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Comparative Evaluation of Dosimetric Parameters in Carcinoma Cervix Patients Undergoing Intensity–Modulated Radiotherapy versus Three–Dimensional Radiotherapy: A Retrospective Analysis

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Abstract:

Objective: Cervical cancer affects many women across the globe and often requires radiation for treatment. This study aimed to compare the dosimetric outcomes of Intensity–Modulated Radiation Therapy (IMRT) and Three–Dimensional Conformal Radiation Therapy (3D–CRT) in managing locally advanced cervical carcinoma.

Methods: We performed a retrospective analysis of 30 patients who received IMRT with weekly cisplatin–based medication**.** Corresponding 3DCRT plans were generated for comparison. Dosimetric parameters for Planning Target Volume (PTV) and Organs at Risk (OARs) were evaluated. Patients were immobilized in a supine position for simulation, according to conventional protocols.

Results: PTV coverage was similar between IMRT and 3D–CRT groups. However, IMRT showed significantly improved dosimetric outcomes for OARs, including the bladder, rectum, bowel, and bone marrow. IMRT reduced doses to critical organs while maintaining comparable PTV coverage.

Conclusion: Patients undergoing IMRT experienced reduced doses to critical organs compared to 3DCRT. Larger–scale trials with longer follow–up periods are needed to corroborate these findings and confirm IMRT's efficacy in cervical cancer treatments.

Keywords: Cervical cancer, Radiotherapy, Intensity–Modulated Radiation Therapy, Three Dimensional Conformal Radiation Therapy, Organs at Risk

Introduction

Carcinoma cervix is the commonest cancer in females in the developing world[1] and radiotherapy plays an important role in the treatment of cervical carcinoma, particularly in managing locally advanced cases with concurrent cisplatin–based chemoradiation and brachytherapy. Conventional radiotherapy methods, such as four–field box–type irradiation, were formerly employed and are still commonly used, but they cause radiation–induced damage in the digestive tract, urinary tract, and hematological system.[2,3] Intensity–modulated radiation therapy (IMRT) and three–dimensional conformal radiation therapy (3D–CRT) are new radiotherapy techniques that have been shown in studies to increase the irradiation dose of the target area while effectively reducing the irradiation dose of surrounding normal tissues and organs, controlling tumors, and reducing body damage.[4,5] The incidence and severity of radiation toxicity are influenced by multiple factors. These parameters include the treated tissue volume, the dose received, and the radiation treatment delivery mechanism. The

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Studies suggest that IMRT effectively minimizes radiation exposure to critical organs like the bladder, rectum, bone marrow, and bowel may lead to decreased toxicity when compared to 3D conformal radiotherapy.[6–9]

A comparison conducted by the Radiation Therapy Oncology Group (RTOG) 1203 evaluated IMRT against 3D–CRT radiotherapy in cervical cancer, revealing significantly reduced scores for gastrointestinal and urinary toxicity with IMRT.[10] Furthermore, studies from Radiation Therapy Oncology Group 418 indicated that IMRT had been associated with decreased incidence of hematological toxicities than 3D–CRT.[11] Aim of this study was to compare the dosimetric outcomes of Intensity–Modulated Radiation Therapy (IMRT) and Three–Dimensional Conformal Radiation Therapy (3D–CRT) in managing locally advanced cervical carcinoma.

Material and Method

We did a retrospective analysis of patients treated for locally advanced cervical carcinoma (stage IIA to IIIB) at the Department of Radiation Oncology from September 2022 to November 2023. Thirty patients undergoing IMRT with weekly concurrent cisplatin–based chemotherapy (cisplatin 40 mg/m2) were included. The corresponding virtual 3DCRT plans (another 30 3DCRT plans) were generated for all patients. The IMRT and 3DCRT plans were compared in terms of dosimetric parameters of planning target volume (PTV) and organs at risk (OARs). According to institutional protocols, 30 patients were selected for combination radiation and concurrent weekly cisplatin–based chemotherapy, following informed consent processes. Patients with a performance status or Karnofsky performance score of greater than 60 and all previously untreated patients with histologically established squamous cell, FIGO stage IIA to IVA cervical cancer were included. Exclusion criteria included patients who had undergone prior treatment such as radiotherapy or hysterectomy, those with other comorbidities, and pregnant patients. The total prescribed dose for external beam radiotherapy was 50.4 Gy in 28 fractions with a schedule of five fractions per week 1.8Gy per fraction.

One week following the completion of external beam radiotherapy all patients received a boost to the primary tumor, administered at a dose of 21 Gy in three fractions of 7 Gy each, spaced at weekly intervals.

Immobilization and simulation

Simulation was conducted with patients in a supine position, secured with a 4–clamp pelvic thermoplastic mask for immobilization. A standard bladder protocol was adhered to during both simulation and treatment sessions. Before simulation, patients were instructed to empty their bladder, followed by consuming 500 ml of water over an 30 Minute and not to void before simulation/treatment. Contrast–enhanced CT simulation was then performed on CT simulator at the conclusion of the hour. A vaginal marker was positioned at the lower extent of the cervical disease during CT imaging. Planning images were generated from the CT scans, and the patient coordinate system was established using three orthogonal lasers. Lead balls were utilized as fiducial markers, marking the crosswire points in the X, Y, and Z planes on patients. Planning CT images were obtained with a slice thickness of 2.5 mm, extending from L2 to mid–thigh.

Radiotherapy Oncology Group (RTOG) guidelines were used for delineation of target volumes and organs at risk . The gross visible tumor and its extensions were delineated as the gross tumor volume (GTV). The entire GTV, including the uterine cervix, uterine corpus, parametrium and vagina, were contoured as the clinical target volume (CTV). Additionally, relevant draining nodal groups (common iliac, internal iliac, external iliac, obturator, and presacral lymph nodes) were outlined as nodal CTV.

For PTV 0.7 mm margin was given from CTV , accounting for uterine motion and any setup errors.[12] The outer contour of the bone marrow was delineated treating it as a solid, continuous structure. The superior extent of the bone marrow contour started at the level of the L3/L4 junction, while the inferior extent extended to the level of the ischial tuberosity.

IMRT Planning:

For IMRT plans, seven to nine fields were used in the same plane, couch at 0°. Only 6MV photon energy was used and didn't use any opposite fields. Specific limits were set for how much dose the target areas (PTV, CTV, and GTV) and the at–risk organs could receive. Although we kept track of bone marrow doses, we didn't set any strict limits because we couldn't always meet the recommended doses when we first planned the treatment. A tool called the Varian leaf motion calculator vs. smart MLC(17.0.1) to figure out how the leaves should move to deliver the right dose dynamically. To calculate the doses precisely, we used AAA algorithm with a small grid size of 0.25 cm. We adjusted the plans using a tool that optimizes the doses.

3D Conformal Radiotherapy Planning:

Four fields were used in the same plane – two on the sides and one from the front and one from the back – all angled at 0°. We made sure the edges of the beams fit exactly around the PTV, leaving a small margin of 0.8 cm. Only used 15 MV energy was used with AAA algorithm method with a small grid size of 0.25 cm. For hot/cold spots in the doses strength of the beams were adjusted as needed.

Plan Evaluation:

During the plan evaluation graphs illustrating the radiation dosage received by the target areas were analyzed. The primary focus was on ensuring that at least 95% and 99% of the target area received the appropriate radiation dosage, avoiding excessive radiation dosage in any specific region. Additionally, the radiation dosage received by adjacent organs was assessed, with precise figures documented for organs such as the bladder, rectum, bowel and others at various points. The uniformity of radiation distribution was also scrutinized to ensure comprehensive coverage of the target area.

Statistical Analysis:

To assess differences in dosimetric parameters, we utilized the Student's t–test. For comparing toxicity between the groups, we employed either the chi–square test. Any p–value below 0.05 was considered significant.

Results

Our study included 30 patients diagnosed with cervical carcinoma with stage IB2 to IVA. Dosimetric results The PTV coverage was similar between both arms. Both treatment plans achieved satisfactory coverage of the planning target volume (PTV), with 95% of the PTV receiving 97.4% and 96.6% of the prescribed dose in 3D conformal radiotherapy and IMRT plans respectively. Additionally, 99% of the PTV received 94.24% and 96.6% of the prescribed dose in the respective plans. Figures 1a and b illustrate the PTV coverage with 99% of the prescribed dose for one of the cases in both plans.

In IMRT plans there is notable reductions in doses to organs at risk compared to 3D conformal radiotherapy and is statistically significant. Further details regarding target coverage, doses to organs at risk for all plans using both techniques are presented in Table 1 & 2

For Organ at risk the average values of D15, D35, and D50 for the urinary bladder were lower in the IMRT group compared to the 3DCRT group. The dose to the rectum was slightly lower with IMRT compared to 3DCRT, but the findings are statistically significant. The volume of the bowel bag receiving 45 Gy was lower in IMRT group. However, the maximum dose received in the femoral head was higher in the 3DCRT group compared to the IMRT group. Detailed dose information for organs at risk is provided in Table 2.

Discussion

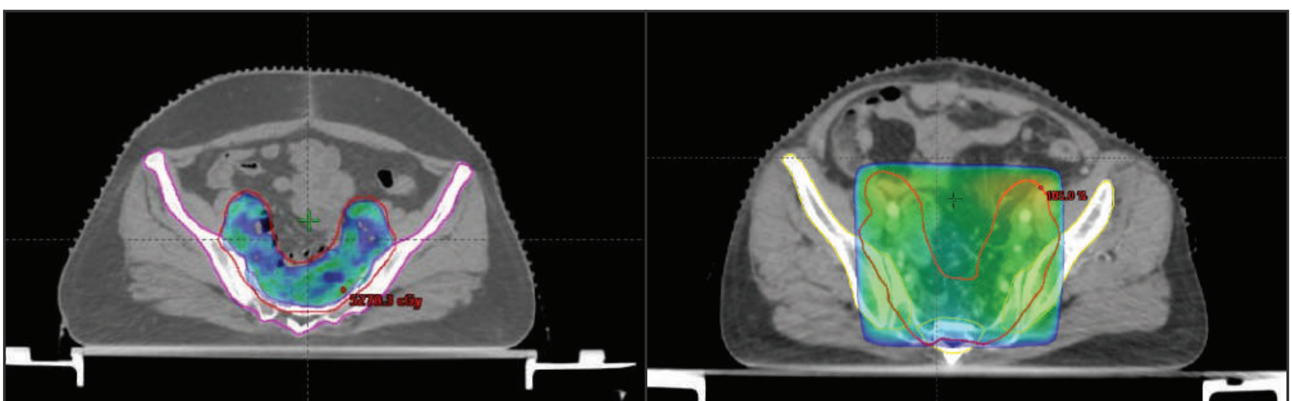
3DCRT remains the mainstay of radiation therapy to carcinoma cervix treatment but over recent years but there has been a significant rise in the application of Intensity–Modulated Radiation Therapy (IMRT) for cervix carcinoma, there are limited studies comparing dose coverage and

Dosimetric parameter (PTV)	3DCRT (Gy)	IMRT(Gy)	P–value
D99	47.5	49.3	0.16
D95	49.1	48.7	0.04
Dmax	53.8	54.8	0.001
Dmin	44.4	40.8	0.009

Table 1: Mean dosimetric parameters for ensuring PTV coverage in both groups

D99: Dose to 99 % volume of PTV; D95: Dose to 95 %volume of PTV, Dmax: Maximum Dose to PTV;

Dmin:Minimum dose to PTV. IMRT= Intensity–Modulated Radiotherapy; 3DCRT=Three Dimensional Conformal Radiotherapy.



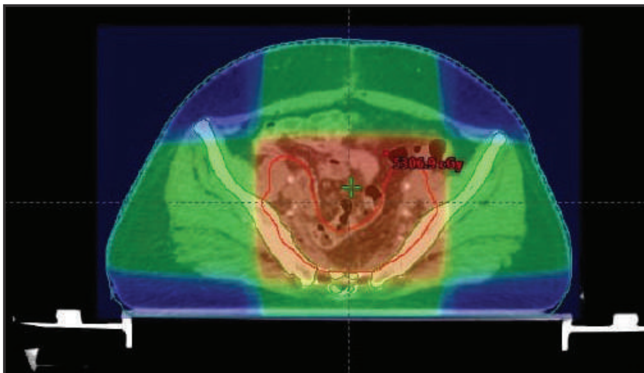
1(a) 1(b)

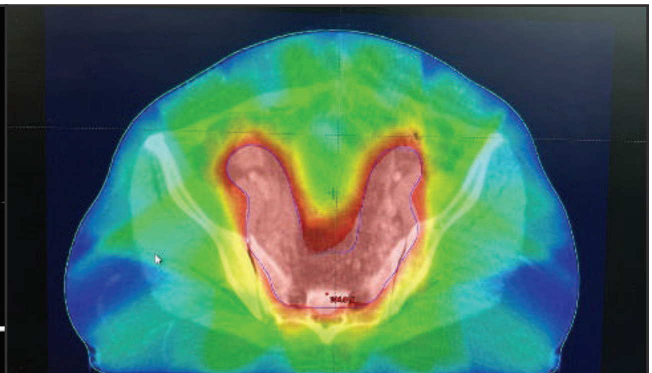
Figure 1a and 1b showing 99% of PTV coverage in Both IMRT and 3DCRT plans

Organ	Dosimetric parameters	3DCRT	IMRT	P value
Urinary Bladder	D15(Gy)	52.8	50.4	0.000
	D35 (Gy)	51.6	48.7	<0.00001
	D50(Gy)	51.2	44.1	<0.00001
Rectum	D15(Gy)	51.4	41.7	0.008
	D35(Gy)	51.2	46.2	<0.00001
	D50(Gy)	50.4	42.3	0.13
Bowel	V45(cc)	382	196	<0.00001
Femur Head (Dmax)	RT (Gy)	51.2	46.7	<0.00001
	LT (Gy)	51.3	47.4	<0.00001
Bone Marrow	V10 (%)	98.4	96.2	0.01
	V20 (%)	92.3	89.1	0.02

Table 2: Mean Dosimetric parameters for organs at risk in both treatment groups

D15:Dose to 15% of the volume, D35:Dose to 35% of the volume, D50:Dose to 50% of the volume,V45: Volume receiving 45 Gy, Dmax: Denotes the maximum dose. IMRT= IntensityModulated Radiotherapy; 3DCRT= Three–Dimensional Conformal Radiotherapy.


2(a)


2(b)

Color Dose wash on CT image in 2(a) 3DCRT and 2(b) IMRT plan.

OAR Sparing in both techniques. In the current study, we compared the dosimetric parameters between IMRT and 3D conformal irradiation techniques.

IMRT plans Improved coverage and Conformity index because of use of utilization of multiple beam angles and computer–optimized intensity–modulated beams. During optimization, these beams are subdivided into numerous small beamlets, with their intensity adjusted via the multileaf collimator (MLC) until the desired dose distribution is achieved. In IMRT beams after entering the patient's body, yield highly conformal dose distributions with better target volume coverage and effectively sparing surrounding normal organs, as shown in Figure 2(b). In 3D conformal radiotherapy, uniform intensity beams are employed, distributing dose not only to the irregularly shaped planning target volume (PTV) but also to adjacent organs at risk, as depicted in Figure 2(a). Consequently, this approach often leads to elevated doses to organs at risk and inadequate conformity of dose distribution around the PTV.

We studied 30 patients for dosimetric analysis and our results showed that IMRT improved the dose delivered to certain organs like the rectum, bladder, and small bowel with better PTV coverage. Which is similar to recent studies have found.[12–13] Sharma et al[14] showed that IMRT D15, D35, and D50 of bladder was less as compare to 3DCRT . In our study in IMRT D15, D35, D50 of the bladder was lower by 4.5%, 5.62%, and 13.86%, respectively compared to 3DCRT and was statistically significant. Similarly, for the rectum, these doses decreased by 18.8%, 9.7%, and 35.6%, respectively, with IMRT compared to 3DCRT and was statistically significant. Yang b et al[6] and Van De Bunt et al[16] have also shown reductions in the volume of bladder and rectum receiving the prescribed dose, ranging from 23 to 44% when comparing IMRT to conventional radiotherapy plans.[15,16] Additionally, the volume of bowel receiving 45 Gy (V45) was much lower (50%) with IMRT compared to 3DCRT and was statistically significant.

A study by Mell et al.[17] also reported that there was a reduction in doses to the bone marrow and small bowel when patients were treated with IMRT. In our study we found same result and was statistically significant. Van De Bunt et al[16] reported that IMRT is superior to conformal and conventional treatment in sparing critical organs with ample target volume coverage and also stated that IMRT remains superior after EBRT regardless of internal organ movement. Fumaiki et al. compared IMRT and 3DCRT in the cervical carcinoma with concurrent chemotherapy and observed that the V45 of the bowel bag in the IMRT arm was 485 mL, whereas that of the 3DCRT arm was 891 mL, a significant reduction and also statistically significant.[18]

Limitation of our study is the short duration of follow–up. Additionally, implementing bone marrowsparing techniques could potentially alleviate the elevated incidence of hematological toxicity observed in patients undergoing intensity–modulated radiotherapy. Furthermore, there is a need for heightened attention to the target margin to ensure sufficient allowance in IMRT planning for PTV expansion.

Conclusion

In summary, patients undergoing IMRT have reduced doses to the bladder and rectum, bowel and Bone marrow compared to those treated with 3D–CRT. We recommend conducting larger–scale studies with extended follow–up periods in future research endeavors to validate our findings.

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Approval: Nil (Retrospective analysis)

Conflict of Interest: There was no conflict of interest

Ethical Declaration: As it is retrospective study so consent and study approval was not required but patients consent was taken before starting of any treatment.

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