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Physical Evaluation and Verification of Different Radiotherapy Techniques for Prostate Cancer

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Abstract:
Introduction: In radiotherapy, cancer prostate can be treated with different advanced radiotherapy techniques (3DCRT, IMRT, and RapidArc). Each of these techniques can be achieved with different plans. To select the optimum plan in these techniques physical evaluation and dose verification should be performed for each plan.
Material and Methods: Computed tomography scans of 18 patients who had completed 3DCRT for intermediate risk of prostate cancer were replanned using two RapidArc plans, four IMRT plans and two 3DCRT plans. Calculated doses to planning target volume (PTV) and organs at risk (OAR) were compared between all plans in physical evaluation (dose homogeneity index (HI), target coverage and conformity indices (PITV, TCI, CI, and CN), dose gradient (GI and GM), critical organ scoring indices (COSI and MCOSI) and an index for overall plan quality factor (QF)). Dose distributions of 8 plans were verified using 2D array in octavious 4D phantom.
Results: by using physical evaluation HI values indicated that 3DCRT has the best dose homogeneity. Calculated values of PITV, TCI, CI, and CN showed that RapidArc produce better dose conformity than other technique. GM and GI values displayed that, RapidArc gives better dose gradient than IMRT and 3DCRT. COSI values displayed that the RapidArc and 3DCRT is the best sparing high dose to OAR. MCOSI values displayed that the RapidArc and 3DCRT is the best sparing from low dose to high dose to OAR. So, none of these physical evaluation indices solely allowed ranking the plans. Calculating QF index allowed ranking the plans. The QF value of Rapid Arc plans give the highest values.
Conclusion: in comparing between 3 technique (3DCRT.IMRT and Rapid Arc) the Physical evaluation of treatment plans can't be achieved by calculating any of the physical evaluation quantities solely. This issue can be solved by calculating treatment plan quality factor. In advanced radiotherapy techniques, in addition to the physical evaluation, dose verification should be performed and analysed.

Keywords: *Radiotherapy, cancer Prostate, IMRT, RapidArc, 3DCRT, Physical Evaluation, critical organ scoring indicies, dose verifications.*

1. Introduction

The primary goal of radiation therapy is to deliver a prescribed dose to a target volume, while minimizing the effect of radiation to normal tissue such as bladder and rectum.[1] This is referred to as conforming the dose to the target. Various techniques are employed to achieve this goal such as 3DCRT, IMRT and RapidArc.

Three-dimension Conformal radiation therapy (3DCRT) is a 3-dimensional picture of the tumor in order to target the tumor as accurately as possible and give it the highest possible dose of radiation while sparing normal tissue as much as possible. IMRT is a radiation treatment technique with multiple beams incident from different directions in which some of the beams have non uniform beam surface due to variation in beam intensity at different parts of beams so that each beam delivers a non-uniform dose to the target.[2] The use of IMRT has repeatedly been shown to reduce dose to OARs compared with 3DCRT.[3,4] RapidArc radiotherapy

technology that improves dose conformity while significantly shortening treatment times which the gantry of linac is rotating with the dose on, not fixed beam like IMRT.[5] Treatment planning system (TPS) have incorporated specialized plan evaluation tools that permit the radiation oncologist and medical physicist to judge more objectively one plan potentially better than another. oncologist can make judgment of the likely efficacy of a proposed treatment plan from a DVH by choosing one and maximized the dose to the tumour while keeping the dose to the normal organs to an acceptable level. However, there are inherent limitations with DVHs which they provide no spatial information (e. g. where are the dose hot or cold spot).

The dosimetric indexes like prescription isodose to target volume (PITV) ratio, homogeneity index (HI), conformity index (CI), target coverage index (TCI), conformity number (CN), critical organ scoring index (COSI), modified critical scoring organ (MCOSI)and quality factor (QF) can evaluate the plans which obtain the data from DVH's. Additionally, we have reviewed dose tolerance for organs at risk including RTOG clinical trial results, QUENTEC data and Emami data [6,7,8] which all satisfies the constrains for OAR.

Furthermore, the delivery of treatment fields with small sub-field components is sensitive to small errors (within tolerance) in the machine, such as the MLC position.[9,10] Treatment plans including a large amount of small sub-field components will result in increased uncertainties with larger differences between planned and delivered dose distributions and are regarded as complex treatment plans that should be avoided to be used for treatment. So, advanced radiotherapy treatment plans such as those involving intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (RapidArc) require dosimetric verification before clinical delivery.[11,12,13]

2. Aim of the Work

The aim of this work is to compare different treatment plans using advanced radiotherapy techniques (3DCRT, IMRT and RapidArc) based on evaluation models and dose verification for each plan in 3 different technique.

3. Material and Methods

In this study, we used de- identified CT data sets from 18 patients that had been previously treated at oncology department, Ain Shams University Hospitals with 3DCRT. Dose distributions were generated for each data set using eight plans; two RapidArc plans, four IMRT plans, and two 3DCRT plan (all plans are detailed below). PTV was contoured by expanding the prostate contour with a 10-mm margin in all directions except in the posterior direction only 8 mm margin was applied to spare additional rectal tissue from receiving radiation dose

3.1. Planning Techniques and Beams Arrangement

For all plans applied, AAA Algorithm was used for dose calculation in eclipse Treatment Planning System Version v13.5. Prescribed dose was 56Gy in phase I to the prostate and seminal vesicles and 20 Gy in phase II to the prostate only.

in 3DCRT, two different plans have been applied.

1) seven beams, with following angles (0^o, 50^o, 90, 130^o, 220^0, 270^o and 310^o) (3DCRT7 field) (fig1A).
2) seven beams with optimized beam angles. optimum angles were obtained by TPS (optimize angulations modules) the angles varied from patient to the other (3DCRT 7 opt). (fig1B)

In IMRT Technique: Four plans with different beam arrangement were used.

1- seven fields with optimized beam angles (IMRT 7 OPT). (fig1C)

2-nine fields with optimized beam angles (IMRT 9 OPT). (fig1D)

3-(IMRT7): seven field arranging with equal angle space (0^0,51^0, 102^0,, 153^0 ,204^0 255^0 and306^0) (IMRT7). (Fig1E)

4-nine field arranging with equal angle space (0^0,40^0,80^0,,120^0 ,160^0 ,200^0 ,240^0,280^0 and320^0)(IMRT9). (Fig1F)

In RapidArc Two plan have been applied.

1- A single arc 300^0 arc that started with the gantry angle at 150° and rotated in a counter clockwise (CW) to gantry angle 210°. The arc deliberately avoided treating through the rectum from the posterior direction. The collimator was set at 30° to minimize MLC tongue and groove effect (FA rectum) (Fig 1G)

2- The full arc utilized an arc that started with the gantry at 179° and rotated in a counter clockwise (CW) to gantry angle 181°, for a total 360° arc. An anterior 60°avoidance sector was applied to avoid the bladder anteriorly. The collimator was set at 30° to minimize MLC tongue and groove effect (FA bladder). (fig 1H)

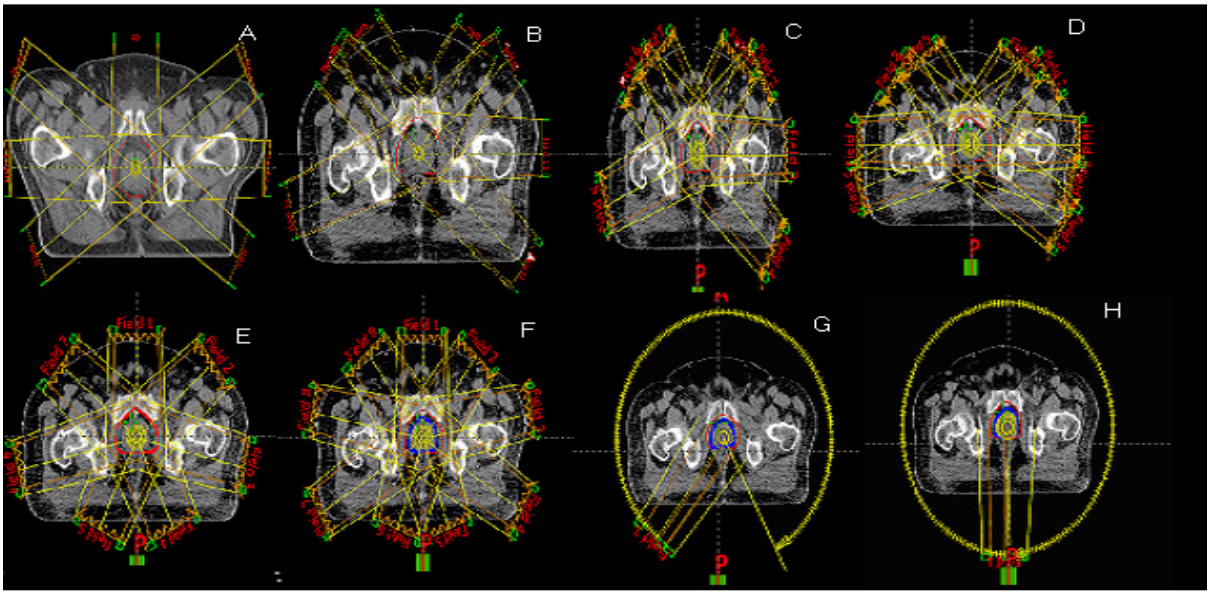

Figure 1: beam arrangement for eight plan

3.2. Dose Constrains

In IMRT and RA we used inverse plan and applied the Dose volume constrains based on QUANTIC summery and RTOG 1005.[6,7]

Volume/organ at risk (OAR)	Dose constraint
Planning target volume (PTV)	• 99% of the volume to get ≥ 95% of the prescription • Minimum dose > 95% of the prescription • Maximum dose <107% of the prescription • The maximum dose must be within the PTV
Rectum	• <50% of the volume to receive 50 Gy • <35% of the volume to receive 60 Gy • <25% of the volume to receive 70 Gy • <15% of the volume to receive 75 Gy
Bladder	• <50% of the volume to receive 65 Gy • <35% of the volume to receive 70 Gy • <25% of the volume to receive 75 Gy • <15% of the volume to receive 80 Gy
Head of femur	• <40% of the volume to receive 40 Gy • <25% of the volume to receive 45 Gy • <0% of the volume to receive 50 Gy

Table 1: Dose Volume Histogram for intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (RapidArc) treatments of the prostate

3.3. Physical Evaluation

3.3.1. Homogeneity Index (HI)

in this study, the homogeneity index calculated by

$$HI=D_{Max}/D_{Min} \quad (2.1)$$

D_{Max} is expressed in terms of D1 and D_{Min} is expressed in terms of D99.This formula of HI is the most sensitive to the variation of dose homogeneity. The lower (closer to one) the index, the better is the dose homogeneity.[14]

3.3.2. Target Coverage Index (TCI)

TCI accounts for the exact coverage of PTV in a treatment plan at a given prescription dose. The target coverage Index (TCI) is defined as the ratio of the target volume receiving at least the prescription dose, V_{tp}, to the total target volume, V_t.[15]

TCI is expressed as:

$$TCI = \frac{V_{tP}}{V_t} \quad (2.2)$$

3.3.3. Prescription isodose to target volume (PITV) ratio

The prescription isodose to target volume PITV ratio, obtained by dividing surface volume surrounded by prescription isodose level (inside and outside the PTV), V_p divided by target volume V_t.[16]

PITV is expressed as;

$$PITV = \frac{V_P}{V_t} \quad (2.3)$$

The PITV ratio is a conformity measure, and a value of 1.0 indicates that the volume of the prescription isodose surface equals that of the PTV. A PITV ratio of 1.0 does not necessarily imply that both volumes are similar. To ensure adequate PTV coverage, this measure should always be used in conjunction with a PTV-DVH .[16]

3.3.4. Conformity Index (CI)

The conformity index (CI) is defined as the ratio of the total volume receiving at least the prescription dose, Vp, to the target volume receiving at least the prescription dose, Vtp .[17]

$$\mathbf{CI} = \frac{\mathbf{V_p}}{\mathbf{V_{tp}}} \quad (2.4)$$

The value of CI is always greater than unity. A value that is closer to unity represents a better target conformity of radiation dose in the treatment plan.

CI is generally used to indicate the portion of a prescription dose that is delivered inside the PTV. CI of 1 indicates that 100% of a prescription dose is delivered to the PTV, and no dose is delivered to any adjacent tissue.[18] The CI is less than 1 for most clinical cases. Higher CI values indicate poorer dose conformity to the PTV.

3.3.5. Conformity number (CN)

Dose conformity evaluates the dose fit of the PTV relative to the volume covered by the prescription dose.[19] Ideally the prescribed dose should fit tightly to the target volume, therefore, reducing the side effects occurred by treating surrounding tissues and organs. The CN simultaneously takes into account irradiation of the target volume and irradiation of healthy tissues.[20] The CN is defined as;

$$CN = TCI\ X\ CI = \frac{V_{tP}}{V_p} X \frac{V_{tp}}{V_t} \quad (2.5)$$

where V_p is, the total volume receiving the prescription, V_t is the target volume, and V_{tp} is the target volume covered by the prescription.[21] A CN value closer to 1 indicates that the dose distribution fits more tightly to the target volume preserving healthy tissue.

3.4. Gradient Index

The gradient index (GI) is defined as the ratio of the volume covered by at least a given percentage of the prescription dose (V_G) to the volume covered by the full prescription dose (V_P).[22] In most of dosimetric studies, the given percentage is set at 50% of the prescription dose. Mathematically, GI is expressed as:

$$GI = \frac{V_G}{V_p} \quad (2.6)$$

The value of GI is greater than unity. A value that is closer to unity represents a faster dose fall-off in normal tissue.

3.4.1. Gradient Measure

Gradient Measure is a quantity calculated by Eclipse treatment planning software to express the dose gradient value in centimeters. Gradient measure is given by the difference between the equivalent sphere radius of the prescription and half prescription isodoses. In this study, GM is given by the difference between the equivalent sphere radius of 100% and 50% isodoses.

3.4.2. COSI Critical Organ Scoring Index

The COSI index accounts for both target coverage and critical organ irradiation. The main advantage of this index is its ability to distinguish between different critical organs.[23]

COSI is expressed as: $COSI = 1 - \sum_i^n w_i \frac{V_i(OAR)_{>tol}}{TCI}$ (2.7)

where Vi(OAR)>TOL is the volume fraction of OAR that receives more than a predefined tolerance dose. TCI is the volumetric target coverage, which is defined as the fractional volume of PTV covered by the prescribed isodose.

organ	Tolerance	risk(TD5/5CGY)
Head of femur	52 GY	necrosis
bladder	60GY	contracture
rectum	60GY	Stricture, ulcer

TABLE 2.2 tissue tolerance of organ at risk.[8]

3.4.3. Modified Critical Scoring Organ (Mcosi)

$$mCOSI = \sum_{i=1} W_i \left(\frac{COSI_{10} + COSI_{20} + \cdots + COSI_{80}}{8} \right)$$

is **expressed as:** (2.8)

Although the COSI index focuses only on OARs that receive high dose region volumes, the modified COSI considers both high dose and low dose regions.[24]

3.5. Quality Factor (QF)

A dosimetrical index that can evaluate the quality of the entire plan, named the quality factor (QF).[15] The QF of a plan can be analytically expressed as:

$$QF = \left[2.718 \exp\left(- \sum_{i}^{n} W_i X_i \right) \right] \quad (2.9)$$

In the above equation, X_i represents all of the PTV indices used for evaluating a plan, including the PITV, CI, HI, TCI, COSI, CN, GI, GM and MCOSI. The values of the weighting factor (W_i) can be adjusted between 0 and 1 for all relatively weighted indices for a user-defined number of indices (N). The eleven indices mention above have been integrated in the quality factor index, as shown in eq. (2.9).

3.5.1. Number of MUs

The total number of MUs needed to deliver each treatment plan was summed and recorded. The total number of MU's is an important factor in selecting the optimal treatment plan, which the higher the total number of MU's is the higher the probability of secondary cancer. In addition to that increasing the total number of MUs increases the treatment delivery time i.e. less comfortable and less accurate treatment.

3.5.2. Dose Verification

Plan Verification has been done for the 8 plans by using verisioft program in Octavius 4D that compare (calculated dose distribution against measured dose distribution). That compare the gamma value in 8 plans.

4. Results

All treatment plans of the three different techniques were able to satisfy all dose-volume constrains prescribed in table (1) for all cases.

4.1. Physical Evaluation

Figure 2 shows HI for all plans. It is obvious that 3DCRT have homogeneity indices more than other technique.

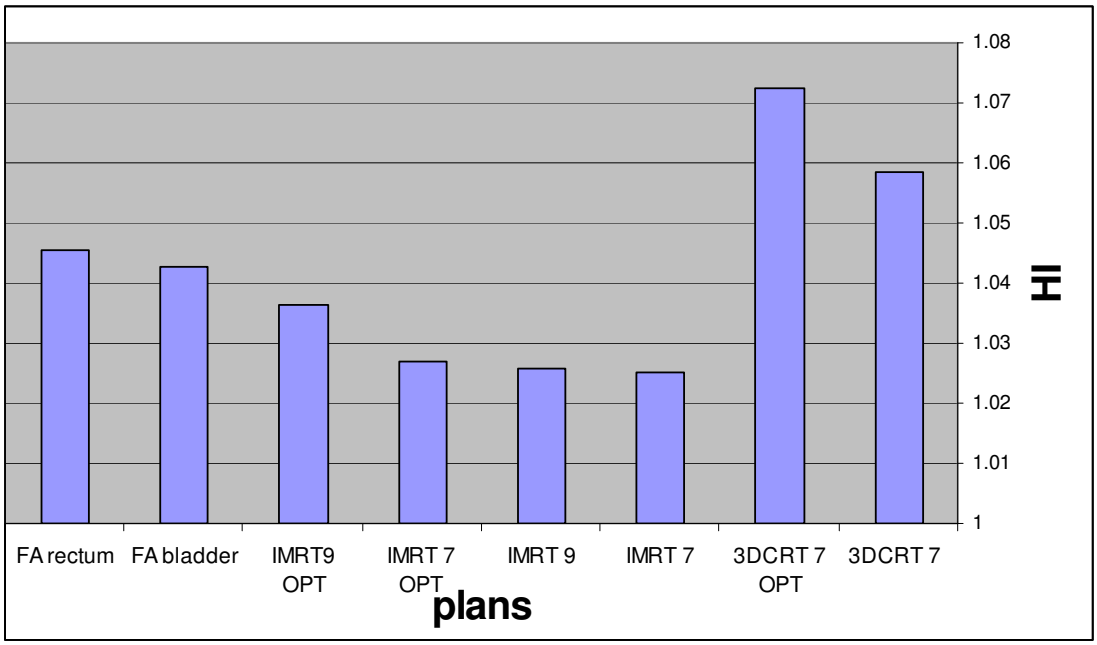

Figure 2: the value Dose Homogeneity Index (HI).

Figure 3.and 4 displays the calculated TCI and PITV for all plans. It is apparent that, IMRT 7 OPT has the lowest TCI and PITV .3DCRT 7 OPT has the highest TCI and PITV. The other plan has very close values for both TCI and PITV.

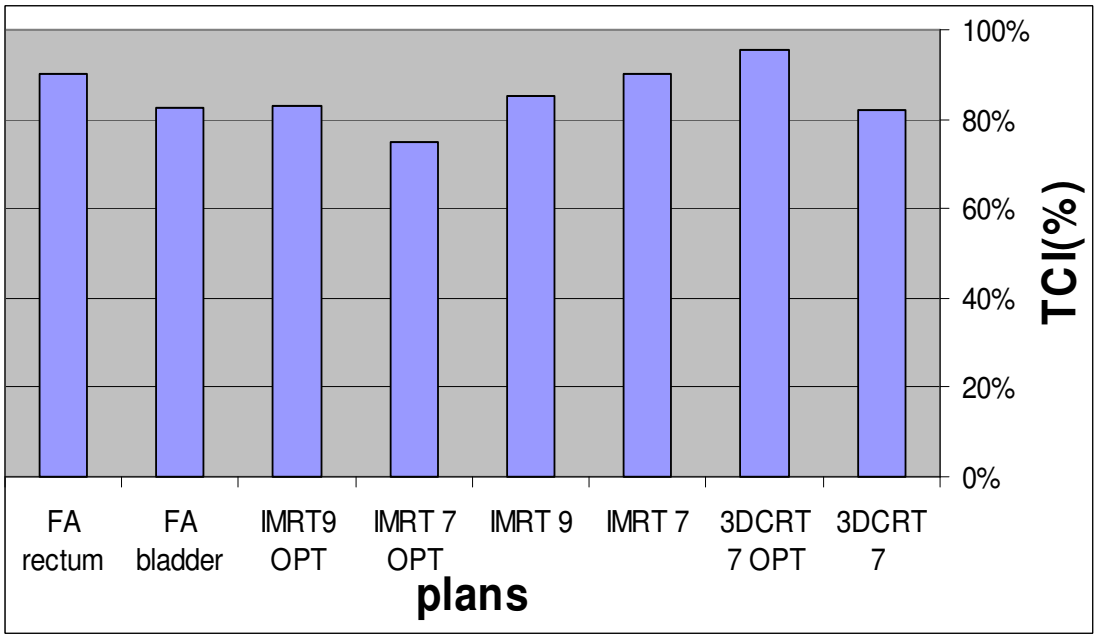

Figure 3: Target Coverage expressed in terms of TCI

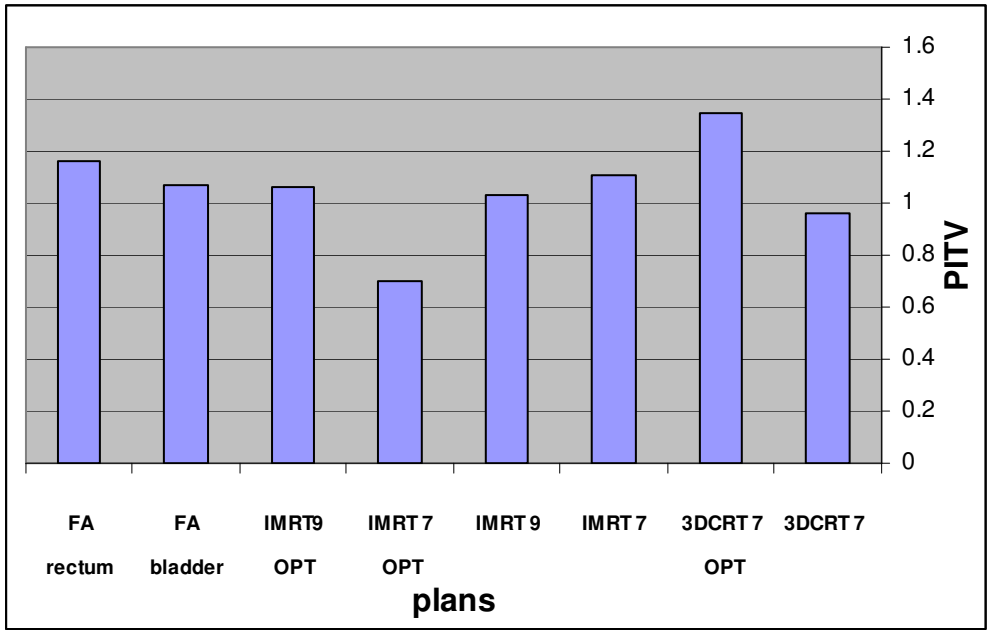

Figure 4: the value of PITV.

Figure 5 shows the CI and CN values of different plans. IMRT 7 OPT has the lowest value in CI and CN ,3DCRT has the highest value in VI and CN and the other plans have very close values for both CI and CN.

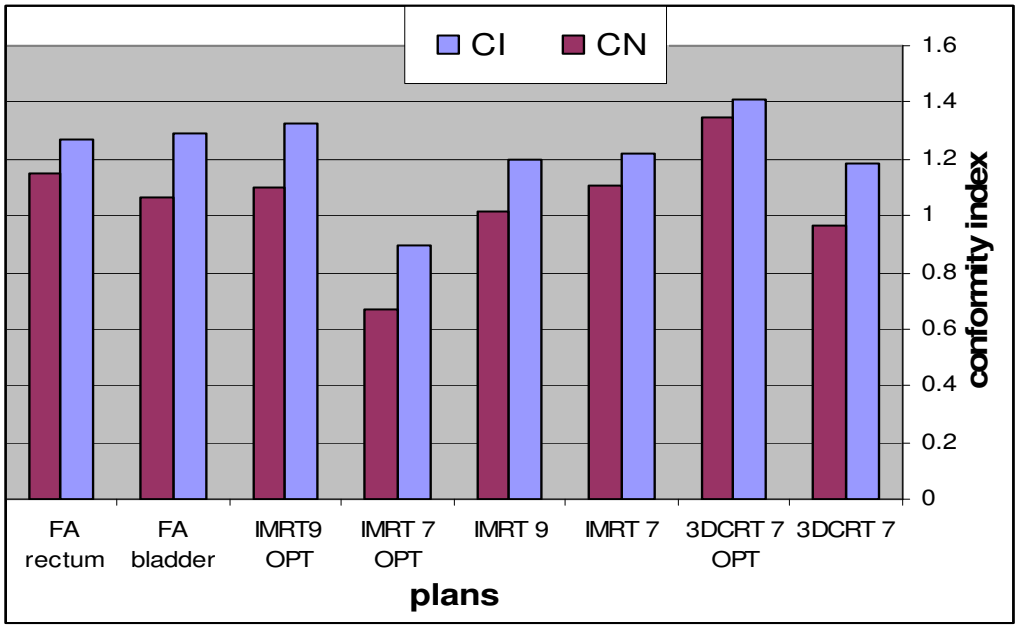

Figure 5: Dose conformity expressed in terms of conformity index (CI) in comparison with conformity number (CN) for all techniques

Figure 6 shows the values of GI of different plans. We can notice that the GI values of all RapidArc plans are very close. While IMRT and 3DCRT have higher GI values. This means that in RapidArc and the dose drop outside the PTV is very quick in comparison with other plans.

Figure 7 shows the Gradient measure values of the six plans. The GM represents the distance of dose drop between PTV and OARs. This means that the higher the GM value is the longer of the distance of dose drop. The RapidArc plans and have almost equal GM values but 3DCRTand IMRT have a higher and significantly different GM value.

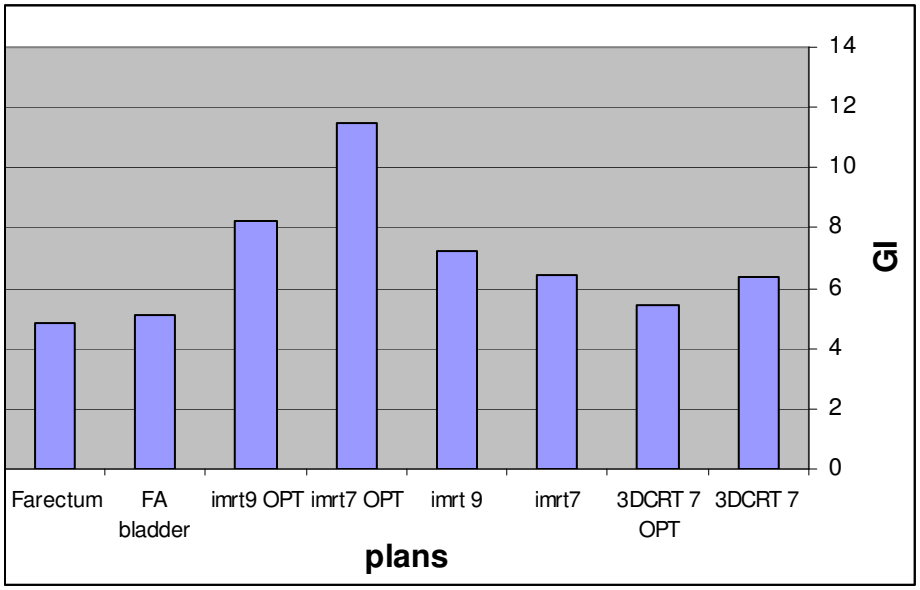

Figure 6: Dose gradient index (GI) for different treatment plans

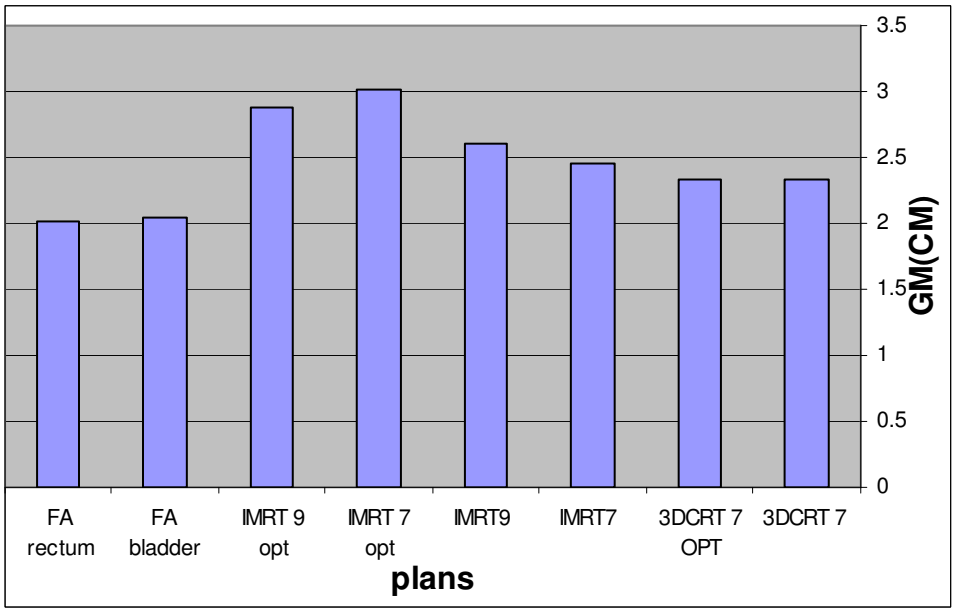

Figure 7: Dose gradient index (GM) for different treatment plans

Figure 8 displays the calculated COSI for all plans. It is apparent that, the COSI values of IMRT has the lowest value and in RapidArc and 3DCRT is the highest value. This mean OAR has high dose in IMRT than RapidArc

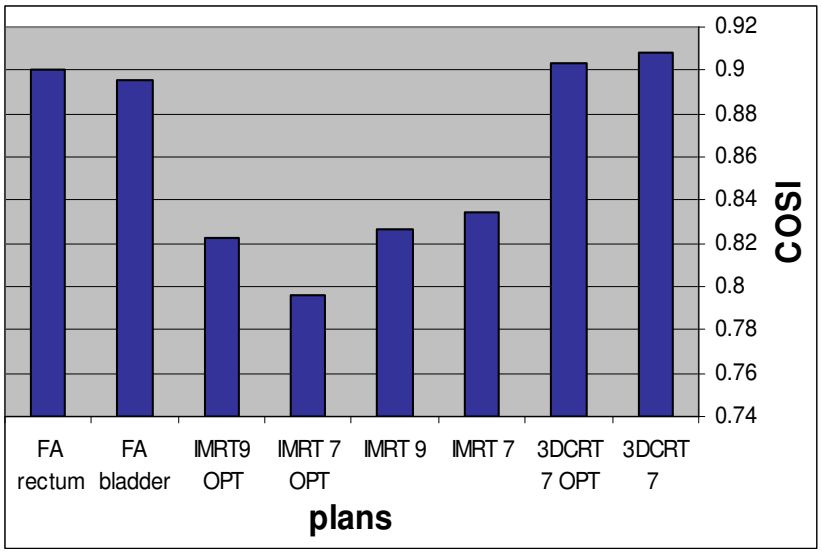

Figure8: critical scoring organ index(COSI) for different treatment plans

Figure 9 displays the calculated MCOSI for all plans. It is apparent that, MCOSI values of all plans with no significant difference and the M COSI values of 3DCRT have the highest values

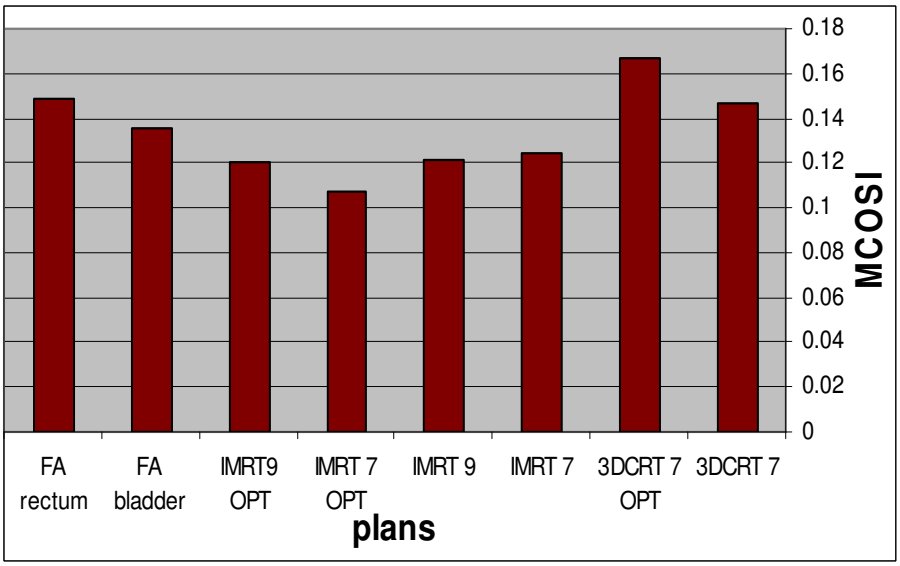

Figure 9: modified critical scoring organ index(MCOSI) for different treatment plans

In spite of the higher dose homogeneity of 3DCRT, we can point out in (figure 10) that the lowest QF value was obtained in IMRT 7 OPT and IMRT 9 OPT. On the other hand, the higher values of QF were obtained in the RA bladder have the highest value of QF

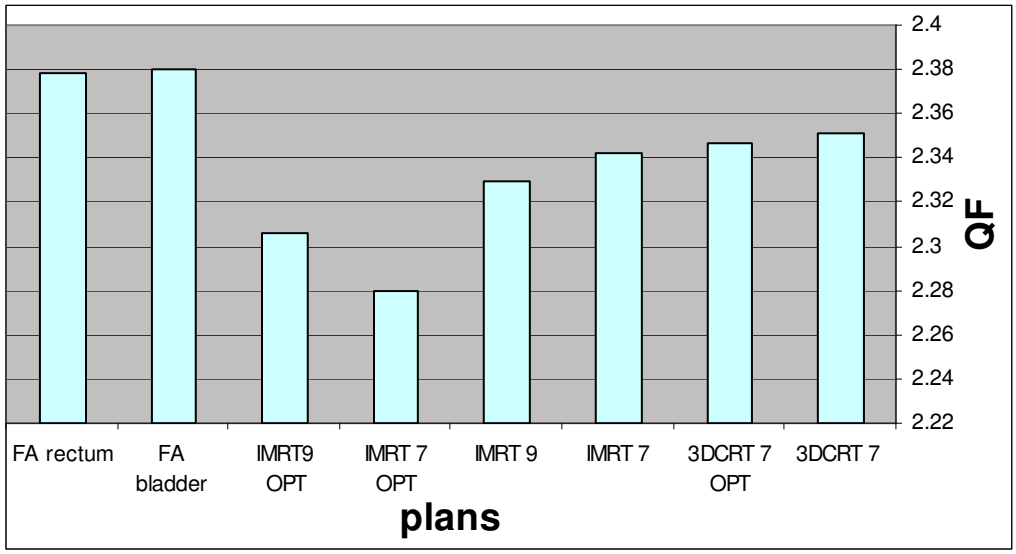

Figure 10: quality factor (QF) for different treatment plans

4.2. Number of MUs

The highest number of MUs was resulted in IMRT technique while the lowest number was resulted in 3DCRT. In different RapidArc plans the number of MUs had mid values between IMRT and 3DCRT (figure 11). The largest number of monitor units (MUs) in IMRT technique means that it has the highest total integral dose and accordingly the highest probability of secondary cancer after curative treatment.

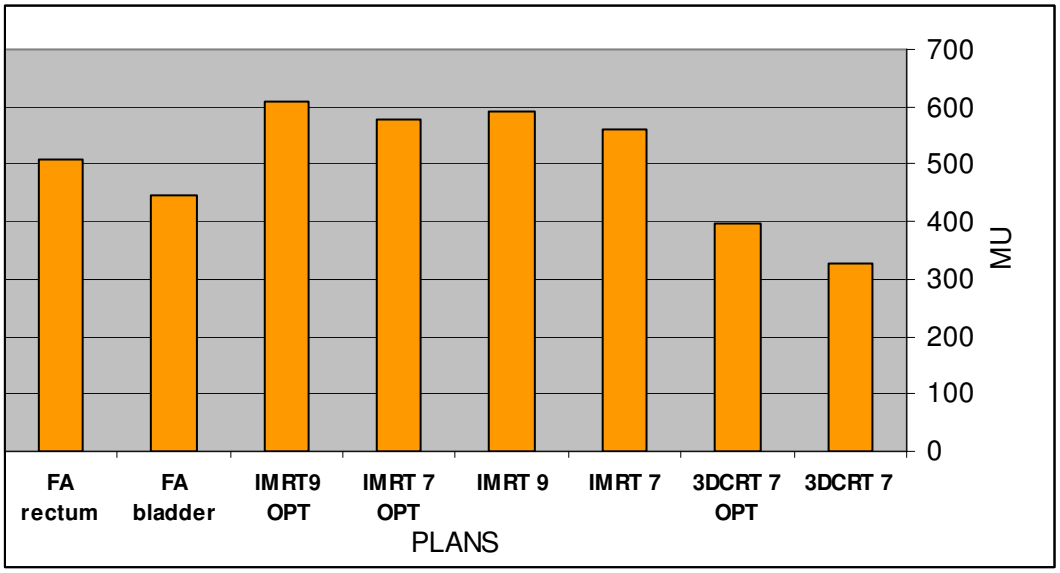

Figure 11: monitor unit(MU)) for different treatment plans

4.3. Gamma Value

In figure 12 we can pointes out the gamma value of all plans are almost equal with no significant difference and the gamma values of RapidArc and 3DCRT have higher values than IMRT technique. in IMRT technique has lowest accurate setup than other techniques

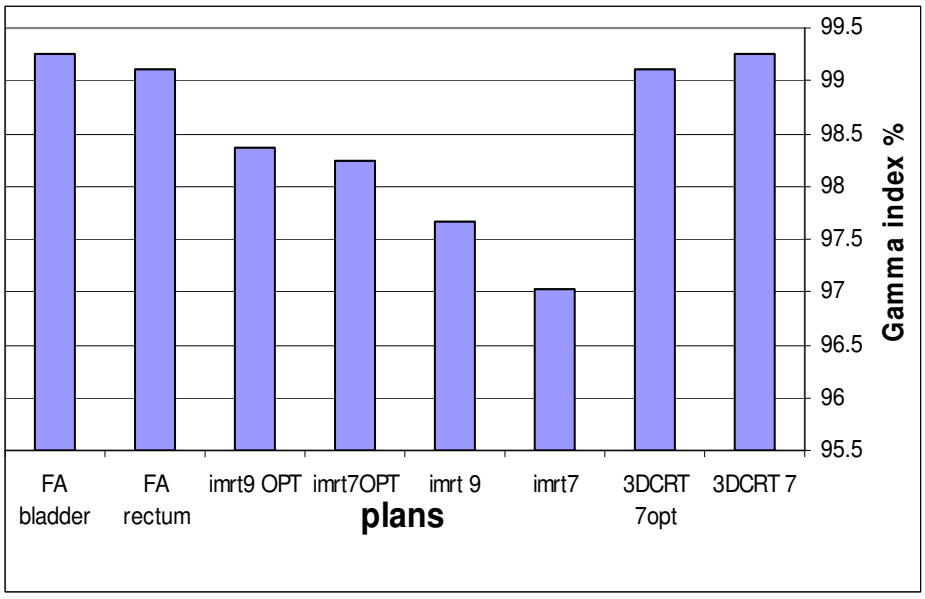

Figure 12: gamma value for different treatment plans

5. Discussion

In this study, we intended to compare different treatment techniques of cancer prostate. All techniques were able to generate a dose distribution that was adequate for treatment. The overall qualities of the plans produced were very close. The similarity in the overall qualities of the plans was also obtained in the evaluation of the DVH's of different targets. All DVH's satisfied the dose-volume constrains. This means that dose distribution and DVH's alone are not capable to rank the treatment plans. In spite of that, in radiation treatment planning analysis, dose volume histograms were the most widely used quantitative results.

We have modified a dosimetric evaluation model suggested by Amin et al (2016) [25] and used it in evaluating the treatment plans. In the modified model, we didn't use the dose statistical parameters (mean, mode, median dose, maximum, minimum dose and standard deviation). These statistical quantities are indicators of target dose homogeneity which can be concluded by calculating the HI index. To avoid a repetition in dose calculation only HI index have been used and we didn't use any other homogeneity index because it is the most sensitive index to the dose variation between the different homogeneity indices used by Amin et al (2016)[25]. In the modified model, we used two more additional quantities. These quantities are COSI and MCOSI indices for evaluating OAR doses above or below its tolerance doses.

The treatment plans should be detected in the pretreatment measurement QA. There are international recommendations to do 3D or at least quasi 3D measurements for pretreatment measurement QA. But there is no specific recommendation on measurement and evaluation methods. The comparison of 3D dose distributions, i.e. the measured and the calculated dose distributions, require an evaluation method that include a large number of data points and preferably express the result in one or a few pass all criteria. A commonly used evaluation method is the gamma evaluation.[9,10,28] Therefore, in addition to dosimetric evaluation we have performed a plan dose verification for all eight plans. The gamma value in 8 plans is pass than 95 %, but the gamma value obtained in both RA and 3DCRT were higher than that obtained in IMRT.

Dosimetric evaluation performed in this study indicated that 3DCRT has better dose homogeneity than IMRT and VMAT because of its high HI value. This result agrees with result obtained cakir et al ,2015 and Amin et al, 2016 and Vaezzadeh et al ,2012).[25.27.28]

In literatures PITV, TCI, CI, and CN indices have been used for target coverage and conformity. These indices are too diverse to achieve the desired objective, i.e., to quantify the quality of a treatment with 100% sensitivity and specificity. All of these indices displayed good PTV coverage and dose conformity in all plans with no significant difference except IMRT7opt. This indicates that computer optimization of beam angle doesn't always give the best dose distribution because of the values of each of this quantities in different plans are very close none of this indicates allowed us to rank the plans

In this study, we have used both of GI and GM indices to predict the dose gradient. Since both of the two quantities are good indicators of both PTV dose conformity and OAR's doses. GM has an advantage of its availability in Eclipse treatment planning system. Better dose gradient was obtained in RapidArc. Dose in surrounding OAR will receive lower dose in RapidArc techniques.

COSI and MCOSI are two indices which allow physic and clicanlc to compare different plans according to the dosimetry of OAR. rapid arc and 3DCRT have better values for organ at risk than IMRT. These results agree with that published by Menhal et al 2006 and Alfonso et al 2015 .[23,29]

Plan comparison studies still remain controversial. The main reason for this is because plan parameters, optimization methods, and OAR constraints are difficult to clearly define. Many researchers have focused on the influence of planning parameters on the results of treatment plans.[30,31] Therefore all the physical evaluation indices have been integrated in one index. This index is the planning quality factor (QF). When we used QF in the physical evaluation, it was sensitive to the variation in dose homogeneity, conformity, gradient and OAR dosimetry. In this study, we modified the QF index which has been used by Amin et al,2016[25] using only one homogeneity index and by adding COSI and MCOSI indices.

The difference in plan quantitative quality was very clear and statistically significant between different plans. The best technique with high QF was RapidArc (FA bladder). This result agrees with Amin et al 2016.
VMAT technique reduced the total MU in comparison with IMRT. This result agrees with Amin et al 2016, Palma et al 2008, Hardcastle et al 2011, Cakir et al 2015.[25,27,32,33.] On the other hand, the total MU in 3DCRT was less than that IMRT and RapidArc as expected.

6. Conclusion

COSI and MCOSI indices are accurate factors for OAR which effect on plan evaluation so the dosemitric evaluation model and the QF factor should take in account these two quantities. Dose verification is a necessary step in advanced treatment planning techniques. The best techniques obtained is Rapid Arc (RAbladder).

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