comparison of 9 fields IMRT over 7 fields IMRT, the difference is observed only in cases of conformity index and dose spillage index. By increasing the number of fields from 7 fields to 9 fields, no advantage was observed for PTV coverage as well as reduction in dose to OARs. In addition, doses to 1%, 95%, 99%, maximum, mean, minimum dose of PTV, maximum, mean and doses at different volumes of OARs are comparable in all three techniques. This is evident from Tables (1-3). Thus, increase in number of fields is not helpful. It should be noted that optimum number of fields in IMRT depends on target and OAR volumes. In general, small target volumes could benefit from multiple fields and vice versa. In the current study, the advantage of IMRT over 3DCRT in case of advanced stage (IIB to IIIB) carcinoma of cervix has been demonstrated. The percentage reduction in OAR doses was less when compared to other studies.[11, 12, 15, 16] This is due to large volumes of OARs overlapping with PTV. With 7 fields IMRT, the reduction in OAR doses compared to 3DCRT, were as follows. The reduction in mean dose for bladder, rectum and bowel are 9.6%, 6.1% and 12.3% respectively. The mean doses of right and left femoral heads were reduced by 44.9% and 37% respectively. There was also a less significant reduction in OAR doses with 9 fields IMRT.

4. Conclusion

IMRT plans reduce the dose to OARs thereby decrease the toxicity of normal organs without compromising the conformity and homogeneity of dose distribution in the target volume compared to conventional 3DCRT techniques. For the target volumes in the current study ranging from 769.2 ml to 1375.6 ml (average target volume of 1071.9 ml), it was found that seven field IMRT gave the optimum dose coverage for target as well as minimal doses to OARs. Even for advanced cervical cancers, IMRT could be possible with optimal number of fields depending upon tumor size.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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