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Comparison of IMRT Plans with and Without Bone Marrow Sparing For the Treatment of Cervical Cancer

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ABSTRACT

Introduction: The present study aimed to compare plans with Bone Marrow sparing (BM-IMRT) and without Bone Marrow Sparing (N-IMRT).

Material and Methods: Fifteen cases of cervical cancer cases were selected for retrospective study. All the cases were previously treated with normal IMRT. For this study, plans with BM-IMRT were created again for all patients following RTOG guidelines. The prescribed dose of 50Gy in 25 fractions was given. The plan having coverage of 95% of PTV receiving 95% of the prescribed dose was accepted. The plans were compared based on PTV coverage (dose to 2%, 98% of target); constraints of OARs (Organs at Risk) were the volume of 40% < 40Gy for normal bladder and rectum (volume receiving dose 5Gy) V_5<95%, V_{10}<80%, V_{20}<60%, V_{30}<50% and V_{40}<35% respectively for Bone marrow and lowest possible doses to bowel were given for planning criteria. Apart from this, HI, CI and R50% were also calculated concerning PTV coverage to analyze plan quality.

Results: There was a statistical difference in P-values of D2, D98, TV_{95}, HI, R50% but the actual difference is less than 2%. In the case of OARs, there were also significant differences in statistical as well longitudinal in values of V_{10}, V_{20}, V_{30} and V_{40} of Bone Marrow (P<0.01) and there was only statistical differences (p<0.05) at V50 of bladder and rectum.

Conclusion: Without scarifying dose coverage for planning target volume, bone marrow can be spared while treating cervical cancer patients using IMRT technique with bone marrow as an extra constraint.

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Introduction

Cervical cancer is the most common cancer in women [1] and it is the fourth most common cancer in worldwide [2]. There are much more advancements in radiation treatment planning, from conventional treatments to modern techniques like Intensity-modulated radiation therapy- IMRT, Image-guided radiation therapy -IGRT, Volumetric modulated arc therapy -VMAT etc. Several studies showed the benefit of IMRT over conventional external beam therapy [3-6].In addition, from the last 10 to 15 years, some studies showed the benefit of IMRT over conventional treatments for sparing bone marrow [7]. Some authors studied the dose escalation with the help of IMRT with bone marrow sparing and maintaining plan quality [8, 9].Platta et al [10] showed a benefit of tomotherapy-based IMRT without compromising dose to planning target volume- PTV with bone marrow as an extra constraint. Few studies [11-13] showed the benefit of IMRT by concurrent chemotherapy. Now a days, studies [14, 15] on protons have been giving better results than modern treatments with photon beams. In the current study, an attempt was made to compare the IMRT (BM-IMRT) (with Organs at risk -OARs-bone marrow, bladder and rectum) with normal IMRT (N-IMRT) (with OARs- Bladder and Rectum only).

Materials and Methods

A 6MV linear accelerator, Clinac 600C (Varian, Palo Alto, CA), having 40 pair MLC (Multi-leaf collimator), each pair projecting 1cm width at isocenter, was used to deliver radiation treatments. A thermoplastic sheet (Orfit) was used for immobilizing the patients. A Philips (big bore)(M/s.Philips Medical Systems, The Netherlands) Computed Tomography scanner was utilized for imaging of the patients and the CT images of 3 mm slice thickness were acquired in the supine position. The CT scans were transferred to the Eclipse treatment planning system (TPS), version 13.6 (Varian Medical Systems, Palo Alto, CA).For all the cases, radiation prescription was given in 25 fractions of 2Gy, per fraction, to a total dose of 50Gy. The gross tumor volume (GTV), clinical tumor volume (CTV), planning tumor volume (PTV) and organs at risks (OARs) were contoured on the CT images by an experienced radiation oncologist following the (Radiation Therapy Oncology Group) RTOG guidelines. All the OARs which were overlapped with PTV and were cropped from the PTV. For dose calculation,

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(Anisotropic Analytical Algorithm) AAA algorithm was used with a grid size of 2.5 mm. Fifteen patients planned and treated with IMRT(N-IMRT) (Bladder, Rectum, Bowel, Left and Right femoral heads as regular constraints) were taken for a retrospective study by re-planning with giving of bone marrow(BM-IMRT) as an extra constraint. The dose constraints for planning are shown in table1. This type of template was created and applied to all the 15 patient plans. In addition, the achievable constraints were changed to obtain a possible minimum dose to critical organs without compromising the PTV coverage of at least 95% dose to 95% of PTV volume. Comparison of dose distribution in PTV and organs at risk were evaluated with and without giving constraint to bone marrow using students t test (Microsoft excel, version 2007). The dose coverage to target and the dose spillage to different organs at risk were evaluated using Dose Volume Histogram (DVH) analysis. The results were compared with those reported by other investigators.

Plan analysis for DVH parameters

The plans were evaluated and compared based on the following dosimetric parameters.

1. The Conformity Index (CI) was evaluated by ICRU [16-18]

CI = 100% Isodose volume / PTV volume

The value of CI varies between 0 to 1 and a value close to unity indicates better conformity of dose to the PTV.

2. The Homogeneity Index (HI) can be defined as follows:

HI = (D2-D98)/ Prescribed Dose

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

3. Dose Spillage Index was defined by the formulae [19, 20]

R50% = 50% Isodose Volume /PTV volume

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

Statistical analysis of the data sets was done between the two techniques. The p-values were calculated using two-tailed students t test (Microsoft excel, version 2007).

Results

The mean of PTV volume was 1018.32cc (SD: 177.18cc).Mean of volumes of OARs were ((Bladder-PTV):112.22cc (SD: 54.52)), ((Rectum-PTV):18.69cc (SD: 8.51)), ((Bowel-PTV):1348.22 (SD: 328.77)), and ((Bone Marrow-PTV):244.79cc (SD: 113.54cc)) respectively. The comparisons of detailed results with and without bone marrow sparing are shown in Table2 and Table3 for PTV coverage and OARs doses, respectively. Figure1 shows a typical comparison of Isodose distribution for IMRT with and without bone sparing. Figure2 shows the DVH comparison using with and without bone Marrow sparing.

Table1. PTV and OARs-Dose Constraints for Treatment Planning.

Structure	Dose-Volume Criteria
Planning Target Volume	95% of the Prescribed dose to 95% of PTV volume
Bladder-PTV	V_{40}< 40%
Rectum-PTV	V_{40}<40%
Bone Marrow	V_5<95%, V_{10}<80%, V_{20}<60%, V_{30}<50%, V_{40}<35%
Bowel	As low as possible

Table 2. Summary of Results of IMRT with and without Bone Marrow sparing for PTV Coverage. TV_{95} is the volume of target covered by 95% Isodose line

	IMRT with Bone Marrow sparing		IMRT without Bone Marrow sparing			
	Mean	STD. DEV	Mean	STD. DEV	P value	Difference in (percentage/Absolute)
D2 (Gy)	52.44	0.57	51.92	0.52	0.01	-1.002%
D98(Gy)	47.93	0.54	48.61	0.37	0.00	1.39%
Dmax(Gy)	54.70	1.62	53.91	0.88	0.13	-1.46%
Dmean(Gy)	50.26	0.14	50.21	0.19	0.55	-0.10%
TV_{95}	98.64	0.82	99.46	0.33	0.00	0.82
HI	0.09	0.02	0.07	0.02	0.00	-0.02
CI	0.64	0.10	0.68	0.11	0.28	0.04
R50	3.77	0.37	4.05	0.48	0.03	0.28

Table 3. Summary of Results of IMRT with and without Bone Marrow for OAR Doses.

	IMRT with Bone Marrow sparing		IMRT without Bone Marrow sparing			
	Mean	STD.DEV	Mean	STD.DEV	P value	Difference in (percentage/Absolute)
Bladder, V30Gy	78.08	13.25	77.41	12.16	0.55	-0.67
Bladder,V40Gy	38.13	4.55	38.78	3.76	0.51	0.65
Bladder,V50Gy	2.27	1.90	1.45	1.40	0.04	-0.82
Rectum, V30Gy	84.15	15.89	83.12	14.61	0.41	-1.03
Rectum,V40Gy	39.29	2.82	40.47	2.88	0.23	1.18
Rectum,V50Gy	0.99	1.12	0.43	0.65	0.03	-0.57
Bone Marrow,V10Gy	94.36	5.84	97.32	4.00	0.00	2.97
Bone Marrow,V20Gy	60.63	2.96	91.15	7.53	0.00	30.51
Bone Marrow,V30Gy	39.87	4.97	63.82	9.58	0.00	23.95
Bone Marrow,V40Gy	19.56	7.34	30.56	12.69	0.00	11.00
Bowel,V30Gy	28.05	12.25	26.91	12.96	0.49	-1.13
Bowel,V40Gy	10.01	6.84	10.83	8.50	0.44	0.83
Bowel,V50Gy	0.31	0.44	0.57	1.56	0.62	0.25
Lt.Femoral Head (Max.dose)(Gy)	49.03	4.22	49.40	3.86	0.66	0.74
Rt. Femoral Head (Max.dose)(Gy)	47.27	4.46	48.10	3.65	0.21	1.73

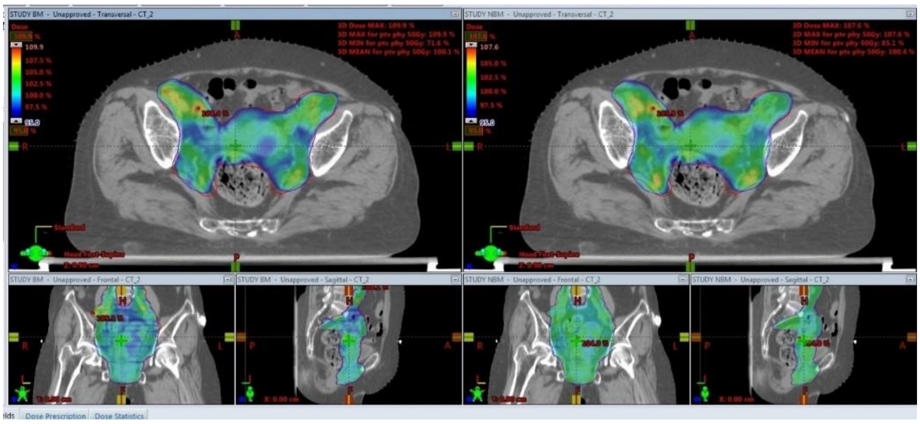

Figure 1.Typical comparison of Isodose distribution using IMRT with bone marrow sparing (left side) and without (right side) bone marrow sparing.

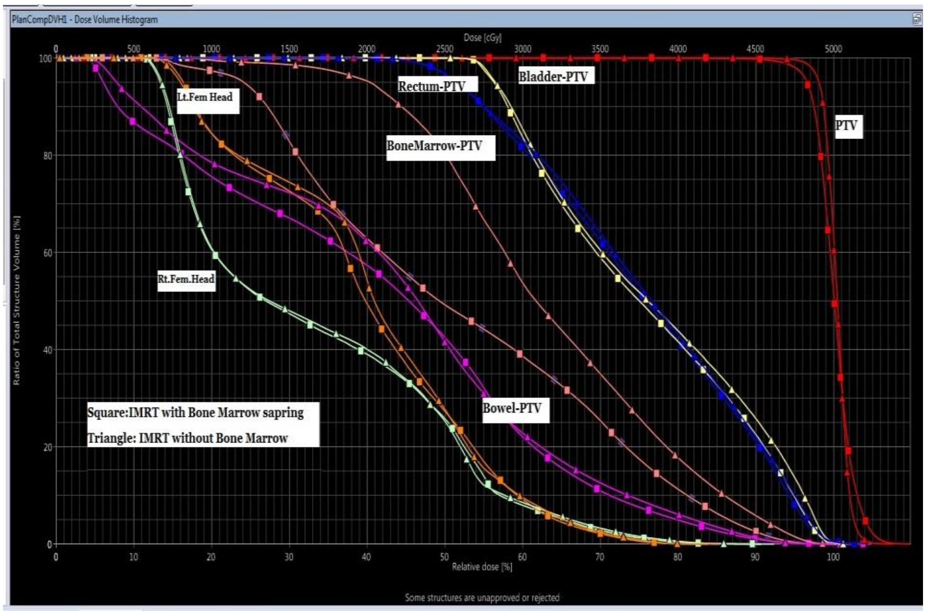

Figure 2. DVH comparison using IMRT with and without bone marrow sparing

Discussion

Roeske et al. [21] showed that irradiated volume of small bowel volume could be reduced using IMRT for the whole pelvis while treating gynecological patients. Mundt et al.[22]showed that dose escalation is possible using IMRT while treating gynecological patients. Chen et al.[23] concluded that volumes of normal tissues can be reduced while delivering higher doses in gynecological patients using IMRT. Selvaraj et al. [24] showed more reduction volumes of bladder, rectum and small bowel using (Intensity-modulated radiation therapy) IMRT compared to (Three-dimensional Conformal Radiation Therapy) 3DCRT.

Similarly, IMRT with bone marrow sparing reduced the volumes of rectum, bladder and bowel compared IMRT without bone marrow sparing using four field box techniques [25].Murakami et al. showed that the averages of V10Gy, V30Gy, and V40Gy were statistically lower with IMRT with bone marrow sparing compared to normal-IMRT [26].

In the present study, as it can be seen from Table 2, it was found that in the case of PTV coverage at upper(D2) and lower(D98),values of PTV is less than 2% even though there was statistical significance($p<0.01$)does exist. Also, there were variations in HI, R50% by -0.02 and0.28 respectively with statistical significance ($p<0.05$).This higher HI (0.02) value shows that there is more homogeneity around PTV in the case of without bone marrow sparing (NBM-IMRT), while lower R50 (0.28) shows a greater fall-off dose in the case of bone marrow sparing (BM-IMRT). There was no statistically significant change ($p<0.05$) for CI, but there is little more decrease in conformity by 0.04 with BM-IMRT than N-IMRT. Also, in the case of OARs, for bladder and rectum doses, there is only statistical dose differences between BM-IMRT vs. N-IMRT at V50Gy and it is also evident from figures 1 and 2.But, in case of bone marrow, there is a significant statistical difference ($p<0.001$) as well as a significant decrease in dose by (V_{20}:30.51%, V_{30}:23.95%, V_{40}:11%) between BM-IMRT versus N-IMRT. In the current study, the advantage of (BM-IMRT) IMRT with bone marrow as extra constraint and bladder and rectum was shown by maintaining the similar plan quality as IMRT without bone marrow sparing. Apart from PTV and OAR doses, in the current study DVH indices like CI, HI and R50% were evaluated to show the difference in plan quality with and without bone marrow as a constraint in IMRT planning for cervical cancer patients.

Conclusion

Without scarifying dose coverage for planning target volume, bone marrow can be spared while treating the cervical cancer patients using (BM-IMRT) IMRT technique with bone marrow as an extra constraint. With bone marrow sparing IMRT, we could able to reduce the future complications related to bone marrow.

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