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Comparative Study of Dose Distribution Homogeneity between 3D-Brachytherapy and Intensity Modulated Radiation Therapy Techniques in Cervix Cancer Tumors

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Abstract

Aim: The purpose of this study was to compare the dosimetric results of the techniques (3D-Brachytherapy and intensity-modulated radiotherapy IMRT) in patients with locally advanced cervical carcinoma (LACC). **Method:** There are 15 patients with locally advanced cervical carcinoma (LACC), after the completion of external beam radiotherapy (EBRT) for the whole pelvic irradiation 45 Gy/25 fractions, followed by 3D-Brachytherapy 24 Gy per weekly fractions and 36 Gy of IMRT per 18 fractions. Coverage of targets volume and doses received by normal tissue were compared in two techniques. **Method:** 15 patients of LACC treated with 3D-Brachytherapy were selected for this study. IMRT plans were also created for all the patients. 3D-Brachytherapy and IMRT plans were compared on the basis of target volume coverage, dose to Organs at risk (OAR's), homogeneity index (HI) and conformity index (CI). **Results:** The results showed that D90% of HRCTV in the 3D-Brachytherapy was covered more than D90% of PTV in the IMRT of prescribed dose, the D_{2CC} and the V60Gy values of Bladder and rectum were significantly lower than in 3D-Brachytherapy. The HI and CI in 3D-Brachytherapy were found better than IMRT. **Conclusion:** 3D-Brachytherapy significantly reduced the irradiated volume of OAR's and improved dose coverage in tumor volume compared to that by IMRT.

Keywords

IMRT, 3D-Brachytherapy, Cervical Cancer

1. Introduction

Cervical cancer is the fourth most frequent cancer in women with an estimated 570,000 new cases in 2018, representing 6.6% of female cancers. About 90% of deaths from cervical cancer occurred in low- and middle-income countries [1].

The human papillomavirus (HPV) is the main cause of cervical cancer. HPV is a common virus that is passed from one person to another during sex. Most sexually active people will have HPV at some point in their lives, but few women will get cervical cancer [2].

Brachytherapy is a method of treatment in which sealed radioactive sources are used to deliver radiation at a short distance by interstitial, intracavitary, or surface applications; a high radiation dose can be delivered locally to the tumour with rapid dose fall off in the surrounding normal tissue [3] [4].

HDR brachytherapy is a single radioactive source which is temporarily placed inside the tumor for a few minutes, and then removed. The source travels inside small catheters controlled by a device called a remote after loader. Since the source position can be precisely adjusted and we can create customized dose distributions to meet each patient's needs, tumors can be treated with very high doses of localized radiation while greatly reducing the doses to surrounding healthy tissues. HDR brachytherapy is most commonly used to treat prostate, cervical, and head and neck cancers [5].

Intensity-Modulated Radiation Therapy (IMRT) refers to a radiation therapy technique in which a non-uniform fluence is delivered to the patient from any given position of the treatment beam to optimize the composite dose distribution. The optimization process involves inverse planning in which segments weights or intensities are adjusted to satisfy prescribed dose criteria for the composite plan. For each target planning target volume (PTV), the user enters the plan criteria (constrain) that include maximum dose, minimum dose, and/or dose volume objective, or the PTV and for organs at risk [3] [6] [7].

2. Material and Method

2.1. Simulation

All patients had undergone a CT scan with 2 mm slice thickness twice at supine and head first position. First: every patient had undergone a CT scan with definite conditions, and then IMRT plan was designed on every patient's CT scan. Second: every patient had undergone the CT scan after fixing a ring CT/MR compatible applicator. This scan has been used in 3D-brachytherapy in every fraction with the same positioning conditions of the first scan. All steps illustrated in flow chart as showed in (**Figure 1**).

2.2. Planning

2.2.1. IMRT

After patients scanning, these images were transferred to the treatment planning system (TPS) Xio (CMS) for IMRT radiotherapy planning. Tumor volumes and

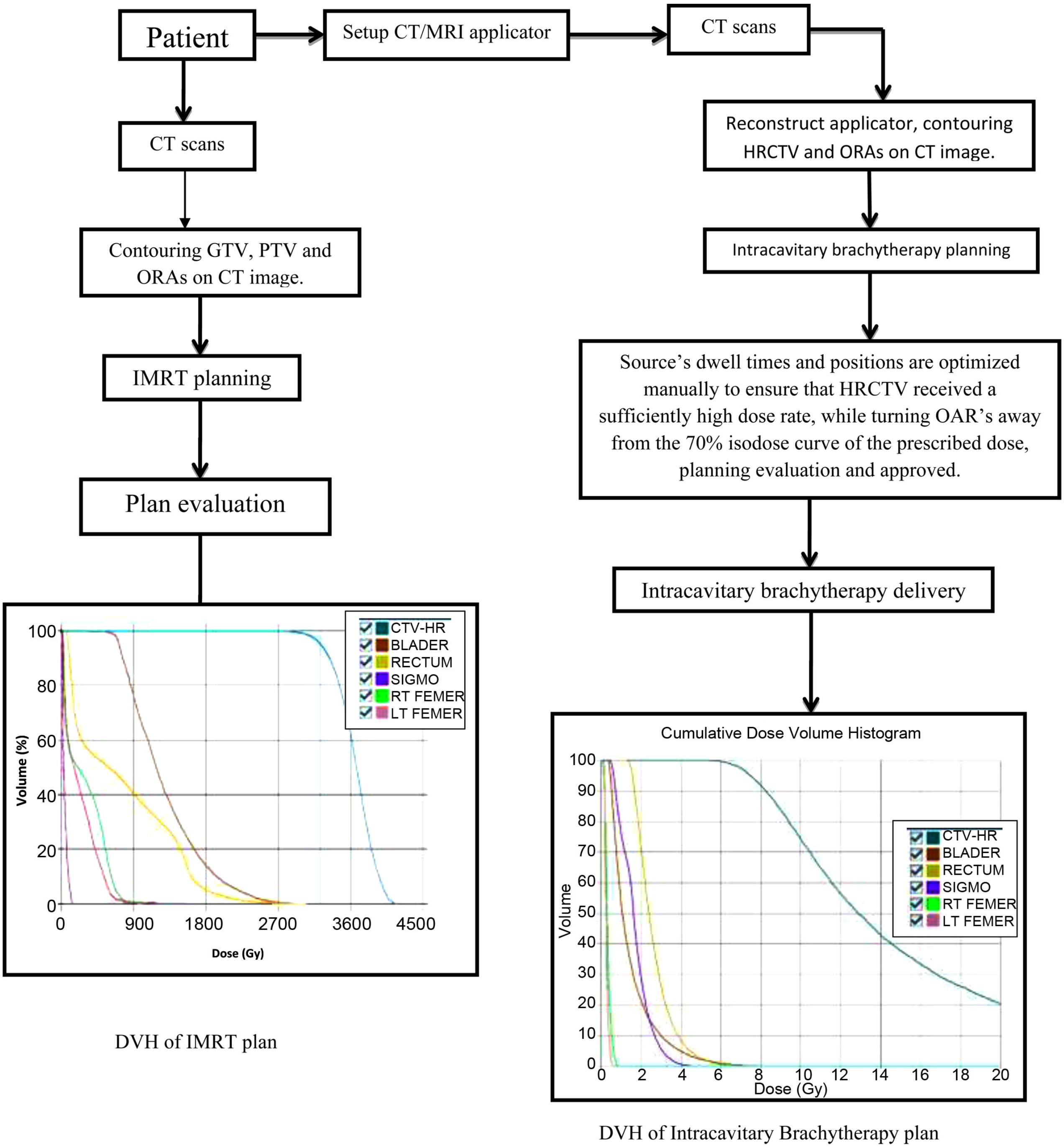

Figure 1. The whole Radiotherapy planning flow chart of Brachytherapy and IMRT techniques.

organs at risk (OAR's) were delineated on CT images for all the patients. RTOG guidelines were used for delineation of target volume and OARs. The total accumulated doses of IMRT and brachytherapy boost were evaluated in terms Biological Effective Dose (BEF) and Equivalent dose in 2 Gy for fraction (EQD2), using $\alpha/\beta = 3$ Gy for OAR and $\alpha/\beta = 10$ Gy for targets [8] [9].

$$\text{BED} = nd\left[1 + \frac{d}{\alpha/\beta}\right] \quad [10]$$

$$\text{EQD2} = \frac{\text{BED}}{1+\alpha/\beta} \quad [10]$$

where n is the number of fractions, α/β is the dose at which the linear and quadratic of cell kill are equal and d is the physical dose per fraction. The calculated physical dose in IMRT is 36 Gy per 18fractions which is equivalent to 24 Gy per 3 fractions/week in Brachytherapy [11] [12] [13] [14].

2.2.2. 3D-Brachytherapy

After the second scanning, the images were sent to the brachytherapy treatment planning system called "Sagi plan". The applicator was reconstructed on the CT images according to GECESRTO recommendations, gross tumor volume (GTV), high risk clinical volume (HRCTV) and OAR's were delineated in CT.

2.2.3. Plan Evaluation

After approval, the dosimetric parameters of all the plans generated from both techniques were compared. The IMRT plans were generated with total prescription dose of 36 Gy in 18 fractions using step-and-shoot technique which equivalent to the total dose of HDR-Brachytherapy of 24 Gy per 3 fractions which calculated by Biological Effective Dose (BED) and Equivalent Dose to 2 Gy (EQD2) [13]. The dose distribution from HDR-Brachytherapy and IMRT plans were compared visually on the axial, sagittal and coronal plans for degree of conformity and homogeneity of prescribed dose to the planning target volume (PTV) and for organs at risk (OAR) as showed in (**Figure 2**) [15].

2.3. Evaluation Parameters

The PTV coverage parameters; D90 Dose to 90% of volume of PTV, V95% and V105% (PTV volume received 95% and 105% of prescribed dose respectively) were compared for both two techniques. Conformity index (CI) and Homogeneity (HI) were calculated for both techniques using.

$$\text{CI} = \frac{\text{V95\%}\left(\text{PTV volume reciving 95\% of PD}\right)}{\text{total volume of PTV}} \quad [8]$$

$$\text{HI} = \frac{\text{D5} - \text{D95}}{\text{D50}} \quad [8]$$

D5, D95 and D50 are the doses received by 5%, 95% and 50% of PTV.

Doses to OAR's were compared in both techniques for the Sigmoid volumes of D30, D50, D70 and D100 (Dose to 30%, 50%, 70% and 100% of organ's volume respectively). D_{2cc} were considered for Bladder and Rectum (dose to 2 cm^3 of organ volume). V60 Gy and V70 Gy represent the volume irradiated to more than 60 Gy and 70 Gy (EQD2) to bladder and rectum by accumulated dose from 3D-Conformal whole pelvis and boost (IMRT or 3D-Brachytrerapy).

3. Results

3.1. Patient

General information: From March 2018 to February 2019 15 locally advanced

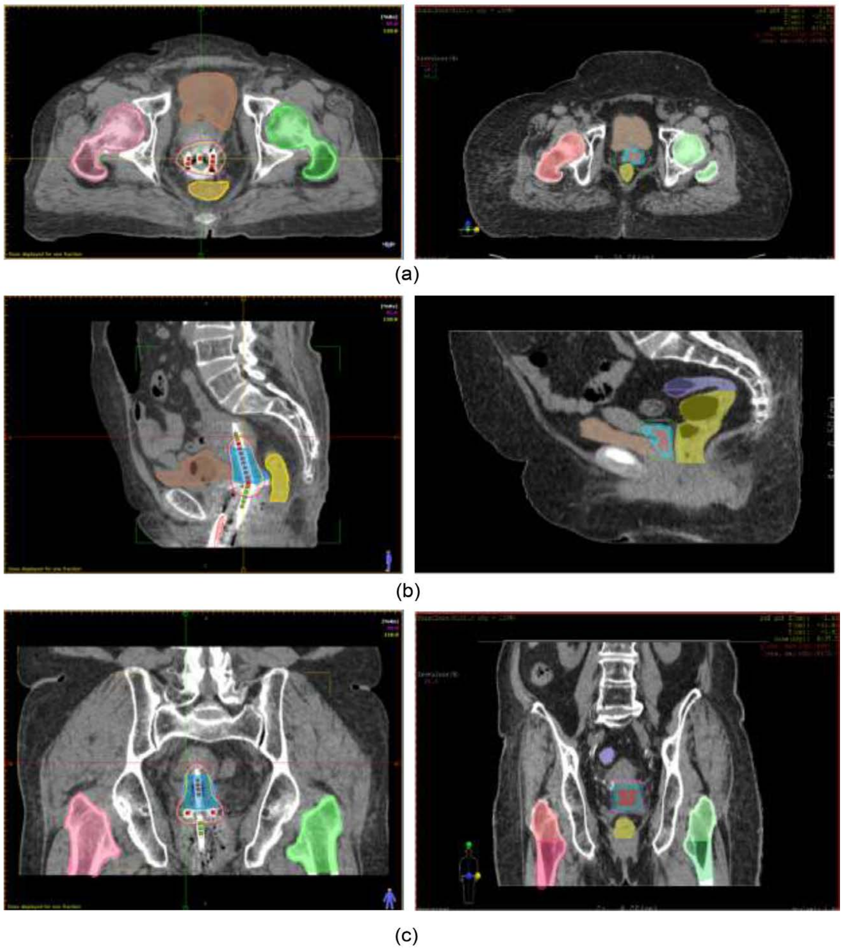

Figure 2. Dose distribution in a patient with cervix cancer (a); axial (b): sagittal and (c) coronal view 3D-brachtherapy technique and IMRT.

cervix carcinoma patients who were diagnosed with parametrial, paravaginal or distal vaginal involvement were receiving radiotherapy at Alexandria Ayadi Al-Mostakbal Oncology Center (AAAOC). Patients' ages: 40 - 77 years (median age: 53 years); stages: IIB of cases 4, IIIA of 3 cases, IIIB of 8 patients (according to 2009 FIGO stage) [11]; tumor volumes: GTV 10.4 cc ± 7.6 cc, PTV 30.65 cc ± 9.32 cc, HRCTV 21.58 cc ± 7.35 cc showed in Table 1.

3.2. Comparison for PTV and HR-CTV

3D-brachytherapy had better coverage than the IMRT where D90% for PTV and HRCTV (102 ± 2.592, 96.45 ± 1.264) for 3D-brachytherapy and IMRT respectively. Homogeneity index (HI) values for 3D-brachytherapy and IMRT were found (320 ± 55.5, 10.35 ± 2.23) respectively the difference between the HI in both the techniques was extremely significant with the p value (P = 0.000*). The Median and Std. deviation (SD) of conformity index (CI) was found to be (97.6 ± 1.046, 94.8 ± 0.658) in 3D-brachytherapy and IMRT respectively, the difference between the CI in 3D-brachytherapy and IMRT was extremely significant with the p value (P = 0.0001). The detailed results of target coverage, HI and CI in all the plans by both the techniques are given in Table 2.

3.3. Comparison for Organ's at Risk

Bladder and Rectum D_{2cc} doses were lower for 3D-Brachytherapy as compared with the IMRT plan. But, the V60 Gy and V70 Gy of rectum in both the techniques were not statistically significant. The result of sigmoid showed that the dose distribution was significant in low isodose line where D10%, D30% and D50% in IMRT were lower than D10%, D30% and D50% in 3D-Brachytherapy, but in a high percentage of dose result showed that the dose distribution was non-significant (Table 3).

Table 1. The patient's features.

Content	Number	Percentage (%)
FIGO stage		
IIB	4	26.7
IIIB	3	20
IIIA	8	53.3
Age (median age: 53)		
<53	7	46.7
≥53	8	53.3
Weight (median age: 74)		
<74	4	26.7
≥74	11	73.3

Table 2. Mean values of PTV coverage, HI and CI for 3D-brachtherapy and IMRT plans of 15 patients.

Dosimetric Parameters	3D-brachtherapy	IMRT	P-Values
D90%	102 ± 2.59	96.45 ± 1.26	0.000*
V95%	96.8 ± 0.49	95.2 ± 2.21	0.440
V105%	44.9 ± 1.83	18.6 ± 19.2	0.005
HI	320 ± 55.5	10.35 ± 2.23	0.000*
CI	97.6 ± 1.046	94.8 ± 0.658	0.0001

*Represents the level of statistical significance $P < 0.05$ (two tails).

Table 3. Mean doses to organs at risk (OAR).

OAR's	Dosimetric Parameters	3D-Brachytherapy	IMRT
Bladder	D_{2cc}	60.48 ± 5.16	71.74 ± 322
	V60 Gy	9.25 ± 6.18	36.45 ± 8.53
	V70 Gy	2.9 ± 1.54	7.78 ± 5.79
Rectum	D_{2cc}	61.48 ± 3.81	67.21 ± 4.04
	V60 Gy	12.25 ± 3.28	14.65 ± 4.19
	V70 Gy	1.55 ± 1.02	1.77 ± 1.48
Sigmoid	D30	54.8 ± 7.7	56.6 ± 1.0
	D50	60.3 ± 3.2	54.9 ± 8.3
	D70	58.2 ± 7.2	56.0 ± 1.15
	D100	62.2 ± 4.0	56.2 ± 1.1
Both femoral head	D_{max}	37.0 ± 1.63	45.3 ± 3.63

4. Discussion

4.1. Target Volume

The results clearly indicated that the 3D-Brachytherapy technique maintained a high dose for tumor volume. In our study, we observed that the IMRT technique was difficult to create the same high dose to tumor volume as 3D-Brachytherapy. This event is mainly due to the fact that IMRT provides a relatively homogeneous dose distribution and conformity but cannot provide a high dose gradients distribution similar to that of 3D-Brachytherapy showed in (Figures 3-6).

4.2. Organ's at Risk

The results also showed the mean rectum and bladder (V60 Gy and V70 Gy) were significantly lower in brachytherapy than IMRT showed in (Figures 7-12). The reason of this difference result of sigmoid in brachytherapy was that we used the ring applicator, so when we optimized Source's dwell times and positions manually to ensure that HRCTV received a sufficiently high dose rate, Tandem (part of applicator) let more low doses to reach to sigmoid.

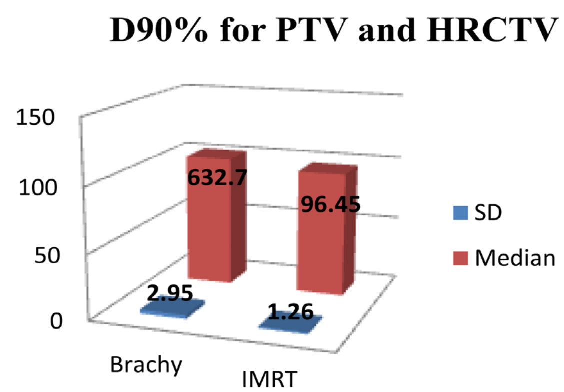

Figure 3. Median and standard deviation (SD±) Dose% received by 90% of PTV for IMRT and 3D-brachtherapy.

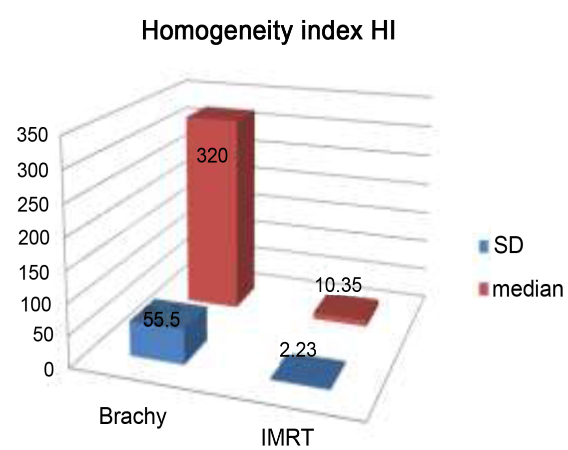

Figure 4. Median and standard deviation (SD±) for homogeneity index (HI) for IMRT and 3D-brachtherapy.

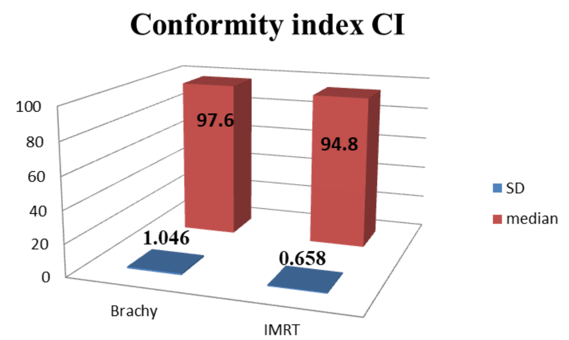

Figure 5. Median and standard deviation (SD±) the Conformity index (CI) for IMRT and 3D-brachtherapy.

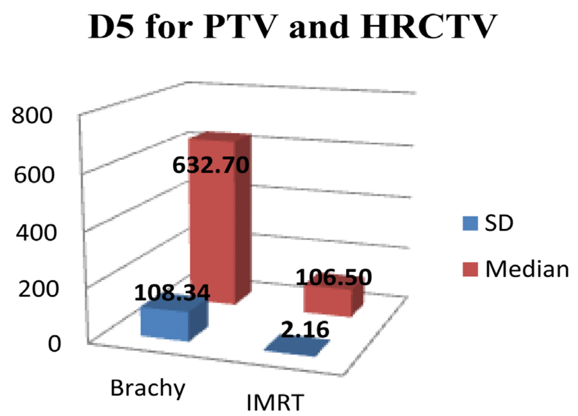

Figure 6. Median and standard deviation (SD±) for Dose% Received by 5% of PTV for IMRT and 3D-brachtherapy.

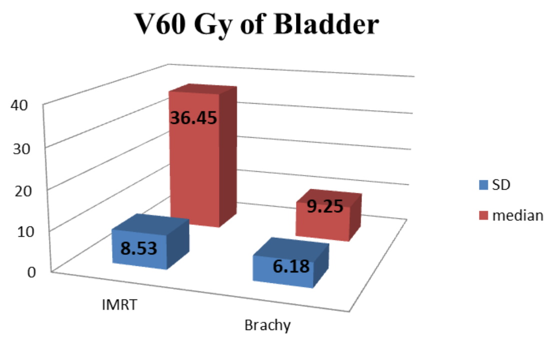

Figure 7. Median and standard deviation (SD±) the volume irradiated to more than 60Gy (EQD2) to bladder by accumulated accumulated dose from 3D-Conformal whole pelvis and boost (IMRT or 3D-Brachytrerapy).

5. Conclusion

For the patients with cervical cancer, 3D-brachytherapy technique not only provides excellent target coverage but also maintains low doses (D_{2cc}) to the rectum and bladder and lower D_{max} to the femoral heads. But in some cases that we can't use brachytherapy regarding to clinical reasons we can use IMR technique.

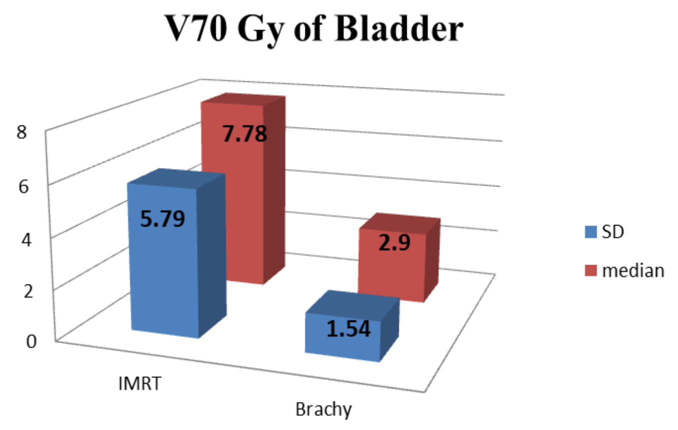

Figure 8. Median and standard deviation (SD±) the volume irradiated to more than 70 Gy (EQD2) to bladder by accumulated dose from 3D-Conformal whole pelvis and boost (IMRT or 3D-Brachytrerapy).

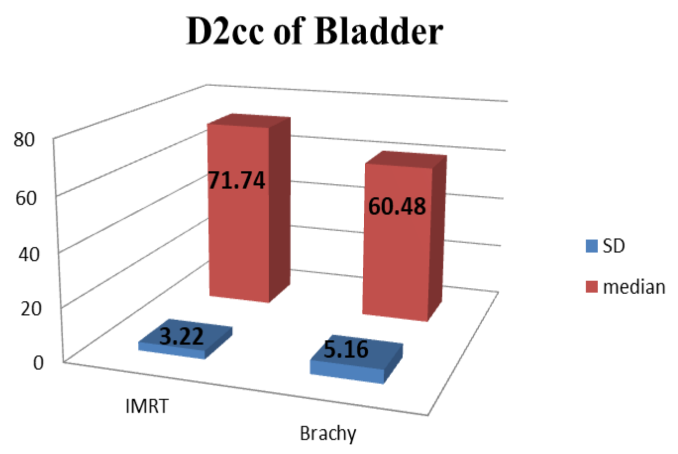

Figure 9. Median and standard deviation (SD±) dose to 2 cm^3 of bladder volume for IMRT and 3D-brachtherapy.

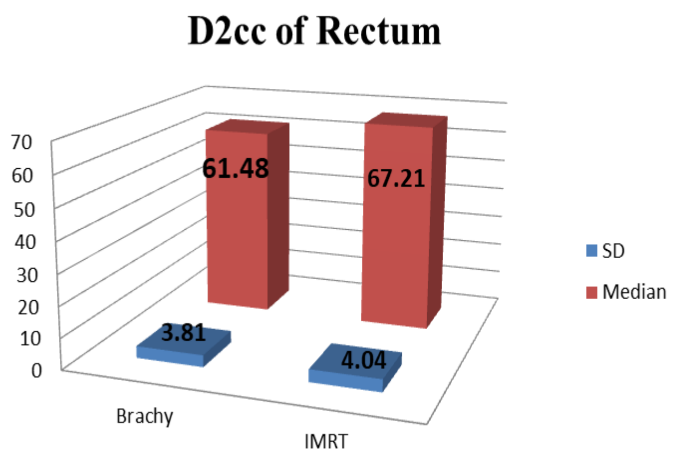

Figure 10. Median and standard deviation (SD±) dose to 2 cm^3 of rectum for IMRT and 3D-brachtherapy.

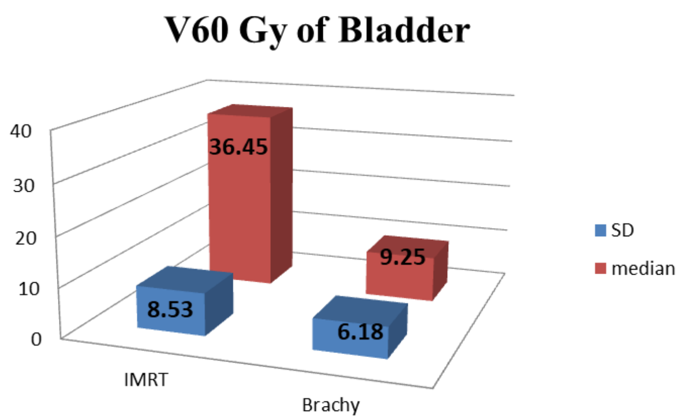

Figure 11. Median and standard deviation (SD±) the volume irradiated to more than 60 Gy (EQD2) to rectum by accumulated accumulated dose from 3D-Conformal whole pelvis and boost (IMRT or 3D-Brachytrerapy).

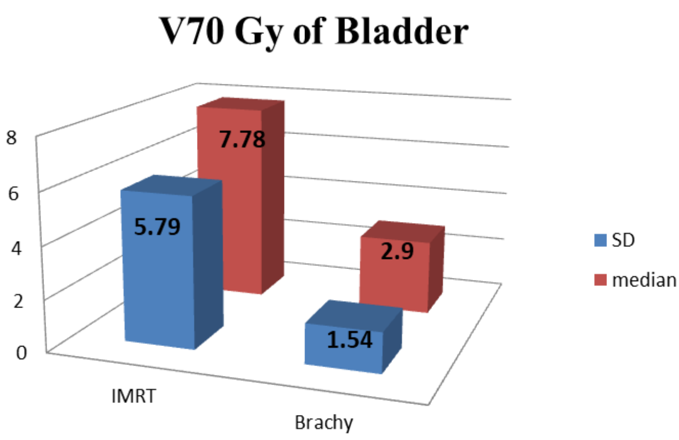

Figure 12. Median and standard deviation (SD±) the volume irradiated to more than 70 Gy (EQD2) to rectum by accumulated dose from 3D-Conformal whole pelvis and boost (IMRT or 3D-Brachytrerapy).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations and Acronyms

IMRT: Intensity-Modulated Radiation Therapy
LACC: Locally Advanced Cervical Carcinoma
EBRT: External Beam Radiotherapy
AAAOC: Alexandria Ayadi Almostakbl Oncology Center
HRCTV: High Risk Clinical Target Volume
OAR's: Organs at Risk
HPV: Human Papillomavirus
PTV: Planning Target Volume
CT: Computed Tomography
TPS: Treatment Planning System
RTOG: Radiation Therapy Oncology Group
GTV: Gross Target Volume
BED: Biological Effective Dose
EQD2: Equivalent Dose in 2 Gy
FIGO: The International Federation of Gynecology and Obstetrics
CMS: Computerized Medical System
XiO: Three Dimensions Treatment Planning System