RESEARCH ARTICLE

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IMRT as an Alternative Technique for Intracavitary Brachytherapy in Patients with Carcinoma of the Cervix: A Feasibility Study Using Unified Dosimetric Index

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Abstract

Objective: Intracavitary brachytherapy (ICBT) plays an important role in the management of carcinoma of the cervix. This study attempts to find the feasibility of intensity-modulated radiation therapy (IMRT) as a boost for patients who are not suitable for ICBT in order to improve their disease-free and overall survival. **Methods:** Twenty patients with carcinoma of the cervix were included in this study. Nine fields of IMRT and ICBT plans were generated for PTV_{Boost}. Various dosimetric indices like coverage, conformity, homogeneity, and gradient index were calculated, and the corresponding unified dosimetric index (UDI) values were generated. Plans were classified based on combined UDI, and the UDI values were compared with those of ICBT. In addition, rectum and bladder doses were compared. **Results:** All the dosimetric indices were within acceptable limits except for the gradient index. The gradient index of the IMRT and ICBT plans were 8.77 ± 0.26 and 1.33 ± 0.06 respectively ($p < 0.0001$). The mean of combined UDI with standard deviation was 32.557 ± 8.940 and plan quality was calculated from these values. Rectum and bladder doses for ICBT were lesser than IMRT ($p < 0.0001$). Conclusion: ICBT is the gold standard for boost RT in carcinoma of the cervix patients. IMRT boost is feasible for patients who are unsuitable on medical grounds for brachytherapy.

Keywords: IMRT Boost- cervix cancer- brachytherapy- dosimetry- UDI

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Introduction

GLOBOCAN data estimates 13.2 million new cases will be detected in India in 2020, out of which 6.78 million are female. Carcinoma of the cervix is the second most common cancer, with an incidence of 18.3%. The management of cervical cancer involves surgery, radiation therapy (RT), and chemotherapy, and the modality of treatment varies with staging. The RT plays an important role in the treatment of advanced cervical cancers. Moreover, studies have proved that the survival outcomes of surgery and RT are similar for early-stage cervical cancers, with the advantage of less morbidity in RT (Landoni et al., 1997; Petignat et al., 2007). In advanced stages of the disease, the combination of chemotherapy and RT yields good disease-free survival.

In RT, both external beam therapy and brachytherapy are used for cervical cancer patients to increase overall survival (Yang et al., 2019). Various external beam therapy techniques like 3-dimensional conformal radiation therapy (3DCRT), intensity-modulated radiation therapy (IMRT), and stereotactic body radiation therapy (SBRT) are available for radiation dose delivery. Commonly, the 3DCRT technique is used for the external beam treatment. The cervical cavity is surrounded by organs like the bladder, rectum, sigmoid, and bowel, which, when irradiated with high doses, will produce complications and affect the quality of life of the patients. Brachytherapy offers the advantage of increased dose delivery to the tumour with rapid dose falloff, which protects the organs in close proximity from radiation. Inclusion of brachytherapy increases disease-free survival and reduces local recurrence (Han et al., 2013; Agrawal et al., 2022; Mehta et al., 2022; Meena et al., 2023).

Brachytherapy may not be feasible in some patients due to the poor response of the tumour to external beam therapy, underlying medical conditions, and the unavailability of facilities. Campitelli et al., (2021) have reviewed various techniques to boost locally advanced cervical cancer, either by brachytherapy or by external beam radiotherapy (EBRT). Advancements in external beam delivery like IMRT and SBRT have been tried by various authors to boost the primary tumour (Shwetha et al., 2011; Lee et al., 2021), while Kundargi et al., (2013) have used surgery after chemoradiotherapy. Though various studies have been undertaken to find a suitable

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substitute for brachytherapy boost, further studies are required to confirm the efficacy of alternative techniques. SBRT and other advanced radiation equipment are very rarely found in government institutions where large numbers of advanced cervical cancer patients are treated.

This study attempts to find out the feasibility of using the IMRT technique to boost the dose to the tumour and associated nodes while controlling radiation to radiosensitive organs within acceptable limits as compared to intracavitary brachytherapy (ICBT) using a unified dosimetric index (UDI). The concept of UDI was introduced by Akpati et al., (2008) and gives the complete nature of the plan and its deviation from the ideal one. The dosimetric indices such as coverage index, conformity index, dose gradient index, and homogeneity index are calculated, and the UDI is derived from these indices.

Materials and Methods

Patient preparation

Twenty cervical cancer patients with stages IIB to IIIB were retrospectively selected for this study. All patients underwent planning computed tomography (CT) scans with proper immobilization devices. The full bladder protocol is followed during CT image acquisition throughout the treatment. The CT images of these patients were used for this dosimetric comparison study. The informed consent has been waived off by the ethics board of the institute, considering this a retrospective dosimetric comparison study with no humans involved.

All patients underwent RT treatment to planning target volume (PTV) using the 4-field 3DCRT technique. The Eclipse Treatment Planning System (Varian Medical Systems, Palo Alto, CA, USA) was used to deliver a prescription dose of 50 Gy in 25 fractions at a rate of 2 Gy per fraction to the PTV, which consists of the primary tumour along with nodal volume. The nodal volume encompasses the obturator nodes, external, internal, and common iliac nodes, and sacral lymph nodes. The OARs delineated were the bladder and rectum. A 15 MV x-ray beam from the Varian Clinac 2100 linear accelerator was utilized for the 3DCRT plans.

Treatment Planning

For dosimetric comparison, 20 patients with stages IIB to IIIB treated with high dose rate ICBT after completion of 50 Gy EBRT were taken. The ICBT dose of 16 Gy in 2 fractions (EQD2 = 24 Gy) was given to the high-risk clinical target volume (HRCTV) that was delineated as per GEC ESTRO recommendations (Pötter et al., 2006). The IMRT boost volume (PTV_{Boost}) was delineated in a CT image set similar to the HRCTV, which includes the entire cervix along with the residual disease. The prescription dose for the PTV_{Boost} was 24 Gy in 8 fractions (EQD2 = 26 Gy).

The IMRT plans for the PTV_{Boost} were generated using 9-fields with gantry angles of 0, 41, 82, 123, 164, 205, 246, 287, and 328 degrees. A 6 MV x-ray beam from the Varian Clinac 2100 linear accelerator was utilized for the IMRT plans, and dose constraints to the bladder and rectum (maximum dose less than the prescription dose) were considered during optimization. The IMRT plans were compared with the ICBT dose distribution created in the Oncentra planning system. Dose volume parameters are obtained from DVH, and dosimetric indices are calculated.

Dosimetric evaluation

The PTV dosimetric evaluation of these plans had been made using dose-volume histogram (DVH) analysis. For the PTV quality comparison, dosimetric indices like coverage index (COI), conformity index (CI), homogeneity dose index (HI), and gradient index (GI) were calculated as stated below. The COI was defined as:

$$COI = \frac{D_P}{D_{98\%}}$$

where D_p is the prescription dose and $D_{98\%}$ is the dose received by 98% of the PTV_{Boost}. The COI value denotes how well the PTV_{Boost} volume is covered by the prescription isodose. The conformal and homogenous nature of the dose distribution is analyzed using the HI and CI. The CI was calculated as:

$$CI = \frac{V_{PTV}}{V_{PTVref}} \times \frac{V_{ref}}{V_{PTVref}}$$

where V_{PTV} is the volume of PTV_{Boost}, V_{PTVref} is the reference isodose (98%) volume within the PTV_{Boost}, and V_{ref} is the volume of reference isodose (98%). The HI was calculated as:

$$HI = \frac{D_{2\%} - D_{98\%}}{D_P}$$

where $D_{2\%}$, $D_{98\%}$ are the doses received by 2%, 98% of the PTVBoost respectively and D_p is the prescription dose. The GI was defined as:

$$GI = \frac{V_{98\%}}{V_{50\%}}$$

where $V_{98\%}$ and $V_{50\%}$ are 98% and 50% isodose volumes, respectively. The ideal value for COI, CI, and GI is 1, and a plan with a value closer to 1 indicates a superior plan. The ideal value for HI is 0, and a plan with a value closer to 0 indicates a superior plan.

A simple plan quality matrix scoring method (UDI) was utilized to calculate an overall score that incorporates all dosimetric parameters evaluated. The UDI was calculated as follows (Akpati et al., 2008):

$$UDI(X) = \{|1.0 - X| + 0.1\} \times 10$$

where X denotes the value of COI, CI, and GI. UDI for HI and combined UDI were calculated as follows and the ideal value for Combined UDI is 1.

$$UDI (HI) = \{|HI| + 0.1\} \times 10$$

Combined UDI = UDI (COI) x UDI (HI) x UDI (CI) x UDI (GI)

The standard deviation and mean were calculated

for the dosimetric indices and for the UDI. The IMRT plans were classified as excellent, good, average, or poor depending on the combined UDI values. The mean (μ) and standard deviation (σ) were calculated for the combined UDI, and the plans were classified as below. If the value of the combined UDI is less than μ-σ, it is an excellent plan in terms of dose coverage, conformity, gradient, and homogeneity. The value of a good, average plan is between μ-σ to μ and μ to μ+σ respectively. A plan is considered poor if the combined UDI value is greater than μ+σ.

The GI and COI were calculated for ICBT plans and compared with those of IMRT plans. $D_{0.1cc}$, D_{1cc}, D_{2cc}, and D_{5cc} doses to OARs such as the bladder and rectum were obtained from IMRT plans. The biologically effective dose (BED) and 2 Gy equivalent dose (EQD2) values for $D_{0.1cc}$, D_{1cc}, D_{2cc}, and D_{5cc} were calculated and compared between IMRT and ICBT plans.

Statistical analysis

The dosimetric results of IMRT and ICBT plans were analyzed using the student's t-test for two samples comparison. The statistical test was two-tailed, with a threshold for statistical significance of $p < 0.05$.

Results

The volumes of HRCTV and PTV_{Boost} used in ICBT and IMRT planning are 25.81 ± 9.60 and 39.16 ± 21.02 cc, respectively. Table 1 shows the dosimetric parameter results for PTV_{Boost} from IMRT plans. Table 2 displays

Table 1. Dosimetric Parameters Results for Boost Planning Target Volume from IMRT Plans

Patient	COI	HI	CI	GI
1	1.013	0.034	0.895	0.271
2	1.028	0.047	0.935	0.212
3	1.033	0.057	0.816	0.206
4	1.018	0.037	0.883	0.223
5	1.017	0.036	0.854	0.247
6	1.021	0.039	0.873	0.196
7	1.031	0.052	0.984	0.252
8	1.026	0.043	0.972	0.275
9	1.042	0.070	0.908	0.225
10	1.037	0.058	0.997	0.237
11	1.017	0.035	0.791	0.215
12	1.020	0.044	0.882	0.219
13	1.012	0.048	0.809	0.237
14	1.017	0.041	0.844	0.177
15	1.036	0.047	1.128	0.191
16	1.028	0.039	0.887	0.222
17	1.029	0.049	0.851	0.208
18	1.017	0.039	0.842	0.205
19	1.035	0.049	0.922	0.193
20	1.022	0.04	0.913	0.236
Mean ± SD	1.025 ± 0.008	0.044 ± 0.009	0.896 ± 0.077	0.220 ± 0.025

COI, Coverage index; CI, Conformity index; HI, Homogeneity index; GI, Gradient index; SD, Standard deviation

Table 2. UDI Results for Boost Planning Target Volume from IMRT Plans

Patient	UDI_COI	UDI_HI	UDI_CI	UDI_GI	Combined UDI
1	1.125	1.343	2.045	8.292	25.640
2	1.282	1.470	1.648	8.882	27.582
3	1.328	1.568	2.837	8.939	52.784
4	1.180	1.373	2.173	8.766	30.863
5	1.173	1.359	2.455	8.527	33.390
6	1.213	1.393	2.273	9.038	34.699
7	1.308	1.524	1.158	8.481	19.579
8	1.264	1.433	1.276	8.251	19.076
9	1.421	1.698	1.921	8.753	40.556
10	1.367	1.576	1.031	8.634	19.172
11	1.172	1.351	3.085	8.849	43.210
12	1.203	1.443	2.179	8.809	33.315
13	1.122	1.475	2.908	8.626	41.528
14	1.167	1.409	2.563	9.229	38.889
15	1.358	1.469	2.280	9.092	41.340
16	1.282	1.385	2.131	8.779	33.234
17	1.292	1.490	2.494	8.917	42.800
18	1.170	1.386	2.578	8.953	37.452
19	1.348	1.492	1.784	9.074	32.566
20	1.223	1.405	1.866	8.644	27.696
Mean ± SD	1.247 ± 0.087	1.449± 0.089	2.053 ± 0.564	8.773 ± 0.259	32.557 ± 8.940

UDI, Unified dosimetric index; COI, Coverage index; CI, Conformity index; HI, Homogeneity index; GI, Gradient index; SD, Standard deviation

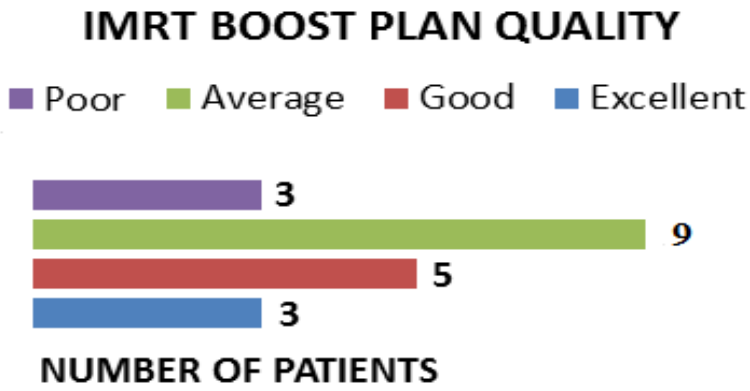

Figure 1. The IMRT Plans Classification Based on the Combined UDI

Table 3. Comparison of UDI_COI and UDI_GI from IMRT and ICBT plans

Parameters	Mean ± SD		
	IMRT	ICBT	P value
UDI_COI	1.247 ± 0.087	1.406 ± 0.052	< 0.0001
UDI_GI	8.773 ± 0.259	1.334 ± 0.059	< 0.0001

UDI, Unified dosimetric index; COI, Coverage index; GI, Gradient index; SD, Standard deviation

the individual and combined UDI results for PTV_{Boost} from IMRT plans. The UDI_COI and UDI_HI were close to the ideal value. The comparisons of UDI_COI and UDI_GI from IMRT and ICBT plans are shown in Table 3. The ICBT plans had superior dose falloff compared to the IMRT plans.

The $D_{0.1cc}$, D_{1cc}, D_{2cc}, and D_{5cc} doses to the bladder and rectum from IMRT plans are presented in Table 4. A comparison of BED and EQD2 doses for bladder and rectum from IMRT, ICBT boost plans and total plan (3DCRT + Boost) is shown in Table 5. The BED and EQD2 values are determined for ICBT and IMRT plans, as the fractional doses are different in both techniques. The bladder and rectum doses were lower in the ICBT plans compared to the IMRT plans ($p < 0.0001$).

Table 4. Dose to Bladder and Rectum from IMRT Plans

Parameters	Mean	SD	Range
Bladder			
$D_{0.1cc}$ (Gy)	23.21	1.093	20.45 – 24.48
D_{1cc} (Gy)	21.287	1.756	18.92 – 24.03
D_{2cc} (Gy)	20.071	2.017	17.19 – 23.58
D_{5cc} (Gy)	17.999	2.636	14.08 – 22.03
Rectum			
$D_{0.1cc}$ (Gy)	21.485	1.76	17.71 – 24.21
D_{1cc} (Gy)	18.954	2.745	13.46 – 23.95
D_{2cc} (Gy)	17.533	2.992	11.78 – 23.74
D_{5cc} (Gy)	14.863	3.182	8.13 – 22.58

SD, Standard deviation

Table 5. Comparison of Bladder and Rectum Doses from IMRT and ICBT Plans

Parameters	Bladder dose			Rectum dose		
	IMRT	ICBT	P value	IMRT	ICBT	P value
BED (Boost plan)						
$D_{0.1cc}$ (Gy)	46.42	40.48	< 0.0001	42.97	26.27	< 0.0001
D_{1cc} (Gy)	42.57	30.72	< 0.0001	37.9	19.18	< 0.0001
D_{2cc} (Gy)	40.14	25	< 0.0001	35.06	15.72	< 0.0001
D_{5cc} (Gy)	35.99	18.56	< 0.0001	29.72	11.29	< 0.0001
EQD2 (Boost plan)						
$D_{0.1cc}$ (Gy)	25.79	22.48	< 0.0001	23.87	14.59	< 0.0001
D_{1cc} (Gy)	23.65	17.06	< 0.0001	21.06	10.65	< 0.0001
D_{2cc} (Gy)	22.3	13.88	< 0.0001	19.48	8.73	< 0.0001
D_{5cc} (Gy)	19.9	10.31	< 0.0001	16.5	6.27	< 0.0001
EQD2 (3DCRT + Boost plans)						
$D_{0.1cc}$ (Gy)	75.53	73.56	< 0.0001	73.42	63.78	< 0.0001
D_{1cc} (Gy)	72.32	66.25	< 0.0001	69.54	58.37	< 0.0001
D_{2cc} (Gy)	70.48	62.72	< 0.0001	67.32	55.63	< 0.0001
D_{5cc} (Gy)	68.81	58.43	< 0.0001	64.58	52.86	< 0.0001

BED, Biologically effective dose; EQD2, 2 Gy equivalent dose

Discussion

The disease-free survival and increase in overall survival of cancer patients depend on the effective and required tumoricidal radiation dose delivery. Various techniques have been tried by many investigators to increase the outcome of radiation therapy. IMRT has been used in cervical cancer to reduce normal tissue complications. Lin et al., (2018) analyzed the efficacy of IMRT over 3DCRT and 2DRT with 1008 patients. They concluded that there was no significant difference in 3-year disease-free and overall survival for all three techniques, with the advantage of reduced acute gastrointestinal toxicity and chronic genitourinary complications for IMRT.

The HRCTV volumes of 20 brachytherapy patients and for both intracavitary applications were found to have an average value with a standard deviation of 25.813 ± 09.554 cc, which is comparable to that reported by Tuntipumiamorn et al., (2018). The HRCTV volumes are best delineated with MRI images, and as our institution does not have MRI machines, a CT data set is used for their delineation as per the guidelines given by Viswanathan et al., (2014). The average volume of PTV_{Boost} in the IMRT boost plan was 39.155 ± 21.016 cc, which is slightly higher than the HRCTV in brachytherapy. This is due to the fact that margins are included in the IMRT boost plan to account for day-to-day variations.

Various authors have discussed the HI for gynecological cancer (Kataria et al., 2012; Lebedenko et al., 2018; Atiq et al., 2019), which gives a clear picture about the dose uniformity within the tumour. Hot and cold spots that affect the radiation outcome can be easily identified using this index. The results of HI calculated are found to have an average value of 0.044 and a standard deviation of 0.009. This value suggests a highly homogenous distribution for the IMRT plan. The values of UDI_COI and UDI_CI were also closer to 1. The value of UDI_GI was on the inferior side, which suggests that the dose falloff from the prescribed isodose to 50% is not rapid. Krishnan et al., (2017) have discussed the dosimetric indices along with the unified dosimetric indices for different sites like the prostate, thorax, and pelvis. The present study's values are in good agreement with them. The individual UDI values for all patients from the IMRT plans are shown in Table 2.

The combined UDI was calculated from the UDI of the individual indices for all the patients and is shown in Table 2. For the plan clasifications the values of μ, μ-σ, and μ+σ were 32.557, 23.617, and 41.497 respectively. Figure 1 shows the number of plans that were classified as excellent, good, average, or poor depending on the combined UDI values.

The ICBT plans had superior dose falloff compared to IMRT. Furthermore, both techniques were able to achieve nearly the same dose coverage. Though IMRT is able to provide conformal plans, it fails miserably in terms of dose falloff. In ICBT, the dose falloff from 100% to 50% was around 1.2 to 1.5 cm, which cannot be achieved by any of the external beam techniques.

In the case of the bladder and rectum, both techniques deliver doses to the organs within tolerance limits. Nevertheless, the ICBT BED values were lower compared to IMRT, and the falloff dose from 0.1 to 5 cc of the organs was more pronounced with ICBT than IMRT. The rectum doses were lower with ICBT due to better separation of the rectum from the tumour. The exclusion of volumetric modulated arc therapy (VMAT) based SBRT was the limitation of this study. However, further investigation including VMAT based SBRT is required.

This study concludes that though IMRT has many advantages like conformal and homogenous dose delivery, reduction in total treatment duration, and surgical intervention-free delivery, ICBT is the gold standard. Nevertheless, the ICBT can be replaced by any other technique if it is not feasible or adaptable clinically in the management of cervical cancer. This study concludes that the IMRT boost plan can be used for patients who are found unsuitable for the ICBT on medical grounds.

Author Contribution Statement

The authors confirm contribution to the paper as follows: study conception and design: G. Balan, V. Ramasubramanian; data collection: G. Balan; analysis and interpretation of results: G. Balan; draft manuscript preparation: G.Balan, V. Ramasubramanian. All authors reviewed the results and approved the final version of the manuscript.

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Ethical Approval

Institutional scientific and ethics board has approved this study. This article does not contain any studies with human participants performed by any of the authors.

Conflict of interest

All authors contributed to this study declare that they have no conflict of interest with respect to the manuscript.

Informed consent

The informed consent has been waived off by the ethics board of the institute considering this as a retrospective study with no human involved. For this type of study formal consent is not required.

Availability of data

All data are presented in the results section of the manuscript.

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