TECHNICAL NOTE

Dosimetric Parameters Comparison of Four-Field and Field-in-Field Radiotherapy Planning in Treatment of Prostate Cancer

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Abstract

Purpose: Prostate cancer is one of the most common malignant cancers. Several radiotherapy planning methods have been suggested for the treatment of prostate cancer. In this study, four-field, and Field-In-Field (FIF) planning methods were compared based on dosimetric parameters.

Materials and Methods: In the radiotherapy Treatment Planning System (TPS) for 10 patients who were treated with the common four-field method, the planning was also performed by the FIF method. Dosimetric parameters were measured for Planning Target Volume (PTV), rectum, and bladder. These parameters included maximum dose, minimum dose, mean dose, V15%, V25%, V30%, and V35%, as well as Homogeneity Index (HI) and Conformity Index (CI). Two treatment planning methods based on dosimetric parameters were compared using paired t-test.

Results: Maximum, minimum and mean dose in PTV, rectum, and bladder were significantly different for the two techniques. There was no significant difference between the two planning techniques in dosimetric parameters of V15%, V25%, V30%, and V35% for rectum and bladder. The FIF technique delivers more doses to the tumor. HI was better in the FIF method than in the four-field method, but CI was not significantly different. In both techniques, the rectum and bladder did not receive doses above 60 Gy.

Conclusion: In the treatment of prostate cancer in both Four-field and FIF planning methods, the dose to the rectum and bladder is less than the tolerance dose. FIF technique is recommended to better control the tumor. Based on dosimetric parameters, no significant findings were obtained that prove the superiority of FIF over the four-field technique in the treatment of prostate cancer.

Keywords: Field In Field Radiotherapy; Prostate Cancer; Treatment Planning; Dosimetry Parameters.

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1. Introduction

Prostate cancer is the most common malignant cancer and the second leading cause of cancer death in men in the United States. This disease is an important threat to health, and mortality and has significant complications for men all over the world in a way that out of every 100,000 people, between 100-170 people are infected with this disease [1]. Approximately 11.6% of men in the United States are affected by prostate cancer at some point in their lives [2]. According to the Iranian Cancer Research, Treatment and Education Institute, prostate cancer is the fourth most common cancer in Iran.

One of the most important factors in the treatment of prostate cancer is the early diagnosis of this disease, so the sooner the diagnosis is made, the better the chances of treatment and survival of the patient [3]. Currently, surgery and subsequent radiation therapy are among the most useful methods of treating prostate cancer, so that it has the least damage and toxicity to the surrounding Organ At Risk (OAR). External radiation therapy with photons as one of the treatment methods has a special role in different stages in the treatment of this cancer [4, 5]. Radiotherapy techniques that use fields with unequal weight, the use of wedges, and multi-field techniques to protect organs at risk are routinely planning procedures [6]. Conformal radiotherapy is one of the most important treatment methods for patients with prostate cancer. Many oncology authorities have shown that biochemical Disease-Free Survival (bDFS) improves dramatically with increasing tumor dose. In the proposed radiotherapy planning techniques to improve the therapeutic ratio, several parameters such as the optimal number of beams, the size, and width of the margin around the Clinical Target Volume (CTV), and the use of effective methods of patient immobilization, are evaluated [7]. An effective radiotherapy treatment planning depends on how much dose has reached a certain area of the anatomical volume and how accurate the delivered radiation dose is to tumor volume [6].

As the dose absorbed increases, tumor control improves dramatically, but the tolerance dose of normal tissues limits the dose increase in radiotherapy [8]. One of the organs that limits the dose increase in the control of prostate cancer is the rectum, which is highly susceptible to toxicities. Primary rectal toxicity usually occurs 90 days after the start of radiotherapy. Symptoms such as loose stools or diarrhea, tenesmus, anorectal pain, hemorrhoidal stimulation, and bleeding following radiotherapy may occur [9]. Rectal bleeding is the most common delay toxicity due to neovascularization and telangiectasia [10, 11]. It is now well established that Intensity-Modulated Radiotherapy (IMRT) and brachytherapy, or a combination of the two, are effective in exacerbating and increasing tumor dose and increasing bDFS [12]. Due to the lack of equipping many radiotherapy centers with IMRT systems, the use of alternative treatment planning to routine methods is very necessary to reduce the complication of normal tissues, especially the rectum and bladder in the treatment of prostate cancer. In radiotherapy centers, three-Dimensional Conformal Radio-Therapy (3DCRT) with four-field is commonly used to treat prostate cancer. Since the use of Field-In-Field (FIF) planning in the radiotherapy treatment of the chest, neck, bladder, anal canal, and rectum has had good results in organ at risk sparing [13], so this study was developed in response to the question of whether the FIF method in the treatment of prostate cancer in comparison with the conventional method, can minimize the dose of sensitive organs.

2. Materials and Methods

This descriptive-analytical study was performed retrospectively in the oncology center of Imam Khomeini Hospital in Sari. In this study, 10 patients in the age range of 73 ± 8 years with prostate cancer were investigated. For this study, radiotherapy planning data in Treatment Planning System (TPS) were extracted for patients with prostate cancer who underwent external radiation using a Siemens primus linear accelerator. For all patients, the Computed Tomography (CT) scan image was obtained using a Siemens helical scanner in 2.5 mm slice thickness and transferred to the treatment planning system in DICOM format. In the radiotherapy treatment planning of prostate cancer, four radiation fields of anterior, posterior, left and right lateral fields using x-ray photons with energy of 15 MV as 3DCRT are commonly used. In the alternative method as FIF, 8 fields were used, so that in each direction, one field and one subfield were defined, and 15 MV energy was used. In the FIF technique for subfields from four directions, a separate prescribed dose and a separate reference point were selected. The main field was selected based on Planning Target Volume (PTV) dimensions and the subfields were selected based on Gross Tumor Volume (GTV). In selecting the dimensions of the subfields, an attempt has been made to remove sensitive organs from the field. The dimensions of the main field in FIF were equal to the dimensions of the field in the four-field method. The main field had blocks but the subfields were open. In the four field and FIF methods, the weight of the lateral fields (right and left lateral) was 100%, the weight of the anterior fields was between 85 and 100, and the weight of the posterior fields was between 100 and 115%. In all patients, the weight of subfields in all directions was 5%. No filter wedge was used in either method. Core Plan treatment system version 3.5.0.5 was used. In this system, the Equivalent Tissue Air Ratio (ETAR) algorithm is used to calculate the dose. In calculating the dose of organs and drawing isodose curves, the calculation grid size (voxel size) was 5 mm. In order to evaluate the dose distribution, taking into account systematic and random errors, the position of the reference point in all directions, anterior-posterior, right-left, and upper-lower direction [14-16] by 2.5 mm and the margin of the PTV and the CTV by 15 mm in the right-left and upper-lower, and 5-10 mm in the anterior-posterior direction was changed for four-field and FIF [17]. In order to correct the performance of the treatment planning system, an on-site audit test was performed. CIRS phantom was used to verify TPS performance. To compare dosimetry parameters in two irradiation techniques four-field and FIF, according to the diagram of differential Dose-Volume Histograms (DVH), mean, maximum, and minimum doses in PTV, rectum, and bladder were calculated. In this study, the percentage of bladder, and rectal volume that received radiation doses greater than 15, 25, 30 and 35 Gy as V15%, V25%, V30%, and V35%, respectively, was obtained for all patients. The Homogeneity Index (HI) was used to determine the dose homogeneity in the PTV (Equation 1) [18].

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (1)$$

In Equation 1, D2%, D50%, and D98% are the minimum doses delivered at 2%, 50%, and 98% of the PTV, respectively. Smaller homogeneity indicates better homogeneity in the target volume [19]. Another dosimetric quantity used to compare treatment plans is the Conformity Index (CI), which is the ratio of the volume of tissue covered by the prescribed isodose to the planning target volume. In this study, Equation 2 was used to calculate CI [20].

$$CI = \frac{V_{PTV} \times V_{TV}}{{TV^2}_{PV}} \quad (2)$$

In Equation 2, V_{PTV} is the PTV volume, V_{TV} is the volume of prescribed isodose lines extracted from the DVH, and TV_{PV} is a volume of V_{PTV} that is located within the volume of VTV. The lower the conformity index, the better the conformity in the target volume [19]. The calculated dosimetric parameters for four-field and FIF treatment methods were evaluated based on descriptive statistics and paired t-test with a 95% confidence interval. In this study, in the treatment of prostate cancer, the prescription dose for eight patients was 46 Gy and two patients received 45 and 44 Gy, respectively. The prescribed dose was the same in both planning methods.

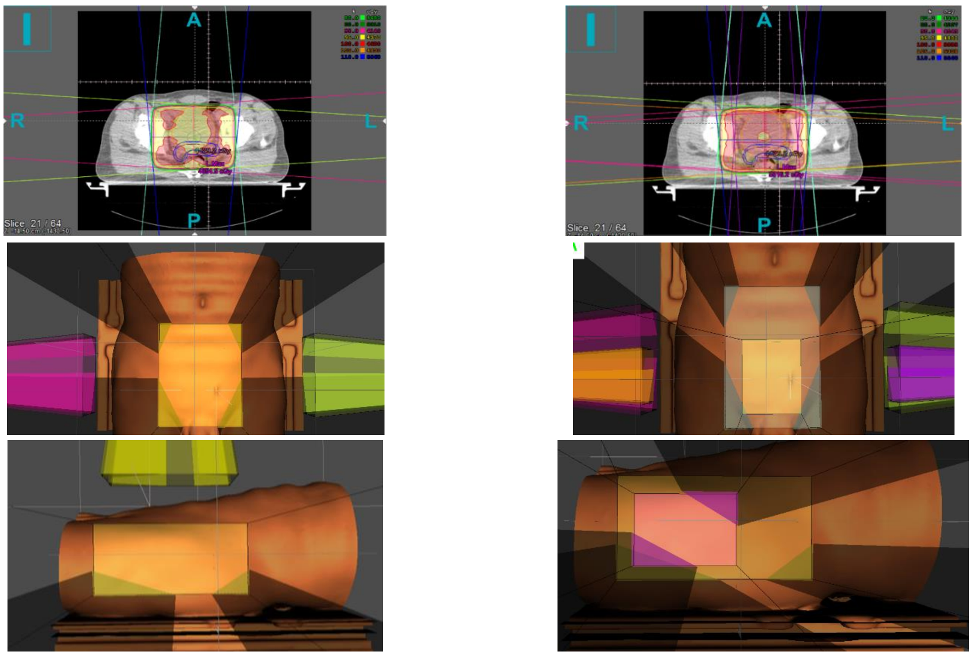
3. Results

In the radiotherapy treatment with four-field method, 4 fields with energy of 15 MV were used. The fields were irradiated from 4 directions as anterior, posterior, and left and right-side fields. No wedge was used in any of the fields. In order to optimize the dose in organs at risk in the pelvis, including the rectum, and bladder, a FIF treatment planning method was proposed. In our study, 8 radiation fields were used for the FIF technique. In this treatment method, a field and a subfield with energy of 15 MV were used in each direction. Figure 1 shows the treatment planning fields for the four-field and FIF methods in the treatment of prostate cancer on an axial CT scan of the pelvis.

According to the DVH diagram, maximum, mean, and minimum doses were obtained in PTV, rectum, and bladder. Table 1 shows these quantities for the four-field and FIF planning methods.

In order to compare the two treatment plans in the dose to the organs at risk, the volume of the rectum and bladder that received a dose of more than 15, 25, 30, and 35 Gy was measured. Table 2 shows the mentioned quantities.

The HI and CI were calculated for both four-field and FIF treatment plans (Figure 2). These two quantities are important dosimetric parameters that well evaluate the quality of treatment planning methods. The findings of our study show that there was no volume of the rectum and bladder that received a dose of more than 60 Gy (V_{60}). In this study, the cumulative dose distribution in tumor volume was compared in the four-field and FIF plans based on the DVH diagrams. Figure 3 shows the DVH diagram for the two methods.



a b

Figure 1. Radiation fields in treatment of prostate cancer in two planning methods A. four-field and B. FIF

Table 1. Comparison of dose parameters received in therapeutic volumes and organs at risk for four-field and FIF treatment plans

Dose parameter	Volume	Four-field plan	FIF[b] plan	p-value
Maximum ± SD (cGy)	PTV [a]	4788.9 ± 53.3	4841.6 ± 57.6	< 0.05*
	Rectum	4811.1 ± 119.4	4841.3 ± 60.2	0.47
	Bladder	4843.2 ± 64.7	4814.3 ± 53.4	0.32
Mean ± SD (cGy)	PTV	4653.6 ± 18.6	4712.9 ± 57.6	< 0.05*
	Rectum	4256.3 ± 324.5	4271.3 ± 306.6	0.31
	Bladder	4626.6 ± 84.1	4625.4 ± 76.8	0.94
Minimum ± SD (cGy)	PTV	4507.6 ± 55.9	4561.7 ± 77.1	< 0.05*
	Rectum	1380.8 ± 356.4	1352.4 ± 244.5	0.073
	Bladder	3414.3 ± 484.5	3398.3 ± 449.9	0.38
Monitor Unit (MU)		228.9 ± 2.8	235.8 ± 7.6	0.15

a PTV: Planning Target Volume, b FIF: Field in Field, *: Statistically significant

4. Discussion

In this study, dosimetric parameters of two radiotherapy planning strategies as four-field (as common methods) and FIF methods in the treatment of prostate cancer were compared. In all the proposed planning techniques to improve the treatment of tumors of the lower abdomen, reducing the toxicity of normal tissues such as the rectum, bladder, intestinal wall, and bone marrow has been considered.

Several methods have been proposed in the radiotherapy treatment of prostate cancer, such as IMRT, FIF, three-field technique, and the use of a balloon to remove the rectum from the field that all of which have desirable results in reducing the dose of organs at risk. In the study of Prabhakar *et al.* [13], the FIF technique and Wedge Filter radiotherapy as a common planning method were compared in the radiotherapy of rectal cancer. In the common technique, 4 anterior, posterior, and left and right lateral fields were used along with the wedge. In the FIF technique, the wedges were removed and the dose distribution was adjusted using Multileaf Collimator (MLC). In this technique, the points with the maximum dose were shielded. Conformity in the FIF method was improved compared to the method with the wedge, but most dosimetric parameters in the two methods were not significantly different. In our study, in the proposed FIF technique 8 fields were used, including 4 open fields and 4 subfields (Figure 1) because it is believed that increasing the number of fields improves the conformity index and reduces the dose of organs at risk [21]. In our study, according to Figure 2, the dose homogeneity in the target volume in the FIF method (with an average of 1.04) was better than in the four-field method (with an average of 1.10), but this difference was not significant (p-value = 0.36). There was no significant difference in conformity between the two technical methods (p-value = 0.15).

According to Table 1, the amount of Monitor Unit (MU) in the FIF planning method was 3% higher than in the four-field method, but the difference was not significant.

In the study of Yavas *et al.* [22], which used the FIF method in the treatment of endometrial cancer, the amount of MU was 1% higher than the conventional method, and in the study of Prabhakar *et al.*, the MU in the FIF method was 30% lower than the wedge method. Reduction in MU minimizes the chance of developing secondary cancers in radiotherapy [13]. The difference in dosimetric parameters reported in different studies is due to the completely different technical procedures used in the FIF plan and a single definition of this method in the treatment of prostate cancer is not provided.

Very few studies are available on the comparison of the FIF and four-field method of prostate cancer without the use of IMRT, and therefore our comparative study with other studies has been very limited. Increasing the number of fields to obtain the desired dosimetric indices, without hardware equipment (such as MLC), makes it

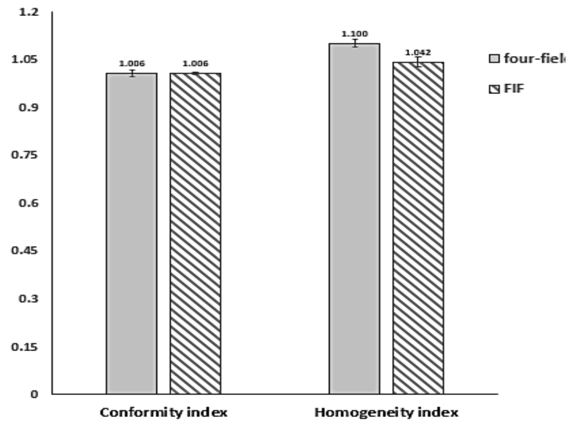


Figure 2. Homogeneity Indices (HI) and Conformity Index (CI) for four-field and FIF planning methods in the treatment of prostate cancer

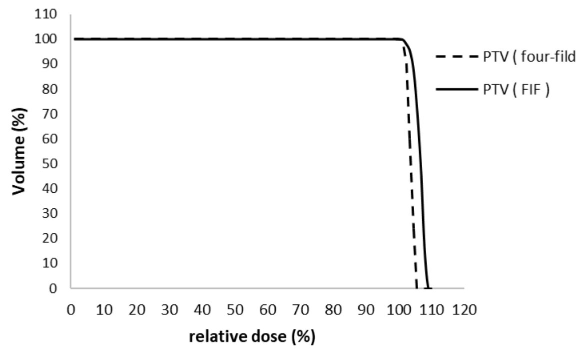


Figure 3. Comparison of the DVH in tumor volume in four-field and FIF treatment planning methods

difficult for the physicist to perform the treatment planning, and also for the radiotherapy technologists and increases the probability of random and systemic errors.

Four-field and FIF techniques in the treatment of prostate cancer are not able to transfer high doses to the tumor and for this purpose, IMRT methods should be used, so that in common treatment techniques if a high dose

Table 2. Volume (%) of organs at risk in two treatment planning methods that received more than a certain dose

Organ at risk	Dose indices	Planning methods		p-value
		Four-field	FIF	
Rectum	V15% [a]	96.13 ± 5.24	96.17 ± 5.24	0.36
	V25 %	92.51 ± 7.56	92.54 ± 7.48	0.36
	V30 %	90.39 ± 9.35	90.39 ± 9.10	1.00
	V 35%	87.71 ± 10.33	87.57 ± 10.13	0.60
Bladder	V15%	100	100	-
	V25 %	100	100	-
	V30 %	99.56 ± 1.13	99.64 ± 0.90	0.36
	V 35%	98.39 ± 3.56	98.57± 3.12	0.32

is transferred to the tumor, it will have serious biological effects on healthy tissues [12]. Zelefsky *et al.* [23] compared the 3DCRT with the IMRT method in the treatment of prostate cancer. Their findings show that in the IMRT method in all patients studied, the dose prescribed to the tumor was 81 Gy. With a 10-year follow-up, Gastrointestinal toxicity (GI) with a grade more than 2 was 13% in patients treated with 3DCRT and 5% in IMRT, which shows a significant difference. Our radiotherapy department does not have an IMRT system and, therefore, we are looking for the best radiotherapy treatment strategy by optimizing the common methods. According to the DVH diagram in Figure 3, the maximum dose to tumor volume (PTV) in the four-field method and FIF was 104% and 107% prescribed dose, respectively, which shows a significant difference; however, in the Prabhakar study, no significant difference was found between the two methods, while in the study of Yavas *et al.*, this amount shows a significant difference and the FIF method applies a lower dose to PTV. Any treatment planning methods that deliver a higher dose to PTV will better control the tumor and have a higher therapeutic ratio.

According to Table 2, the percentage of bladder and rectum volume that received doses greater than 15, 25, 30, and 35 Gy did not show a significant difference. The dose transferred to the rectum and bladder in four-field and FIF methods in the treatment of prostate cancer has a much lower dose than the dose tolerance reported in the Emami report [24] so that no area of the rectum and bladder received more than 60 Gy. However, delivering a dose of 60 Gy is allowed to be less than 35% of rectal volume and less than 50% of bladder volume.

5. Conclusion

The dose transferred to the rectum and bladder as sensitive organs in the treatment of prostate cancer in FIF and four-field planning methods was less than the tolerated dose. Increasing the number of fields in the FIF technique increased the MU by 3% compared to the four-field method. The FIF technique is recommended for better controlling of the tumor and increasing the dose of PTV in the treatment of prostate cancer. No significant findings were found that increase the tendency to use the FIF technique with 8 fields in the treatment of the prostate. The decision to use the FIF method in the control of prostate tumors in radiotherapy departments that do not have an IMRT system needs further study. Increasing the number of fields and using subfields in the FIF method compared to the four-field method did not show a significant change in dosimetric indices except in a few parameters.

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References

1- Lindsey A Torre, Rebecca L Siegel, Elizabeth M Ward, and Ahmedin Jemal, "Global cancer incidence and mortality rates and trends—an update." *Cancer Epidemiology and Prevention Biomarkers,* Vol. 25 (No. 1), pp. 16-27, (2016).

2- Beatriz Sánchez-Nieto *et al.*, "External photon radiation treatment for prostate cancer: Uncomplicated and cancer-free control probability assessment of 36 plans." *Physica Medica,* Vol. 66pp. 88-96, (2019).

3- Hossein Rafimanesh, Mahshid Ghoncheh, Hamid Salehinia, and Abdollah Mohammadian Hafashjani, "Epidemiology of prostate cancer and its incidence trends in Iran." *Journal of Sabzevar University of Medical Sciences,* Vol. 23 (No. 2), pp. 320-27, (2016).

4- Faiz M Khan, Paul W Sperduto, and John P Gibbons, Khan's Treatment Planning in Radiation Oncology. *Lippincott Williams & Wilkins,* (2021).

5- Edward C Halperin, Luther W Brady, David E Wazer, and Carlos A Perez, Perez & Brady's principles and practice of radiation oncology. *Lippincott Williams & Wilkins,* (2013).

6- Linda W Chan *et al.*, "Proposed rectal dose constraints for patients undergoing definitive whole pelvic radiotherapy for clinically localized prostate cancer." *International Journal of Radiation Oncology* Biology* Physics,* Vol. 72 (No. 1), pp. 69-77, (2008).

7- P Milecki, T Piotrowski, and M Dymnicka, "The comparison of radiotherapy techniques for treatment of the prostate cancer: the three-field vs. the four-field." *Neoplasma,* Vol. 51 (No. 1), pp. 64-69, (2004).

8- Bahman Emami *et al.*, "Tolerance of normal tissue to therapeutic irradiation." *International Journal of Radiation Oncology* Biology* Physics,* Vol. 21 (No. 1), pp. 109-22, (1991).

9- Martin Hauer-Jensen, Junru Wang, and James W Denham, "Bowel injury: current and evolving management strategies." in *Seminars in radiation oncology*, (2003), Vol. 13 (No. 3): *Elsevier*, pp. 358-71.

10- PS Hasleton, N Carr, and PF Schofield, "Vascular changes in radiation bowel disease." *Histopathology*, Vol. 9 (No. 5), pp. 517-34, (1985).

11- Luis Felipe Fajardo, "The pathology of ionizing radiation as defined by morphologic patterns." *Acta oncologica*, Vol. 44 (No. 1), pp. 13-22, (2005).

12- Nicholas A Serrano, Noah S Kalman, and Mitchell S Anscher, "Reducing rectal injury in men receiving prostate cancer radiation therapy: current perspectives." *Cancer management and research*, Vol. 9pp. 339-50, (2017).

13- R Prabhakar, PK Julka, and GK Rath, "Can field-in-field technique replace wedge filter in radiotherapy treatment planning: a comparative analysis in various treatment sites." *Australasian Physics & Engineering Sciences in Medicine*, Vol. 31 (No. 4), pp. 317-24, (2008).

14- EK Osei, R Jiang, R Barnett, K Fleming, and D Panjwani, "Evaluation of daily online set-up errors and organ displacement uncertainty during conformal radiation treatment of the prostate." *The British journal of radiology*, Vol. 82 (No. 973), pp. 49-61, (2009).

15- Jackson Wu *et al.*, "Positioning errors and prostate motion during conformal prostate radiotherapy using on-line isocentre set-up verification and implanted prostate markers." *Radiotherapy and Oncology*, Vol. 61 (No. 2), pp. 127-33, (2001).

16- Bo Sterckx, Isabell Steinseifer, and Markus Wendling, "In vivo dosimetry with an electronic portal imaging device for prostate cancer radiotherapy with an endorectal balloon." *Physics and Imaging in Radiation Oncology*, Vol. 12pp. 7-9, (2019).

17- Felix Böckelmann, Florian Putz, Karoline Kallis, Sebastian Lettmaier, Rainer Fietkau, and Christoph Bert, "Adaptive radiotherapy and the dosimetric impact of inter-and intrafractional motion on the planning target volume for prostate cancer patients." *Strahlentherapie und Onkologie*, Vol. 196 (No. 7), pp. 647-56, (2020).

18- Katharina Bell, Yvonne Dzierma, Melanie Morlo, Frank Nüsken, Norbert Licht, and Christian Rübe, "Image guidance in clinical practice–Influence of positioning inaccuracy on the dose distribution for prostate cancer." *Physica Medica*, Vol. 46pp. 81-88, (2018).

19- Tingting Cao, Zhitao Dai, Zhen Ding, Wuzhou Li, and Hong Quan, "Analysis of different evaluation indexes for prostate stereotactic body radiation therapy plans: conformity index, homogeneity index and gradient index." *Precision Radiation Oncology*, Vol. 3 (No. 3), pp. 72-79, (2019).

20- Ian Paddick, "A simple scoring ratio to index the conformity of radiosurgical treatment plans." *Journal of neurosurgery*, Vol. 93 (No. supplement_3), pp. 219-22, (2000).

21- MI El Gohary, EM Attalla, and IM Hassan, "Evaluation of 3D Conformal Radiotherapy for Prostate Cancer Using Dosimetric Indices." *Egyptian Journal of Biomedical Engineering and Biophysics*, Vol. 17 (No. 1), pp. 53-65, (2016).

22- Guler Yavas *et al.*, "Dosimetric comparison of 3-dimensional conformal and field-in-field radiotherapy techniques for the adjuvant treatment of early stage endometrial cancer." *Physica Medica*, Vol. 29 (No. 6), pp. 577-82, (2013).

23- Michael J Zelefsky *et al.*, "Incidence of late rectal and urinary toxicities after three-dimensional conformal radiotherapy and intensity-modulated radiotherapy for localized prostate cancer." *International Journal of Radiation Oncology* Biology* Physics*, Vol. 70 (No. 4), pp. 1124-29, (2008).

24- Bahman Emami, "Tolerance of normal tissue to therapeutic radiation." *Reports of radiotherapy and Oncology*, Vol. 1 (No. 1), pp. 123-7, (2013).