Egypt. J. Biophys. Biomed. Eng., **Vol.24 ,** No.1, pp.13- 30 (2023)

Physical and Radiobiological Evaluation of Patient SetupErrors in the Radiotherapy Procedure for Prostate Cancer

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Background: Radiobiological and dosimetric indices-related effects of patient setup errors were evaluated for prostate patients treated using the volumetric modulated arc therapy (VMAT) technique.

Materials and Methods: Ten patients were treated and evaluated during the course of treatment. Each one was treated with 2 Gy for 39 fractions. The setup verification of each patient was determined using an electronic portal imaging device (EPID) for 5 fractions during the treatment course. The mean of setup errors for those 5 fractions was calculated for each patient. Dose-Volume Histograms of the planning target volume (PTV), femoral heads, bladder, and rectum were generated, and the conformity index (CI), homogeneity index (HI), tumor control probability (TCP), and normal tissue complication probability (NTCP) were determined.

Results: The population random set-up errors were (3.61), (3.24), and (3.87) mm in vertical, longitudinal, and lateral directions respectively. Radiobiological indexes were evaluated with and without the introduction of random errors. In the original plan, the average EUD in the VMAT plans was 77.59 Gy, and the average of TCP was 98.24%; but with the introduction of the errors, the average EUD became in the order of 60.24 Gy, while the average of TCP was in the order of 84.24%. Significant differences were observed between the two plans.

Conclusion:The dosimetric and biological impacts were evaluated and indicated that setup errors during VMAT treatments can lead to a non-significant change of conformity and homogeneity but can lead to changes in the dose distribution influencing the target volume coverage and altering the delivered dose to the organs at risk (OAR).

Keywords: Dosemtrical indices, Radiobiological indices, Setup errors, Systematic error, Randomized error, Prostate cancer.

Introduction

Radiation therapy's primary goal is to administer enough radiation to the tumor to stabilize it while avoiding irradiating the organ at risks (OARs) to a level that would cause severe complications. Increased tumor dose results in better tumor control, according to clinical evidence, particularly in prostate cancer [1, 2]. External beam radiation therapy (EBRT) advancements such as intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) enable high-dose delivery to the target while reducing the dose to vital structures [3-5]. The VMAT is a rotational radiation therapy technique that delivers the radiation dose continuously with the simultaneous variation of gantry rotation speed, dose rate, and multi-leaf collimator field aperture, while IMRT is an advanced type of 3-dimensional conformal radiation therapy (3DCRT) that incorporates intensity modulated radiation beams [3]. VMAT has recently gained widespread recognition as the technique of choice for prostate cancer patients undergoing EBRT because it can achieve IMRT-quality dose distributions with less treatment time and fewer monitor units [3-

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Received 12/12/202 , accepted 20/12/2022
DOI :10.21608/EJBBE.2022.176331.1060

5]. Several studies comparing VMAT versus IMRT preparation for prostate cancer have been conducted by several scientists. Previous research analyzed the findings primarily in terms of physical volume, radiobiological and physical dose [6-12]. Thus VMAT will be the technique used in the current work. The tumor control probability (TCP) and normal tissue complication probability are two radiobiological models that enable quantification of the effects of radiation treatment on cancer and healthy cells (NTCP) [13, 14]. TCP is thus calculated using the planned target volume (PTV) and NTCP is calculated for all OARs. The planning target volume (PTV) represents the clinical target volume (CTV) with an added margin to account for any geometrical uncertainty in its shape and any variations in its location relative to the radiation beams due to organ mobility, organ deformation, and patient setup variations. [15, 16]. To reduce such margins, image guidance has been widely used in position verification to reduce patient set-up uncertainty. On the other hand, treatment plan robustness is the degree of resilience of the required dose distribution to these uncertainties and varies with the treatment site, technique, and method. TCP and NTCP are useful parameters in the evaluation of plan robustness [17]. Therefore in our study, both parameters will be used to evaluate the difference between the corrected and uncorrected patient setup errors in patient positioning during the radiotherapy treatments. In addition, plan qualities will be also investigated in each of the studied cases. Stroom et al, showed that shifts in the position of the isocenter as large as 3 mm tend to have modest impacts on the quality of the VMAT plans [18]. On the contrary, Algan et al stated that the mean V_{95} (Volume of CTV receiving 95% of the prescription dose) values for corrected patient setup rises to 99.9% compared to the uncorrected one (87.3%) [19]. The importance of this subject is ascribed to the fact that this can impact the setup margins that are typically used for patients and this was a motivation to conduct our institutional investigation. It should be mentioned that there are two types of setup uncertainties: systematic errors (Σ) and random errors (σ). Both of them should be considered when deriving the margins used in generating the PTVs. Systematic errors are repeatable consistent errors that occur in the same direction and magnitude, whereas Random (day-to-day) errors can differ in direction, and magnitude, and are unpredictable. Cone-Beam CT and Electronic Portal Imaging Device (EPID) are two options that can be used for setup error evaluation [20]. Our study will mainly focus on the random errors occurring with prostate patient positioning as evaluated by our EBID system.

Materials and Methods

Patient selection and preparation

We selected ten high-risk prostate cancer patients that were treated at Ain-Shams University's hospital of Nuclear Medicine and Radiation Oncology from March 2019 to March 2021. CT images are acquired for all patients with an empty rectum and full bladder and with 3 implanted fiducial markers. Images were then imported into the Eclipse (version 13.5.35) treatment planning system, and the CTV and OARs were contoured by the responsible physician. The patient's PTV was generated by expanding the CTV with an isotropic margin of 7mm.

Image Guided Radiotherapy (IGRT)

Before treatment, patients were positioned with a suitable immobilization device and then they were set up for treatment using in-room lasers and patient skin marks. Orthogonal portal images were acquired using EPID. The image quality of our EPID system is 1024768 × Pixels. For portal acquisition, 1 monitor unit (MU) was delivered per field with a dose rate of 600 MU per minute. Electronic portal images (EPIs) were compared to the digitally reconstructed radiographs (DRRs) serving as our reference image created for the orthogonal portal at 0^0 (anterior) and 90^0 (lateral) using the treatment planning system (TPS). Reference bony landmarks for the comparison of the EPIs and DRRs in the lateral direction are pubic symphysis, obturator foramen, iliac crest, and fiducial markers. In the anterior and posterior (AP) direction, landmarks were Coccyx bones, L5-S1, pubic symphysis, and fiducial markers. Online setup error corrections were carried out for each prostate patient. Matching DRRs and portal images were performed using the anatomy matching software (ARIA-record & verify system). EPIs were taken 5 times during the course of each patient's treatment. The random set-up error was assessed along the three transitional directions (vertical (Z), longitudinal (Y), and lateral (X)). We calculated the individual random errors for each of the ten patients and then calculated the population random setup error.

Treatment planning

All treatment plans were done using the VMAT technique and were delivered to the linear

accelerator (Unique©Varian Clinic-iX) with 6MV photon beams. For each patient, after the initiation of patient treatment using the plan generated in Eclipse, extra 5 plans were generated utilizing the errors reported during each of the 5 times that EPIs were taken. Then a final composite plan was generated representing the dose distribution that would occur if no corrections were done during patient treatment. This composite plan will be named "shifted plan" or "plan with error" throughout this paper

Radiobiological evaluation:

The EUD (equivalent uniform dose model) based mathematical model is simple because it's based mainly on two-equation, and versatile because the same model may be used for both TCP and NTCP calculations *Niemierko's* EUD-based TCP, NTCP [14, 25] are defined as equations (1),(2).

$$TCP = \frac{1}{1+\left(\frac{TCD_{50}}{EUD}\right)^{\gamma_{50}}} \quad (1)$$

$$NTCP = \frac{1}{1+\left(\frac{TD_{50}}{EUD}\right)^{\gamma_{50}}} \quad (2)$$

where the TCD_{50} is the dose to control 50% of the tumors when the tumor is homogeneously irradiated, and TD_{50} is the tolerance dose for a 50% complication rate at a specific time interval (eg.5 years in the *Emami et al*. organ at risk (OARs) tolerance data [26] when the whole organ of interest is homogeneously irradiated), and γ_{50} describes the slope of the dose-response curve [14, 25, 27]. According to *Niemierko's* phenomenological model, the EUD [14, 25] is defined as equation (3):

$$EUD = \left(\sum_{i=1} (v_i EQD_i^{\,a})\right)^{\frac{1}{a}} \quad (3)$$

where:(v_i) is that the three-quarter organ volume that receives a dose (*Di*) and (*a*) may be a tissue-specific parameter describing the amount of impact. The dose constraints of the treatment plan for each patient were indicated in the table (1).

TABLE 1. Dose specifications for rectum, bladder, and femoral heads.

Normal organ limit*	$D_{15\%}$	$D_{25\%}$	$D_{35\%}$	$D_{50\%}$
Rectum	< 75 Gy	<70 Gy	< 65 Gy	< 60 Gy
Bladder	< 80 Gy	< 75 Gy	< 70 Gy	< 65 Gy
Femoral heads			Mean dose <45Gy	

Normal organ limit refers to the volume of that organ that should not exceed the dose limit. $Dx_{\%}$: Dose received by "$x_{\%}$" of total OAR volume, where $x_{\%}$ = 15, 25, 35, and 50; *OAR*: Organ at risk in equation (3), *"a"* is a unit less model parameter that is specific to the normal structure or tumor of interest, and "*v"* is a unit less and represents the i^{th} partial volume receiving dose D_i in Gy [14]. Since the relative volume of the whole structure of interest corresponds to 1, the sum of all partial volumes v_i will equal 3 [14]. Furthermore, in equation (3), the EQD [25] is the biologically equivalent physical dose of 2 Gy and is defined as:

$$EQD = D \times \frac{\left(\frac{\alpha}{\beta} + \frac{D}{n_f}\right)}{\left(\frac{\alpha}{\beta} + 2\right)} \quad (4)$$

where,n_f and d_f, which ($d_f = D/n_f$), are the numbers of fractions and dose per fraction size of the treatment course, respectively. The α/β is the tissue-specific Linear Quadratic (LQ) parameter of the organ being exposed [14 -18, 21-25]. During the study, parameters (*a*), TD50, γ_{50} and

α/β are important for the late response. For comparative aim, the values for TCD_{50}, TD_{50}, (a), and α/β ratio for radiotherapy were investigated to evaluate TCP values and NTCP with physical indices from DVH. A MATLAB code [6] was used to conduct these calculations to analyze DVH for each patient. The first column corresponds to the increasing absolute dose and the second column to the corresponding absolute volume. The alpha-beta ratio of 1.2 was used to measure the EUD and TCP values for the prostate tumor, and the EUD and NTCP values for the OARs were determined in the same way. The alpha-beta ratios used in this analysis for the rectum, bladder, and femoral heads were 3.9, 8.0, and 0.85, respectively. Table 2 summarized the parameters used to calculate Niemierko's EUD-based TCP and NTCP

TABLE 2. Parameters used to calculate Niemierko's EUD-based TCP and NTCP.

Organ	Volume type	n_f	a	γ_{50}	TD_{50}(Gy)	TCD_{50}(Gy)	D_{pf}(Gy)	α/β
Prostate	Tumor	39	-10	1.0	-	28.34	2	1.20
Rectum	Normal	39	8.33	4	80	-	2	3.90
Bladder	Normal	39	2	4	80	-	2	8.00
Femur	Normal	39	4	4	65	-	2	0.85

n_f: Number of fractions, α/β Alpha-beta ratio, D_{pf}: Dose per fraction, EUD: Equivalent uniform dose, TCP: Tumor control probability, Femur: Femur heads, TD: Tolerance dose, TCD: Tumor dose to control, NTCP: Normal tissue complication probability.

Physical indices evaluation:

Dosimetric parameters used included, prescribed dose, prescription isodose volume, maximum dose, homogeneity index (HI), and conformity index (CI). The homogeneity index and conformity index were calculated as follows:

Homogeneity index:

$$(HI) = \frac{D_2 - D_{98}}{D_{50}} \quad (5)$$

Conformity index:

$$(CI) = \frac{(PTV)_{pD}}{PIV} \quad (6)$$

where D_2, $D_{50,}$ and D_{98} are the doses covering 2%. 50% and 98% of the target volume, respectively, and PIV represents prescription isodose surface volume, and $(PTV)_{PD}$ represents PTV coverage at the prescription dose.

Errors Statistical Analysis

The setup errors were defined as deviations between the actual and expected patient position normally calculated as the shift in the isocenter position when an image is compared against its corresponding reference. The systematic error is calculated as the mean of the setup error for individual patients. For each individual, the random errors were defined as the standard deviation of the setup errors around the corresponding mean. We recorded the isocenter errors for each patient and calculated the mean value in X" laterals", Y "longitudinal «and Z "vertical" directions and finally, we calculated the individual random for all patients in the three dimensions.

The individual mean set-up error

It is calculated by summing the measured set-up error for each imaged fraction ($\Delta_1 + \Delta_2 + \Delta_3 +\ldots$) and then dividing by the number of imaged fractions (n) [28].

$$m_{individual} = \frac{(\Delta_1+\Delta_2+\Delta_3+...+\Delta_n))}{n} \quad (7)$$

Individual random error:

It is the SD of the set-up errors around the corresponding mean individual value (m) derived from the previous equation (7) [28].

$$\sigma^2_{individual} = \frac{(\Delta_1-m)^2+(\Delta_2-m)^2+(\Delta_3-m)^2+...+(\Delta_n-m)^2)}{(n-1)} \quad (8)$$

where: is imaged fraction number

Population random error:

It is the mean of all the individual random errors (σ_1, σ_2, σ_3 …) [28].

$$\sigma_{(set\text{-}up)} = \frac{(\sigma_1+\sigma_2+\sigma_3+...)}{p} \quad (9)$$

where: is the patient number

Comparing physical and radiobiological indexes to the reported random errors

The chart flow in figure 1 summarizes the steps done for each patient. Thus, in Summary, the prostate patient is selected and then a plan is generated. Once the patient starts the course of treatment, we will select 5 days distributed along the course of his or her treatment. The isocenter shifts determined by portal images taken on each of those days will be recorded. Then in eclipse, those shifts will be used to generate a new plan simulating the situation of uncorrected shifts for each day, thus a total of 5 plans will be generated and a composite plan will be generated to represent the final dose distribution resulting from the errors that occurred during those 5 days.

Results

The population random set-up error was (3.61), (3.24), and (3.87) mm in vertical, longitudinal, and lateral directions respectively. Table (3) shows the recorded error shifts for all patients. Each one referred to the mean error value of the EPIDs along the course of treatment. Table (4) shows the calculated individual and population random errors.

The radiobiological and dosimetric evaluation:

The isodose distributions of the VMAT plans and the corresponding DVHs of targets and OAR for the original and shifted plans for one of the studied patients are shown in figures (2) and (3) respectively.

Prostate tumor:

Table 5 shows the results of EUD& TCP while table 6 & 7 shows the value of doses before and after error verification, For prostate tumors, the average EUD values in the VMAT plans without errors (77.59 Gy) were slightly higher than in the VMAT plans with errors (60.24 Gy). The average TCP value without errors for the prostate tumor in the VMAT plans was 98.24 and with errors in VMAT plans was 84.24 as shown in Table (5). It is worth mentioning, that in case number (2) & (5), the volume of the prostate tumor was very small with large setup errors during the sessions.

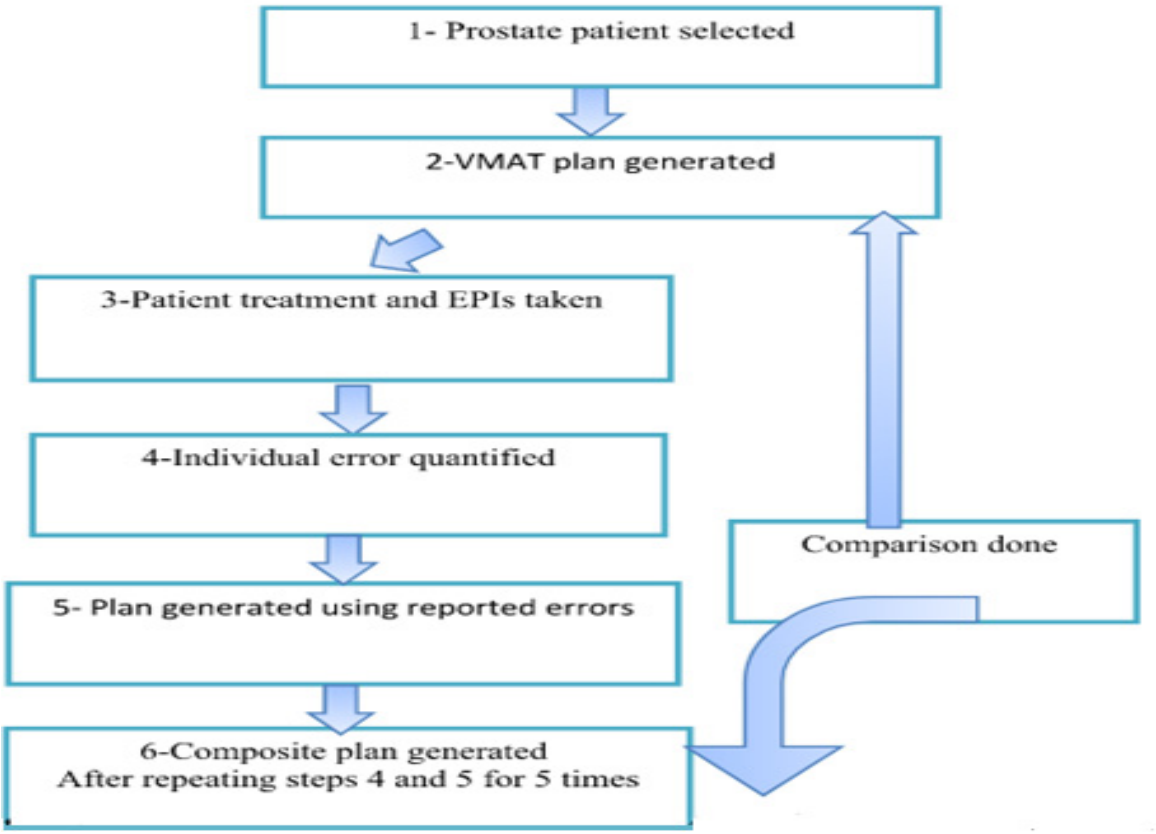


Fig. 1. the flow chart of this work for each patient.

TABLE 3.The mean isocenter error shift of the ten cases.

Patient	Mean error	X "laterals" mm	Y "longitudinal" mm	Z "vertical" mm
Patient 1	M_1	0.5	4.0	-0.25
Patient 2	M_2	-1.67	2.0	-2.33
Patient 3	M_3	-0.75	-3.0	-11.25
Patient 4	M_4	-0.75	2.87	1.87
Patient 5	M_5	0.28	-0.57	0.28
Patient 6	M_6	-1.58	1.33	-0.92
Patient 7	M_7	-4.67	3.5	-1.0
Patient 8	M_8	-6.28	-2.71	-2.71
Patient 9	M_9	-0.25	-2.5	-1.5
Patient 10	M_{10}	2	-3.71	-1.57

TABLE 4.individual random errors for ten patients and population random setup error.

patient	Random error	X "laterals" mm	Y "longitudinal" mm	Z "vertical" mm
Patient 1	σ_1	4.7	5.1	3.3
Patient 2	σ_2	4.9	6.0	2.52
Patient 3	σ_3	6.3	4.16	10.1
Patient 4	σ_4	3.01	1.24	1.88
Patient 5	σ_5	1.25	0.7	0.7
Patient 6	σ_6	6.11	3.2	4.77
Patient 7	σ_7	2.94	2.07	2.68
Patient 8	σ_8	3.59	1.97	2.69
Patient 9	σ_9	1.71	3.32	2.08
Patient 10	σ_{10}	4.08	4.57	5.28
Population random set-up error	$\sigma_{set\text{-}up}$	3.87	3.24	3.61

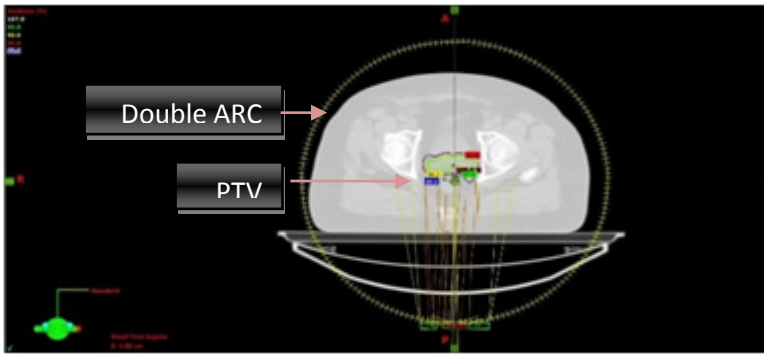


Fig. 2. Transversal view of isodose distribution for prostate cancer case planned in Eclipse treatment planning system using VMAT double ARC (ARC angle: 1810CW 1790 with collimator angle 300, 1790CCW 1810 with collimator angle 3300.

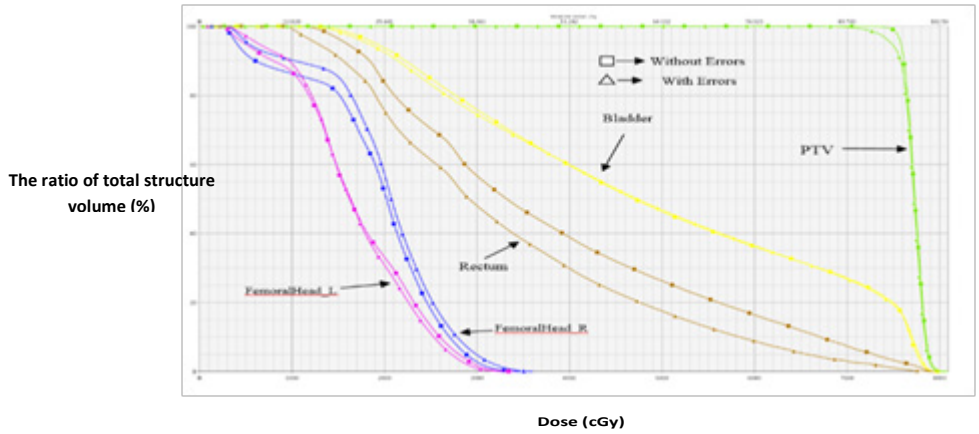


Fig. 3. The corresponding DVHs of targets and OARs for the original and shifted plans.

TABLE 5. EUD and TCP for Prostate cancer in VMAT plans in case of errors and without errors.

Case No	EUD(Gy)		(TCP)%	
	Without errors	With errors	Without errors	With errors
Case 1	76.26	74.52	98.13	97.95
Case 2	77.20	20.37	98.22	21.05
Case 3	77.52	64.98	98.24	96.51
Case 4	77.50	56.91	98.24	94.20
Case 5	77.7	27.621	98.26	47.44
Case 6	80.63	73.261	98.50	97.81
Case 7	77.76	76.351	98.27	98.14
Case 8	76.76	76.14	98.17	98.12
Case 9	76.16	53.91	98.12	92.91
Case 10	78.44	78.30	98.32	98.31
Average	77.593	60.24	98.247	84.24
SD	1.277	20.92	0.103	27.14

TABLE 6. PTV-High without errors in prostate cases.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv.SphereDiameter (cm)
Case 1	187.8	72.09	83.51	77.98	77.80	77.93	1.12	7.1
Case 2	120.5	71.92	80.91	77.33	77.03	77.34	0.95	6.1
Case 3	198.6	63.25	81.52	76.99	77.11	77.04	1.05	7.2
Case 4	95.7	70.73	83.24	78.40	78.49	78.41	1.08	5.7
Case 5	151.1	70.86	83.34	79.74	79.93	79.84	1.06	6.6
Case 6	227.2	61.59	81.50	77.28	77.53	77.50	1.50	7.6
Case 7	163.4	68.97	82.39	77.60	77.49	77.56	0.93	6.8
Case 8	156	70.07	82.75	77.90	78.11	78.03	1.24	6.7
Case 9	156.1	66.11	83.56	77.85	77.82	77.87	1.18	6.7
Case 10	189.6	67.58	82.02	77.93	78.05	78.00	0.99	7.1
Average	164.6	68.317	82.474	77.9	77.936	77.952	1.11	6.76

TABLE 7. PTV-High in prostate cancer patients with errors.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv.SphereDiameter (cm)
Case 1	187.8	57.12	83.32	77.53	77.71	77.74	1.71	7.1
Case 2	120.5	65.08	80.56	77.08	77.61	77.24	1.30	6.1
Case 3	198.6	40.81	80.62	72.38	77.52	76.41	7.56	7.2
Case 4	95.7	55.61	85.61	79.29	79.89	79.66	2.13	5.7
Case 5	151.1	56.71	83.48	78.26	79.74	79.56	3.8	6.6
Case 6	227.2	56.74	81.83	76.86	77.54	77.36	2.23	7.6
Case 7	163.4	17.64	82.69	75.51	77.58	77.53	7.59	6.8
Case 8	156	42.63	84.20	77.34	78.14	78.08	3.47	6.7
Case 9	156.1	38.22	83.48	77.11	77.71	77.71	3.65	6.7
Case 10	189.6	25.51	81.30	65.34	77.61	70.85	13.79	7.1
Average	164.6	45.607	82.709	75.67	78.10	77.21	4.723	6.76

Rectum

For the rectum, the average EUD values in the VMAT plans without errors 60.45 Gy were lower than in the VMAT plans with errors 61.46 Gy, and the average NTCP values of the rectum without error in the VMAT plans 1.30 % and with error in the VMAT plans 5.7% are shown in Table(8).

For dosimetric response, the average volume in VMAT plans without errors 65.6 cc, the average minimum dose is 6.91Gy, the average maximum dose 81.25Gy, the average mean dose 41.09Gy, the average modal dose is 28.16 Gy, the average of median dose 37.63Gy, the average of STD 20.97Gy, and the average of equivalent sphere diameter 4.69cm are shown in Table (9).

TABLE 8. results of EUD and NTCP.

Case No	EUD(Gy)		(NTCP)%	
	Without errors	With errors	Without errors	With errors
Case 1	59.92	59.98	0.97	0.99
Case 2	61.25	58.75	1.38	0.71
Case 3	61.78	65.28	1.57	3.72
Case 4	62.10	62.08	1.71	1.70
Case 5	62.12	75.06	1.72	26.49
Case 6	54.97	44.67	0.25	0.009
Case 7	62.52	61.28	1.90	1.39
Case 8	56.13	50.83	0.34	0.07
Case 9	61.46	73.41	1.450	20.16
Case 10	62.26	63.28	1.78	2.29
Average	60.451	61.462	1.307	5.7529
SD	2.70	9.13	0.59	9.44

TABLE 9. Rectum organ without errors in prostate cases.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv.SphereDiameter (cm)
Case 1	69.9	1.05	82.17	42.26	8.25	45.59	24.31	5.1
Case 2	46.8	10.69	79.94	38.09	18.93	33.18	18.03	4.5
Case 3	44.2	9.79	79.71	44.62	77.66	42.09	20.29	4.4
Case 4	48.3	4.40	82.42	40.40	6.74	38.87	24.76	4.5
Case 5	77.7	4.38	81.48	33.54	7.43	33.22	20.31	5.3
Case 6	80.1	10.08	79.68	37.39	20.48	28.82	21.40	5.3
Case 7	55.4	8.89	81.34	44.02	77.75	38.38	18.80	4.7
Case 8	91.6	5.85	82.45	48.30	34.71	45.47	18.43	5.6
Case 9	84.7	6.82	83.20	41.58	7.71	38.68	22.45	5.4
Case 10	57.3	7.24	80.16	40.72	21.98	32.01	20.92	4.8
Average	65.6	6.919	81.255	41.092	28.164	37.631	20.97	4.96

The average volume in VMAT plans with errors 65.6cc, the average minimum dose 6.43Gy, the average maximum dose 80.92Gy, the average mean dose 42.15Gy, the average modal dose 30.49Gy, the average of median dose 41.33Gy, the average of STD 21.01Gy, and the average of equivalent sphere diameter 4.96cm are shown in Table (10).

Bladder

The average EUD values for the bladder in the VMAT plan without error 45.11 Gy were higher than in the VMAT plans with error 39.36 Gy, and the average NTCP values of the bladder without error in the VMAT plans 0.07, 0.1 % and with error in the VMAT plans 0.01, 0.02% are shown in Table (11).

TABLE 10. Rectum organ in prostate cases when there are errors.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv.SphereDiameter (cm)
Case 1	69.9	1.00	80.47	41.01	6.21	44.85	24.22	5.1
Case 2	46.8	9.23	79.99	33.23	18.97	29.13	16.27	4.5
Case 3	44.2	9.79	79.71	44.62	77.66	42.09	20.29	4.4
Case 4	48.3	3.86	83.55	38.60	7.04	34.81	25.61	4.5
Case 5	77.7	4.08	76.76	29.78	6.68	30.71	16.99	5.3
Case 6	80.1	10.48	79.31	37.71	20.00	28.97	21.17	5.3
Case 7	55.4	7.17	80.93	39.64	8.43	35.45	19.63	4.7
Case 8	91.6	4.64	81.99	51.78	73.78	52.18	20.61	5.6
Case 9	84.7	6.22	83.23	40.40	8.01	37.78	23.41	5.4
Case 10	57.3	7.91	83.29	64.76	78.19	77.42	21.95	4.8
Average	65.6	6.438	80.923	42.153	30.497	41.399	21.01	4.96

TABLE 11. results of EUD and NTCP for Bladder.

Case No	EUD(Gy)		(NTCP)%	
	Without errors	With errors	Without errors	With errors
Case 1	39.28	40.27	0.001	0.002
Case 2	41.56	34.50	0.003	0.0001
Case 3	47.91	39.14	0.027	0.001
Case 4	36.85	34.23	0.0004	0.0001
Case 5	55.08	28.98	0.254	0.000009
Case 6	32.77	36.05	0.00006	0.0003
Case 7	48.26	48.26	0.031	0.031
Case 8	50.57	50.55	0.065	0.065
Case 9	56.42	43.49	0.37	0.006
Case 10	42.42	38.43	0.004	0.0008
Average	45.11	39.39	0.076	0.01
SD	7.812	6.60	0.129	0.02

For dosimetric response, the average volume in VMAT plans without errors 171.52 cc, the average minimum dose is 8.79 Gy, the average maximum dose is 81.77 Gy, the average mean dose is 43.15 Gy, the average modal dose is 65.33Gy, the average of median dose 40.21Gy, the average of STD 21.09 Gy, and the average of equivalent sphere diameter 6.63cm are shown in Table (12).

The average volume in VMAT plans with errors is 171.52 cc, the average minimum dose is 7.93 Gy, the average maximum dose is 80.42 Gy, the average mean dose is 37.18 Gy, the average modal dose 40.48Gy, the average median dose is 32.91 Gy, the average of STD 21.77 Gy, and the average of equivalent sphere diameter 6.63cm are shown in Table (13).

TABLE 12. Bladder organ in prostate cases without errors.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv.Sphere-Diameter (cm)
Case 1	122.9	6.71	82.31	48.92	77.78	48.59	23.46	6.2
Case 2	64.1	11.92	80.44	49.19	76.72	46.94	20.70	5
Case 3	78.3	18.38	79.90	57.24	76.59	56.20	15.65	5.3
Case 4	234.6	5.16	81.88	40.11	78.58	38.53	21.72	7.7
Case 5	263.8	2.92	82.02	30.77	27.63	27.49	19.03	8
Case 6	358.8	4.29	80.40	37.75	77.49	33.06	19.93	8.8
Case 7	81	9.19	82.27	37.81	77.55	28.98	22.85	5.4
Case 8	169	4.20	83.73	43.08	77.71	37.23	25.40	6.9
Case 9	281	2.36	82.79	31.85	4.41	30.93	23.86	8.1
Case 10	61.7	22.82	82.02	54.78	78.91	54.21	18.32	4.9
Average	171.52	8.795	81.766	43.15	65.337	40.216	21.092	6.63

TABLE 13. Bladder organ in prostate cases when there are errors.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv.Sphere Diameter (cm)
Case 1	122.9	5.78	82.48	44.58	77.84	42.48	42.22	6.2
Case 2	64.1	11.61	80.28	49.00	77.04	47.30	21.02	5
Case 3	78.3	17.77	79.23	46.34	37.45	43.31	12.73	5.3
Case 4	234.6	4.67	83.73	35.21	8.01	33.50	22.14	7.7
Case 5	263.8	3.10	82.64	33.38	79.68	29.20	20.53	8
Case 6	358.8	4.49	80.44	38.76	77.50	34.08	20.05	8.8
Case 7	81	6.82	82.69	29.92	8.75	20.93	22.04	5.4
Case 8	169	3.21	84.20	32.23	4.54	23.32	25.68	6.9
Case 9	281	2.12	82.68	28.89	4.70	23.33	23.39	8.1
Case 10	61.7	19.73	65.89	33.53	29.31	31.67	7.98	4.9
Average	171.52	7.93	80.426	37.184	40.482	32.912	21.77	6.63

Left Femoral head

The average EUD values for the left femoral head in the VMAT plans without an error of 10.04 Gy were higher than those in the VMAT plans with an error of 9.69 Gy the average NTCP values of femoral head-L without error in the VMAT plans were 0.0% and with error in the VMAT plans 0% are shown in Table (14).

For dosimetric response, the average volume in VMAT plans without errors is 171.2 cc, the average minimum dose is 2.82 Gy, the average maximum dose is 34.94 Gy, the average mean dose is 16.24 Gy, the average modal dose is 11.78 Gy, the average of median dose 16.75 Gy, the average of STD 6.99 Gy, and the average of equivalent sphere diameter 6.9 cm are shown in Table (15).

TABLE 14. the EUD and NTCP for the left femoral head.

Case No	EUD(Gy)		(NTCP)%	
	Without errors	With errors	Without errors	With errors
Case 1	9.82	9.12	0	0
Case 2	8.40	7.66	0	0
Case 3	13.01	13.01	0	0
Case 4	9.42	9.42	0	0
Case 5	13.90	13.12	0	0
Case 6	9.25	8.66	0	0
Case 7	10.92	10.16	0	0
Case 8	10.30	9.94	0	0
Case 9	9.28	9.92	0	0
Case 10	6.07	5.84	0	0
Average	10.04	9.69	0	0
SD	2.23	2.20	0	0

TABLE. 15. left Femoral Head organ in prostate cases without errors.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv.SphereDiameter (cm)
Case 1	169.4	3.17	37.21	17.99	16.76	18.01	6.63	6.9
Case 2	169.6	2.46	34.02	16.92	13.80	16.21	6.63	6.9
Case 3	188.6	3.39	33.25	17.49	17.65	17.71	5.58	7.1
Case 4	191.4	6.96	27.38	10.96	12.79	12.07	5.30	7.2
Case 5	152.4	1.78	34.44	15.53	13.80	15.32	6.23	6.6
Case 6	144.5	1.36	32.02	14.94	2.13	15.78	7.95	6.5
Case 7	184	3.38	30.06	15.31	15.43	15.68	5.41	7.1
Case 8	155.4	1.21	40.50	17.81	1.94	19.35	10.16	6.7
Case 9	194.9	0.76	35.97	14.63	1.11	16.30	7.92	7.2
Case 10	162.7	3.77	44.64	20.84	22.44	21.07	8.14	6.8
Average	171.29	2.824	34.949	16.242	11.785	16.75	6.995	6.9

The average volume in VMAT plans with errors is 171.2 cc, the average minimum dose 2.44Gy, the average maximum dose is 34.09 Gy, the average mean dose is 15.90 Gy, the average modal dose is 11.14 Gy, the average median dose is 16.30 Gy, the average of STD 6.37 Gy, and the average of equivalent sphere diameter 6.9 cm are shown in Table (16).

Right Femoral head

The average EUD values for femoral head-R in the VMAT plans without error 10.29 Gy were higher than those in the VMAT plans with error 10.61 Gy the average NTCP values of femoral head-R without error in the VMAT plans, 0.0% and with error in the VMAT plans 0.0% are shown in Table (17).

TABLE 1 6. left Femoral Head organ in prostate cases when there are errors.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv.Sphere Diameter (cm)
Case 1	169.4	3.59	35.06	17.66	16.40	17.63	5.86	6.9
Case 2	169.6	2.99	33.58	16.90	13.76	16.32	6.04	6.9
Case 3	188.6	3.19	32.02	15.28	14.83	15.46	4.82	7.1
Case 4	191.4	1.15	26.54	10.88	12.53	11.91	4.97	7.2
Case 5	152.4	1.73	32.89	14.95	13.27	14.81	5.93	6.6
Case 6	144.5	1.25	29.93	14.07	2.02	14.94	7.69	6.5
Case 7	184	3.38	28.78	14.67	15.05	15.02	4.77	7.1
Case 8	155.4	1.54	40.81	19.10	2.16	20.44	9.22	6.7
Case 9	194.9	0.83	35.91	14.87	1.16	16.27	7.64	7.2
Case 10	162.7	4.76	45.41	20.70	20.24	20.22	6.78	6.8
Average	171.29	2.441	34.093	15.908	11.142	16.302	6.372	6.9

TABLE 17. EUD and NTCP of the right femoral head .

Case No	EUD(Gy)		(NTCP)%	
	Without errors	With errors	Without errors	With errors
Case 1	9.42	10.03	0	0
Case 2	9.22	10.21	0	0
Case 3	12.15	13.22	0	0
Case 4	9.45	9.09	0	0
Case 5	13.46	14.25	0	0
Case 6	9.83	10.15	0	0
Case 7	11.33	12.10	0	0
Case 8	11.27	11.86	0	0
Case 9	9.93	8.16	0	0
Case 10	6.89	7.08	0	0
Average	10.295	10.61	0	0
SD	1.83	2.24	0	0

For dosimetric response, The average volume in VMAT plans without errors is 171.2 cc, the average minimum dose is 2.20 Gy, the average maximum dose is 35.01 Gy, the average mean dose is 16.65 Gy, the average modal dose is 13.07 GY, the average of median dose 17.59 Gy, the average of STD 7.04 Gy, and the average of equivalent sphere diameter 6.9cm are shown in Table (18).

The average volume in VMAT plans with errors is 171.2cc, the average minimum dose is 2.50 Gy, the average maximum dose is 38.21 Gy, the average mean dose is 17.42 Gy, the average modal dose is 14.39 Gy, the average median dose is 18.02 Gy, the average of STD 6.97 Gy, the average of equivalent sphere diameter 6.9cm are shown in Table (19).

TABLE 18. right FemHeadorgan in prostate cases without errors.

No of Cases	Volume (cc)	Min Dose (Gy)	Max Dose (Gy)	Mean Dose (Gy)	Modal Dose (Gy)	Median Dose (Gy)	STD (Gy)	Equiv. Sphere Diameter (cm)
Case 1	164.2	3.81	37.30	19.50	21.86	20.75	6.49	6.8
Case 2	168.5	2.41	34.75	19.07	20.64	20.21	6.97	6.9
Case 3	184.5	3.31	32.72	16.26	12.58	15.33	5.41	7.1
Case 4	188	0.83	29.16	11.68	1.36	13.40	6.32	7.1
Case 5	155.1	1.70	33.73	16.48	18.54	17.40	6.67	6.7
Case 6	149.2	1.41	32.56	15.14	20.09	16.55	7.51	6.6
Case 7	185	3.54	32.63	16.72	18.88	17.31	5.58	7.1
Case 8	157.1	1.16	36.94	18.18	1.82	20.96	9.28	6.7
Case 9	194.3	0.86	36.89	14.46	1.23	16.06	7.87	7.2
Case 10	166.1	3.01	43.43	19.09	13.75	18.02	8.38	6.8
Average	171.2	2.204	35.011	16.658	13.07	17.599	7.048	6.9

TABLE 19. FemHead-R organ in prostate cases when there are errors.

No of Cases	Volume (cc)	Min Dose (GY)	Max Dose (GY)	Mean Dose (GY)	Modal Dose (GY)	Median Dose (GY)	STD (GY)	Equiv.SphereDiameter (cm)
Case 1	164.2	4.65	40.95	20.57	22.16	21.50	6.32	6.8
Case 2	168.5	2.91	36.08	20.18	20.36	20.74	6.52	6.9
Case 3	184.5	3.29	38.41	16.48	13.49	15.09	5.75	7.1
Case 4	188	1.00	29.85	12.16	15.35	14.03	6.31	7.1
Case 5	155.1	1.69	36.13	16.65	17.64	17.42	6.86	6.7
Case 6	149.2	1.40	34.37	15.52	2.20	16.92	7.98	6.6
Case 7	185	4.12	38.09	17.90	16.08	18.04	5.57	7.1
Case 8	157.1	1.64	45.49	20.07	21.61	21.73	8.55	6.7
Case 9	194.3	0.91	35.70	14.53	1.28	16.02	7.36	7.2
Case 10	166.1	3.45	47.07	20.23	13.80	18.78	8.51	6.8
Average	171.2	2.506	38.214	17.429	14.397	18.027	6.973	6.9

The mean CI and HI for the prostate targets in the shifted and original VMAT plans are shown in Table (20). It was shown that CI and HI are not greatly altered with the introduced shifts. This could be because the random error will result in a blurring in the dose distribution with less noticed overall changes in CI and HI

Discussion

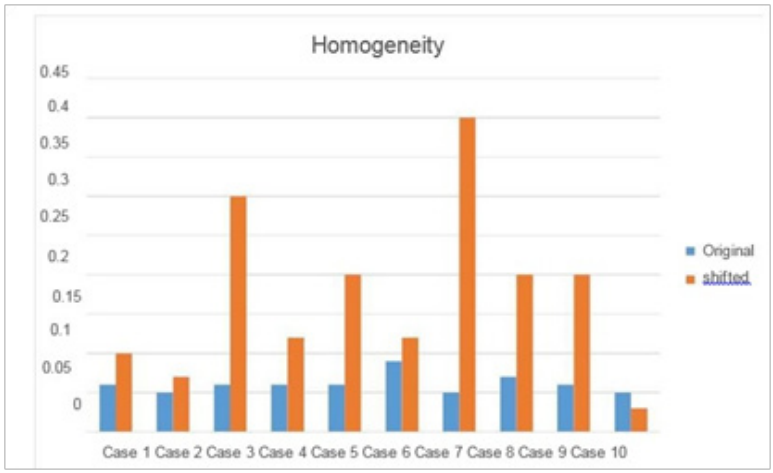
In literature, some works were focused on the dosimetric or radiobiological assessment of systematic isocenter shift errors for different types of cancers. [17, 18, 24]. This work aimed to evaluate both the dosimetric and radiobiological effects of the random setup error that usually occurs during the position of prostate patients. Particularly, we compared the radiobiological and dosimetric impacts of setup errors during VMAT of high-risk prostate cancer. Based on our results, the TCP values between treatments with and without error was showing a significant difference, a noticeable difference was also shown with EUD calculations. However similar NTCP values were seen for femoral heads and bladder with and without setup errors. (% 0.07 vs. 0.01 %), Higher average NTCP values were seen for the rectum with and without setup error (5.75 % vs. 1.307 %). DVH parameters have been always the dosimetric tool to evaluate the quality of any treatment plan. It was also a useful tool in our study to evaluate the consequence of uncorrected setup errors. Our results showed that uncorrected setup errors can result in delivering a higher dose to the rectum. The effect of uncorrected setup errors was also revealed with the radiobiological evaluation using TCP and NTCP indicating a difference in tumor control and predicting changes in normal tissue response. It should be mentioned that one of the study limitations is that no consideration has been done to the deformable changes in the target shape. Also, the critical structures were not deformed or moved during re-planning and were assumed to be in the same relative position to the target as that seen during initial planning.

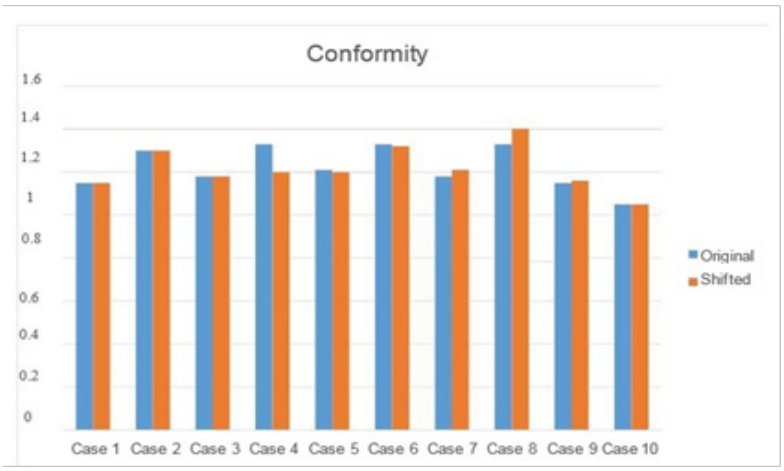
Conclusion

The dosimetric and biological impacts in this study were evaluated and indicated that the setup errors during VMAT can result in a change of conformity and homogeneity as well as changes in the dose responses altering target coverage and affecting the OAR doses.

TABLE 20. The mean CI and HI for the prostate targets in the shifted(Simulated) and original (treatment) plans

No of Cases	Homogeneity index		Conformity index	
	Original	Shifted	Original	shifted
Case 1	0.06	0.1	1.15	1.15
Case 2	0.05	0.07	1.3	1.3
Case 3	0.06	0.3	1.18	1.18
Case 4	0.06	0.12	1.33	1.2
Case 5	0.06	0.2	1.21	1.20
Case 6	0.09	0.12	1.33	1.32
Case 7	0.05	0.4	1.18	1.21
Case 8	0.07	0.2	1.33	1.4
Case 9	0.06	0.2	1.15	1.16
Case 10	0.05	0.03	1.05	1.05
Average	0.061	0.174	1.221	1.217





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(*Received* 12 / 12 / 2022 ;
accepted 20/12 /2022)

تقييم اللآ ثار البيولوجية والدوزومترية نتيجة أخطاء الأوضاع العلاجية في إجراءات العلاج الإشعاعي لمرضي سرطان البروستاتا

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يهدف العلاج الإشعاعي إلي توصيل أقصي جرعة للورم وتوصيل أقل جرعة ممكنة لبعض الآماكن الاخري المحيطة بالورم . وتعتبر أخطاء ضبط وضعية العلاج للمرضى جزء متأصل ومؤثر في عملية العلاج الإشعاعي. ويمكن استخدام تقنية العلاج الإشعاعي الموجه بالصور مثل أجهزة التصوير الإلكترونية المتحركة (EPIDs) لزيادة التوافق بين خطة العلاج التي يتم تحديدها والجرعة الواقعية التي تصل الي المريض.فى هذا البحث تم تقييم أخطاء ضبط وضعية المرضى للعلاج باسنخدام جهاز التصوير المتحرك وصور إشعاعية معاد بناؤها رقميا (DRR). وقد تم تطبيق أخطاء الضبط علي خطط العلاج الخاصة بتقنية العلاج الاشعاعي متغير الشدة لمرضي سرطان البروستاتا وذلك عن طريق تغيير نقطة المركز لخطة العلاج لتقييم مدى تأثير أخطاء الضبط والتحقق من هذا التأثير علي الورم.

وقد أظهرت النتائج أن أخطاء الضبط العشوائية لحالات سرطان البروستاتا " ٣,٨٧ ,٣,٢٤ ,٣,٦١ " مم وذلك في الاتجاهات الاتية بالترتيب x y z .كما تم تقييم معايير الجرعات الإشعاعية بواسطة قياس الجرعة القصوي والحد الآدني للجرعة والجرعة المتوسطة لجميع الأعضاء في حالة ما قبل العلاج وما بعد تقييم الأخطاء الضبطية للمرضى كذلك تقييم معايير الجرعات البيولوجية من خلال بعض التقنيات مثل MATLAB الذي من خلاله يتم التقييم لتحقيق الهدف من العلاج الإشعاعي وهو وصول الجرعة كاملة للأعضاء المصابة وحماية بقية الأعضاء، وذلك عن طريق حساب إحتمالية السيطرة علي الورم (TCP), وإحتمالية مضاعفات الأنسجة الطبيعية (NTCP), والجرعة المكافئة (EUD) وذلك في وجود أخطاء وبدون أخطاء.