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Dosimetric influence of Flattening Filter (FF) and Flattening Filter Free (FFF) 6 and 10 MV photon beams on Volumetric Modulated Arc Therapy (VMAT) planning in case of prostate carcinoma

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ABSTRACT

Background: In the treatment of prostate cancer, radiotherapy is the potential to increase second primary cancers such as bladder and rectal cancers. The reasons for this potential are more monitor units (MUs), therefore a larger total body dose because of leakage radiation, a bigger volume of normal tissue is exposed to lower radiation doses. This study was designed to compare the integral dose of using Flattening Filter (FF) and Flattening Filter-Free (FFF) 6 and 10 MV photon beams via volumetric modulated arc therapy (VMAT) for prostate cancer patients. ***Materials and Methods***: Twenty prostate cancer patients were selected retrospectively for this planning study. VMAT plans were developed using the Eclipse (Varian Medical System, Palo Alto, California, USA) Treatment Planning System (TPS) with 6 MV FF, 6 MV FFF, 10 MV FF and 10 MV FFF for each patient. Conformity index (CI), homogeneity index (HI), Integral dose (ID), the volume receiving 5 Gy (V5%) and monitor units (MUs) were compared. ***Results:*** The use of 10 MV FF had 206 liter*Gy integral dose to Body-CTV volume. Using 10 MV FFF had 204 liter*Gy integral dose to normal structures. When 10 MV FF or 10 MV FFF were used instead of 6 MV FF and 6 MV FFF integral dose decreased as -7% and -8%, respectively. The dosimetric difference were statistically significant ($p<0.05$). The use of 10 MV FFF rather than 10 MV FF had limited influence on the integral dose for rectum, bladder, penile bulb and femoral heads. ***Conclusion:*** This study showed that high energy photons (10 MV FF, 10 MV FFF) have lower integral dose than low energy photons (6 MV FF, 6 MV FFF). The relationship between low energies, high energies and integral doses is significant, although there is no significant relationship between V5% doses of all energies. In comparison to different treatment plans, we showed that V5% alone did not provide enough information when possible secondary cancer risks were calculated.

Keywords: *Integral radiation dose, secondary cancer, flattening filter free beam, volumetric modulated arc therapy, prostate cancer.*

INTRODUCTION

About 50% of all cancer patients in the world receive radiotherapy during their treatment. The aim of radiotherapy is to keep local tumor control and tolerable normal tissue complications for early and late effects [1-2]. Secondary malignancies are late complications arising after radiotherapy and chemotherapy. In all studies, atom bomb survivors, Chernobyl accident, irradiated patients, animal experiments show that ionizing radiation is a carcinogenic

factor [3-4]. Several studies have shown that the risk increases with dose. Hall and Cheng-Shie expressed by increasing the volume of normal tissue receiving low doses, the incidence of secondary cancer might increase. A linear relation exists between cancer and dose from about 0.1 Sv up to about 2.5 Sv [5-6]. These data represent the gold standard for our knowledge concerning radiation-induced cancer. In most cases, assessment of risk of secondary cancers in radiotherapy patients is difficult. Because there is no control group treated without radiation expect for cancer of prostate and cancer of the cervix, in which surgery is a viable alternative to radiotherapy [7-8]. Prostate cancer is one of the most frequent malignant cancer for men in the world [9]. Radiotherapy has an important role in the treatment of prostate cancer. In the last two decades, two-dimensional and three-dimensional conformal radiation therapy (3D-CRT) techniques were applied [10-11]. In recent years, intensity modulated radiation therapy (IMRT) and intensity modulated arc therapy (VMAT) have been increasingly utilized to treat prostate cancer to give more conformal dose distribution. The basic principle of IMRT involves irradiation from a number of different directions with beams of non-uniform energy fluences, which have been optimized to deliver a high dose to the target volume and acceptably low dose to the surrounding normal structures [11-12]. IMRT increases the volume of normal tissue exposed to some radiation; however it can also reduce total dose received by critical structures [13]. Because high energy photons (greater than 10 MV) have dosimetric advantages in some situations due to their greater depth of penetration and skin-sparing potential, and such energies are commonly used in 3D-CRT. With the introduction of technologically advanced radiotherapy, the volume of healthy tissues receiving high doses will be reduced [13-15]. Conversely, the volume of healthy tissues receiving low doses will increase. On the other hand, delivery of a specified dose to the isocenter from a modulated radiation field by IMRT would require more monitor units (MUs) and longer treatment time. This will cause increased leakage radiation in the total body. VMAT uses a dynamic modulated arc to deliver IMRT. The VMAT technology simultaneously coordinates gantry rotation, MLC motion and dose rate modulation, facilitating highly conformal treatment and optimal sparing of the normal tissue near the target [16]. VMAT, based on the original investigation of K. Otto has been recently introduced in clinical practice in several institutes after an intensive validation at planning level, compared to IMRT or other approaches. Rapid Arc (RA), the Varian solution of VMAT are implemented as the Progressive Resolution Optimization (PRO) algorithm in the Eclipse planning system by Varian Medical System (Palo Alto, California, USA). The optimization process is based on an iterative inverse planning process aiming to simultaneously optimize the instantaneous multi leaf collimator (MLC) positions, the dose rate, and the gantry rotation speed to achieve the desired dose distribution [17].

VMAT has the dual advantages of lower MUs and less scattered dose to the body [18]. As the consequence of medical progress, cancer patients have higher number of long term survivals after treatments. Radiation-induced tumors in radiotherapy patients will become increasingly important as younger patients are treated.

Radiotherapy for prostate cancer has been linked to the late occurrence of second malignancies both in the true pelvis and outside the targeted area due to low-dose radiation scatter. Secondary malignancies following prostate irradiation include predominantly bladder cancer and, to a lesser extent, colon cancer [19-21]. Those secondary radiation-induced bladder tumors are usually aggressive and sometimes lethal.

A new linear accelerator called TrueBeam STx (Varian Medical Systems, Palo Alto, CA) with flattening filter-free (FFF) beams was introduced into clinical operation. There are two main advantages of removing the flattening filter: 1) fast delivery time because of the high dose rates, which means the possibility of fast beam delivery in Stereotactic Body Radiotherapy (SBRT) treatment, and 2) reduction of the out-of-field dose as a result of reduced head scatter and leakage, which leads to reduced

exposure of normal tissue to scattered doses outside the target field [22].

There are so many articles published about 3D-CRT and IMRT, VMAT technique comparisons in many cancer treatments. Some authors have reported dosimetric comparisons of 3D-CRT, IMRT and VMAT for prostate treatment. They mostly used comparison for PTV conformity, homogeneity and OAR dose constraints. There is no energy-related integral radiation dose.

The aim of this study was to compare the planning target volume (PTV) coverage, organ at risk (OARs), and non-tumor integral radiation dose from 6 MVFF, 6 MVFFF, 10 MVFF and 10 MVFFF for VMAT in the treatment of prostate cancer.

MATERIALS AND METHODS

Varian TrueBeam STx linear accelerators

Varian TrueBeam STx is a radiotherapy device using 3 dimensional Conformal, IMRT, IGRT, VMAT, Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiotherapy (SBRT). This linear accelerator is designed as a digital linear accelerator with 6 MV, 10 MV, 15 MV filter (Flatting Filter-FF) and 6 MV, 10 MV (Flattening Filter Free-FFF) beams. The dose range of filtered beams is 100-600 MU / min, 400-1400 MU / min for 6 MV FFF and 400-2400 MU / min for 10 MV FFF. The maximum area dimensions used for active MLC, with minimum 0.5 x 0.5 cm and maximum 40 × 40 cm area dimensions, are 22 × 40 cm.

TrueBeam STx linear accelerator has multileaf (MLC) consisting of 120 tungsten materials. The MLCs are 2.5 mm thick in the isocenter and have 32 pairs of MLC and 28 pairs of 5 mm MLC that surround the treatment field. The tongue-and-groove effect has the same design as the Millennium MLC and the High Definition MLC (HD-MLC) in terms of rounded leaf edge properties. HD-MLC, irregularly shaped areas of 40 cm length and 22 cm long can be formed.

Patient preparation on CT simulation

CT data-sets of 20 patients with localized prostate cancer (T1-2N0M0) who received radiotherapy in our institution were used in this comparative planning study. All planning CT scans were obtained by using CT simulator (Siemens-Somatom Definition AS Munchen-Germany) with 5-mm slice thickness, without a gap from the iliac crest to 8 cm below the ischial tuberosities. Patients were instructed to void the bladder and rectum about 1-1.5h before the CT their individual urinary conditions. The clinical target volume (CTV) was defined as the entire prostate in this study. A 5-mm margin was used to expand the CTV to the planning target volume (PTV) based on measured localization uncertainties, inter-user reproducibility and intra-fraction motion. For the beam margin, accounting for the beam penumbra, was set to be 0.5 cm from the PTV in the coplanar direction and 0.7 cm from the PTV for the direction perpendicular to the beam direction plane (along the z-direction). Normal structures including bladder, penile bulb, and rectal wall were outlined on the planning CT images. The contoured rectal wall extended from the bottom of the ischial tuberosities to the rectosigmoid flexure. The “normal tissue” volume was defined as the whole patient volume minus the CTV. Routine institutional image-based patient position verification protocols foresee 2D-2D matching of orthogonal kV-MV images acquired with the on-board imaging system installed at the accelerator with evaluation performed by radiographers and application of couch shifts if total vector length of displacement is smaller than 5 mm. CT as Cone Beam CT imaging is becoming part of our routine protocol and is now performed once a week in addition to the 2D -2D matching (kV-MV) as the most common procedure. VMAT plans were developed using the Eclipse (Varian Medical System, Palo Alto, California, USA) Version 13.0 Treatment Planning System (TPS) with 6 MV FF, 6 MV FFF, 10 MV FF and 10 MV FFF for each patient. AXB (Acuros XB Algorithm, Varian Medical System, Palo Alto, California, USA) was used to compute the dose distributions. The dose constraints were set for the rectal wall, penile bulb, femoral head, bladder, and unspecified normal structure table 1.

Table 1. Optimization parameters for volumetric modulated arc therapy treatment plans.

Structure	Criterion Dose (cGy)	%Volume
Planning target volume (PTV)	7400	≤95%
Rectum	5000	<40%
	6000	<17%
	7000	<15%
	7500	<8%
Bladder	5000	<50%
	7000	<30%
Penile Bulb	4500	<50%
	3700	<70%
Femoral Heads	5000	<10%

Volumetric modulated Arc therapy (VMAT) planning process

VMAT planning is performed through inverse planning techniques similar to that of dynamic gantry IMRT. This is further complicated due to increased number of dynamic variables involved during delivery. Varian's solution is the introduction of a new resolution-based optimization algorithm to aid in the inverse planning process. The clinical advantages of rotational techniques seem to be establishing themselves as a systematic process providing a turnkey solution for the inverse planning process to be elaborated. As a result, there is a strong correlation between the experience of the planner and the resulting plan quality.

All VMAT plans require some degree of collimator rotation to reduce the cumulative effects of tongue and grove leakage throughout gantry rotation, and to allow spatial modulation in the transverse plane. The jaws are set to be open to largest PTV throughout the entire the gantry rotation, with an extra margin of approximately 10 mm. The Arc1 is set to run from 179 through to 181 in a counterclockwise (CCW) direction and Arc2 is set to run from 181 through to 179 in a clockwise (CW) direction selected for all photon energies. The above field setup allows the optimization algorithm as the largest range of parameters so that the change of the best plan being produced is maximized. Following optimization, dose calculation is done using the optimized MU value and the AXB dose calculation algorithm with a dose grid size of 2.5 mm. The dose distribution is then evaluated and the DVHs are examined for the planer ability to meet any dose constraints. If target volume coverage does not meet ICRU 83 criteria, there may be a need to renormalize the whole plan by adjusting the plan normalization value, usually by no more than 1-2%. During planning, the primary goal was to achieve similar PTV coverage for all techniques and the secondary goal was to reduce OAR doses individually as much as possible. Conformity index (CI) and homogeneity index (HI) were used for PTV coverage. Dose Volume Histograms (DVHs) were used to compare treatment plans including PTV, OARs, Body $V_{5\%}$ and integral radiation dose from different energies.

Dose-volume histograms and plan evaluation

Conformity Index (CI)

The RTOG conformity index is defined as ratio of prescription isodose volume (V_{Rx}) to the PTV volume. Ideal value of CI is unity and generally it is greater than one.

$CI=V_{Rx}/V_{PTV}$

The CI ranges from 0 to 1, where 1 indicates perfect overlap (identical structures). A value near 0 indicates total absence of conformation in which the target volume's not being irradiated.

Homogeneity index (HI)

The dose homogeneity of PTV, is described as $HI = (D_{2\%} - D_{98\%}) / (D_{50\%})$ where $D_{2\%}$, $D_{50\%}$, and $D_{98\%}$ are the dose values by 2%, 50% and 98% volumes of PTV, respectively. The HI ranges from 0 to 1, where 0 is the ideal value. A higher HI indicates poorer homogeneity.

For statistical analyses, the Kruskal-Wallis test was used. All computations were performed using the SPSS program (SPSS Inc., Chicago, IL,

USA). A p-value below 0.05 was considered significant. In the paired group comparisons of quantifiable data, if parametric conditions were provided the Bonferroni Modified test was applied, otherwise the Mann-Whitney *U* test was used.

Integral dose

Integral dose is the volume integral of the dose deposited in a patient, and is equal to the mean dose times the volume irradiated to at any dose. Integral dose is also the area under the curve of a differential absolute dose volume histogram. It is often stated that the large number of beamlets and monitor units used in IMRT leads to an increase in integral dose. Higher energy photon beams substantially reduce the integral dose.

RESULTS

We observed that 100% of the PTV structure received 95% of the prescription dose of 78 Gy for all twenty patients for all selected energy levels. All VMAT plans were optimized to keep the maximum dose within the target to <110% of the prescription dose (Dmax<110%), and all plans were able to meet this objective. Figure 1 a -d shows that axial VMAT planning slice of the patient who was included in our study.

In terms of the OAR, the Dose-Volume objectives were easily met in all cases table 2). Table 2 shows the summary of PTV D_{min}, PTV D_{max}, PTV D_{mean}, Rectum $V_{60\%}$, $V_{40\%}$, $V_{25\%}$, Bladder $V_{60\%}$, $V_{40\%}$, $V_{25\%}$, Penile bulb $V_{45\%}$, Femoral Head $V_{10\%}$ and Conformity Index, Homogeneity Index were shown for all VMAT plans. Table 3 shows Monitor Unit, Body-CTV integral dose and Body $V_{5\%}$ (5Gy receiving of the volume) for different energies.

Although there were small differences, and some of dosimetric differences were statistically significant.

Table 2 shows that PTV D_{min} dose is higher with the 10 MV FF, but lower with 10 MV FFF beam. In the case of PTV D_{max} 10MV FF had lower maximum dose.

For bladder, 6 MV FFF and 10 MVFFF were able to provide a higher $V_{25\%}$ (Volume of receiving 25Gy) than 6 MVFF and 10 MVFF.

Table 2 shows that all the values for rectum ($V_{25\%}$, $V_{40\%}$, $V_{60\%}$) dose constraint categories present a lower dose when using 10 MVFFF (51±10.4, 35.9± 5.8, 25±3,8 respectively).

The Left and Right Femoral Head D_{mean} dose 10 MV FF and 10 MV FFF were lower mean dose.

The mean Integral dose of Body-CTV tissue are summarized in Table 3. Regarding the integral dose of normal structures, the use of 6 MV FF and 6 MV FFF revealed similar results.

With respect to the dose to the OARs, sparing for the bladder and the rectum was slightly better with the 10 MV FF and 10 MV FFF beam plans than with the 6 MV FF and 6 MV FFF beam plans. However, this difference was negligible except for rectum volume that received the Rectum D_{mean} dose. Table 2 shows that the moderate dose volume to the Rectum was 3.2% less on average for the 10 MV FF and FFF beams than for the 6 MV FF and FFF beams. There was no significant difference in dose volumes between the left and right femoral heads for all plans generated by different beams.

Figure 2 a-f shows that mean value of integral radiation dose of (Body-CTV) Normal Tissue, Bladder, Rectum, Penile bulb, Left Femoral head and Right Femoral head.

The use of 10 MV FF had 206 liter*Gy integral dose to Body-CTV volume. Using 10 MV FFF had 204 liter*Gy integral dose to normal structures. When 10 MV FF or 10 MV FFF were used, integral dose decreased to -7% and -8%, respectively. The dosimetric differences were statistically significant ($p<0.05$). The use of 10 MV FFF rather than 10 MV FF had limited the influence on the integral dose for rectum, penile bulb and femoral head. There was no significantly difference between FF and FFF planning in the same energy levels (Figure 3a-b). Likewise, Figure 3-a shows that in 6 MV FF and 6 MV FFF, there is no dosimetric difference in 6 MV FF and 6 MV FFF ($p>0.05$). Figure 3-b shows that 10 MV FF and 10 MV FFF same dosimetric results ($p>0.05$). However, Figure 3-c represents 6 MV FFF and 10 MV FFF dosimetric data are statistically significant ($p<0.05$).

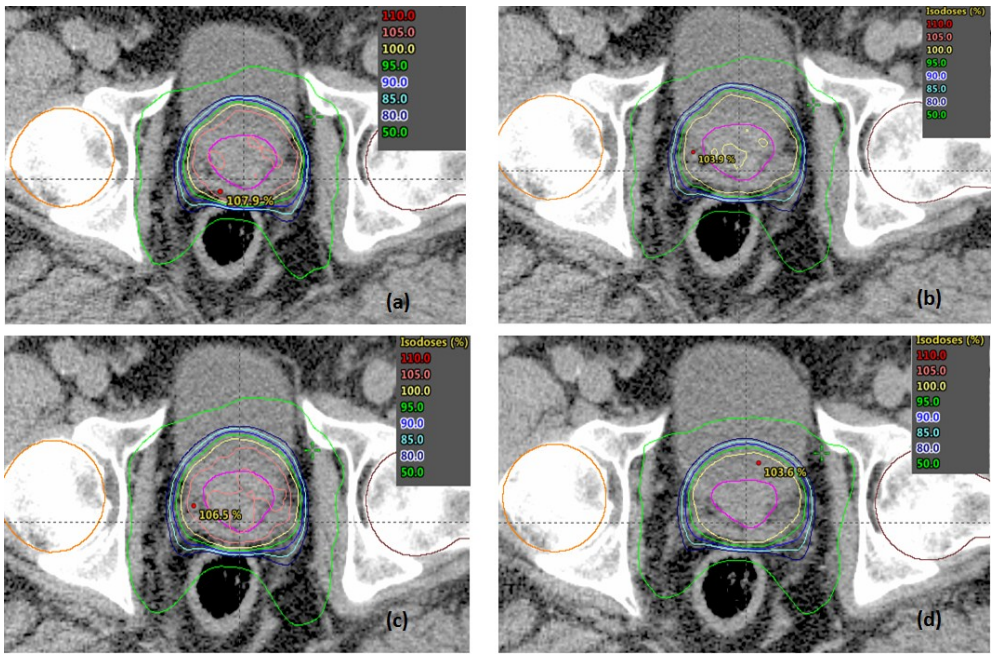

Figure 1. Axial VMAT planning slice of the patient who was included in our study a) 6 MV FF b) 6 MV FFF c) 10 MV FF d) 10 MV FFF.

Table 2. Average dose volume histogram (DVH) analysis for twenty patients.

	6 MV FF (Mean±SD)	6 MV FFF (Mean±SD)	10 MV FF (Mean±SD)	10 MV FFF (Mean±SD)	p-value
PTV D_{min}	68.09±4.3	68.16±3.8	68.43±3.9	67.01±4.1	0.058
PTV D_{max}	80.99±4.5	80.25±4.4	79.74±3.3	80.45±4.2	0.075
PTV D_{mean}	77.18±3.8	77.15±3.7	77.44±4.3	77.44±3.4	0.227
Bladder V_{25}	57.50±3.7	58.40±4.2	56.10±3.9	58.30±3.2	0.068
Bladder V_{40}	41.90±3.2	42.12±3.3	41.80±3.7	42.10±4.1	0.077
Bladder V_{60}	28.78±3.6	28.36±4.2	28.00±3.2	28.94±3.4	0.344
Bladder D_{mean}	41.49±4.2	41.90±3.9	41.22±3.3	41.51±3.6	0.062
Rectum V_{25}	52.00±2.7	51.90±2.9	51.80±3.1	51.00±3.3	0.069
Rectum V_{40}	36.40±3.3	37.50±2.7	36.50±3.2	35.90±4.1	0.089
Rectum V_{60}	25.60±3.4	26.30±3.3	25.80±4.1	25.08±3.3	0.066
Rectum D_{mean}	36.73±4.2	37.04±3.9	36.50±3.4	36.17±3.2	0.055
Penile Bulb V_{45}	10.45±2.1	9.9±2.7	11.20±3.1	10.28±2.9	0.088
Penile Bulb D_{mean}	10.78±2.3	10.25±2.4	10.90±2.8	10.45±2.8	0.078
L Femoral Head D_{10}	19.38±0.75	20.43±0.65	17.66±0.72	17.67±0.66	0.044
L Femoral Head D_{mean}	18.20±0.78	18.15±0.67	16.90±0.65	15.84±0.72	0.040
R Femoral Head D_{10}	19.69±0.66	20.41±0.58	17.62±0.55	17.64±0.72	0.038
R Femoral Head D_{mean}	18.77±0.72	18.53±0.64	16.85±0.77	15.88±0.67	0.034

Table 3. Comparison of MUs, Conformity Index (CI), Homogeneity Index (HI), (Body-CTV) Dmean dose, Body V5% and (Body-CTV) non-tumor Integral Dose (ID).

Category	6 MV FF (Mean±SD)	6 MV FFF (Mean±SD)	10 MV FF (Mean±SD)	10 MV FFF (Mean±SD)	p-value
Monitor Unit	804±15	900±13	687±11	800±17	0.024
Conformity Index	1.05±0.01	1.04±0.03	1.02±0.02	1.01±0.02	0.014
Homogeneity Index	0.12±0.02	0.11±0.01	0.10±0.02	0.11±0.03	0.562
(Body-CTV) D_{mean}	707±9	706±8	660±10	651±14	0.025
Body $V_{5\%}$	27±1	27±1	27±1	26±1	0.060
Integral Dose (liter*Gy)	221± 3.8	221± 2.4	206 ±3	204± 2	0.042

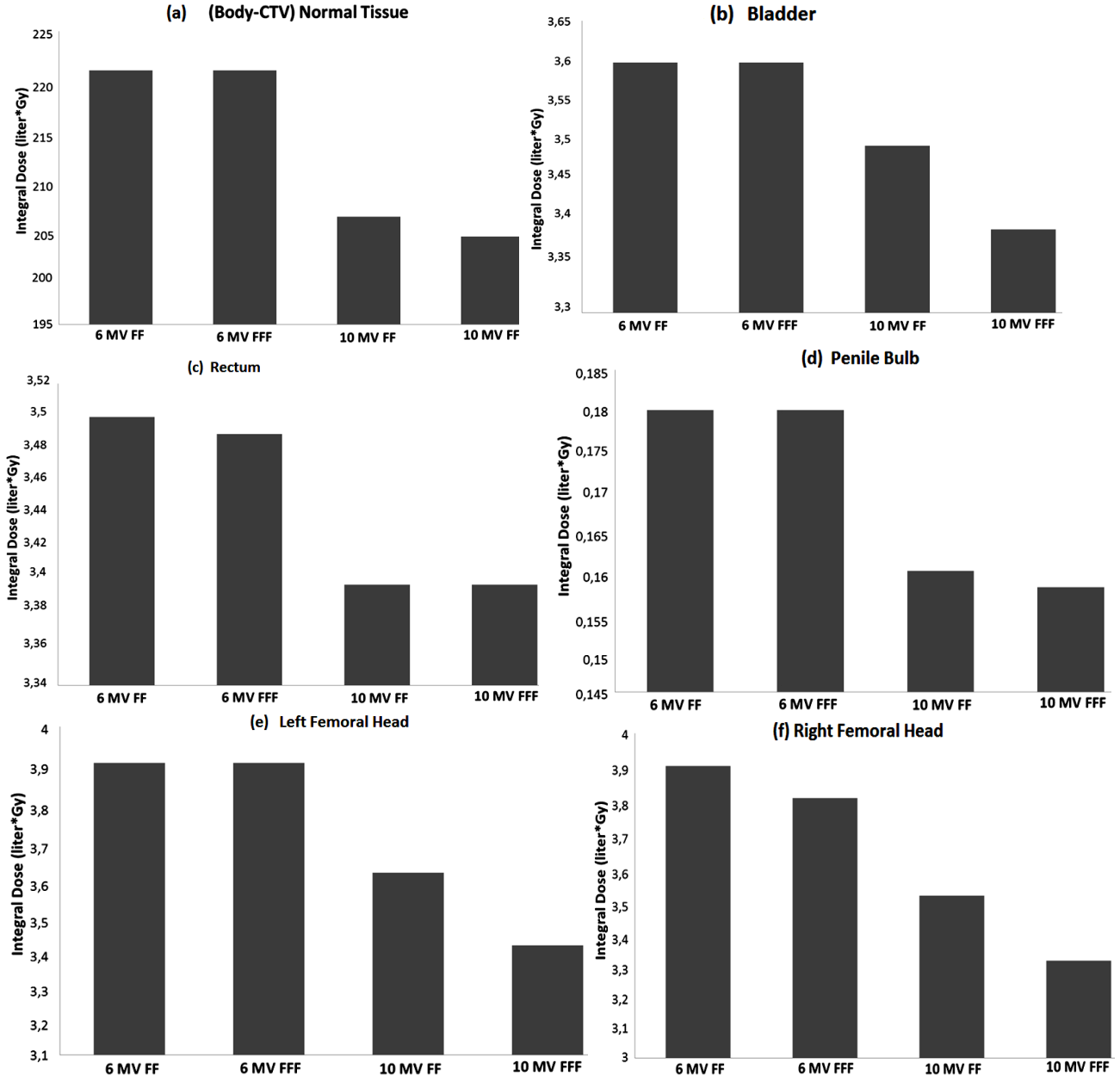

Figure 2. Mean value of integral radiation dose of **a)** (Body-CTV) normal tissue, **b)** Bladder **c)** Rectum **d)** Penile Bulb **e)** Left Femoral Head **f)** Right Femoral Head

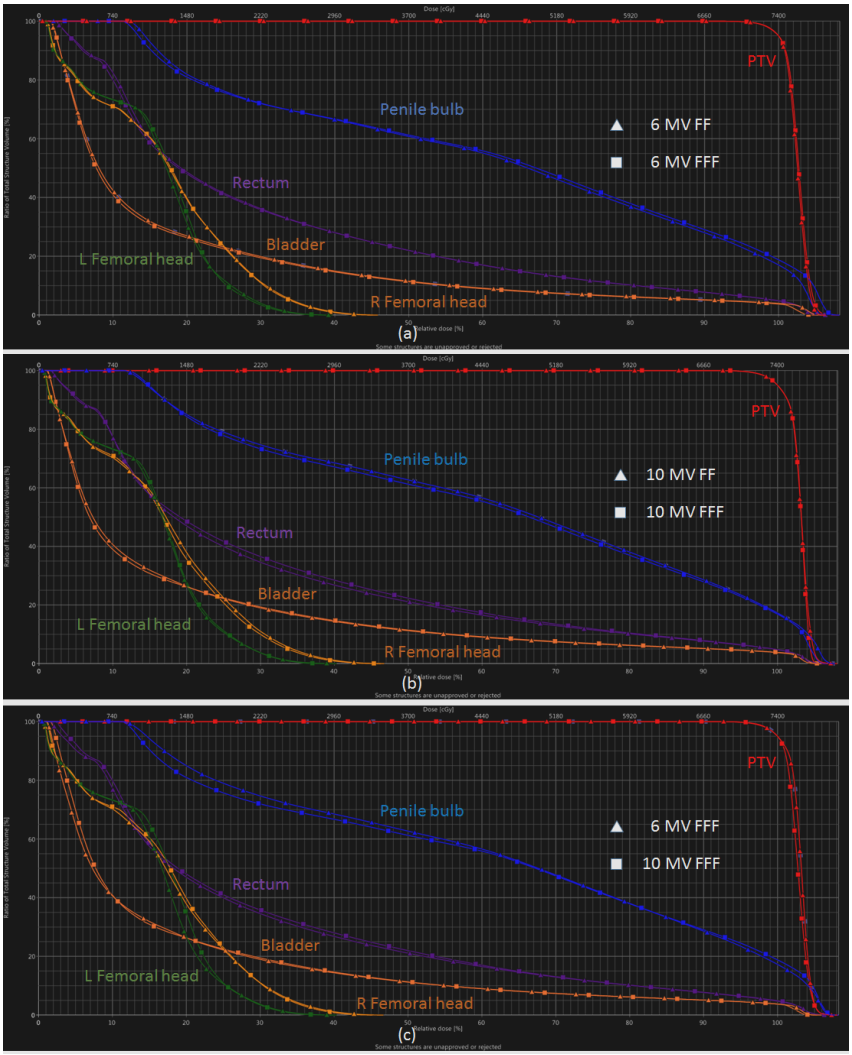

Figure 3. Dose volume histogram (DVH) comparison for **a)** 6 MV FF&FFF **b)** 10 MV FF&10 MV FFF **c)** 6 MV FFF&10 MV FFF.

DISCUSSION

Many radiation-induced secondary cancers appear to occur in organs and tissues in the high -dose volume, but some may also appear in the low dose volumes. There are pronounced differences in the types of radiation-induced secondary cancers among children, young adults and elderly patients treated with radiotherapy [18].

The risk of radiotherapy-induced secondary cancers after radical radiotherapy of most adult cancers is well below 1%. The risk of dying from uncontrolled local recurrences within a few years after radiotherapy is much higher than the risk of developing a secondary cancer 10 or 20 years later. In adult cancer patients, more than 90% of secondary cancers occurring after radiotherapy is the consequence of increased life expectancy due to cure from the first cancer [18].

Improvement in early cancer detection and advances in therapy have resulted in increasing number of cancer survivors. Prostate cancer is the most common malignancy among men. Radiotherapy is an important part in the treatment of prostate cancer. Radiotherapy is associated with a modest increase in secondary cancers. The risk of secondary malignancies using IMRT technique is higher than photon doses of 3D CRT. In the last few years, IMRT and VMAT were increasingly utilized to treat prostate cancer to permit more conformal dose

distribution and dose escalation. On the other hand, volumes of normal tissue low doses of radiation with IMRT and VMAT are larger than conventional conformal techniques. Hall and Wuu are among the frontiers to discuss how a shift from 3D-CRT to IMRT may result in an increase in second malignancies [3]. Because IMRT uses more radiation fields that involve a bigger volume of normal tissue exposed to lower doses of IMRT, the accelerator is required to be powered for longer MUs resulting in more total body dose due to scatter radiation. The amount of scatter radiation generated is a linear function of the amount of MUs. IMRT is associated with a 3 to 5-fold higher number of monitor units compared with conventional treatment. The potential cancer induction maximum in the 1-5 Gy range would make an impact in multi field therapy. Organ-specific dose volume histograms could be helpful for risk assessment. Prospective and uniform out-of-field dosimetry during planning would be preferable over dose reconstruction.

In this study, 10 MV FF and 10 MV FFF plans provided very similar and highly conformal plans for tumor coverage. The dose homogeneity within the PTV was slightly improved by the 10 MV FF and 10 MV FFF photon energy when compared with 6 MV FF and 6 MV FFF, although the difference was not statistically significant.

There are so many articles published about 3D-CRT and IMRT, VMAT technique comparisons in many cancer treatments [19-21]. Some authors have reported dosimetric comparisons of 3D-CRT, IMRT and VMAT for prostate treatment, and therefore, direct comparison with our study is difficult [22-25]. They used different comparison parameters. The comparison was mostly for PTV conformity and OAR dose constraint. There is energy-related integral radiation dose. All studied intensity modulated techniques yield treatment plans of significantly improved quality and higher MUs when compared to 3D-CRT. Palma et al. (hakemler "et al." yerine bütün yazarların adının yazılmasını istemişler) compared 3D-CRT, Dynamic IMRT and VMAT using Varian's Rapid Arc. They reported better treatment efficiency for the VMAT (491.6 and 454.2 MUs for constant and variable dose rates, respectively) vs.788.8 MUs for Dynamic IMRT. They also reported overall similar dose distributions with limited advantages regarding dose to OAR and conformity for the plans with variable dose rate during rotation. A detailed analysis of dose exposure to non PTV normal tissue was not performed [10]. Zelefsky *et al*. reported approximately 700 MUs for dynamic IMRT and 300 MUs for 3D-CRT prostate cancer treatment [2]. Shaffer et al. reported 949 MUs for VMAT and 1814 MUs for nine field IMRT with a integrated boost to the prostate bed [26]. Wolff et al. reported 252±8 MUs for 3DCRT, 544±56 MUs for step-and-shoot IMRT, 386±29 MUs for (one 360º rotation) VMAT and 371±34 for (one 360º rotation and two 100º rotation) VMAT [27] for prostate treatment. Tsai et al. compared treatment and dosimetric advantages between VMAT, step-and-shoot IMRT and Helical Tomotherapy (HT) [28]. They reported that all VMAT, IMRT and HT plans were to meet the goals for PTV and the dose constraints for specific organs. They also reported the mean MUs 309.7 for VMAT, 336.1 for step-and-shoot IMRT and 3368 for HT [28]. Studies show that VMAT has similar coverage of PTV and doses of normal tissue with IMRT (step-and-shoot or dynamic). VMAT had significantly lower MUs than IMRT. It means shorter beam on time. The risk of developing a secondary malignancy increased 0.4%, 1% and 2.8% for 3D-CRT, step-and-shoot IMRT and HT by 6MV photon irradiation, respectively [25]. VMAT with its shorter treatment time may be less affected by intra-fractional movement.

Many studies suggest that IMRT results in increased secondary cancer risk. This has often been attributed to an increase in MUs requirements and head leakage. Indeed, it has been shown that, compared to 3D-CRT, IMRT results in increased leakage. Moreover, increased beam on time results in increased collimator head scatter, both of which contribute to an increase in out-of-field dose.

Studies involving proton treatments have consistently shown reduced secondary cancer risks compared to 3D-CRT and IMRT, largely due to a reduction in exit doses resulting in the volume of normal tissues irradiated, thus leading

to improved conformity. Similarly, the risk of secondary cancer has been shown to be lower with proton arc therapy (PAT) compared to photon VMAT [29]. IMRT technique has been estimated to be 2 or 3 times higher than conventional radiation therapy [5]

The effect of the dose difference on the OARs was inconsistent; however, the D_{mean} dose difference was within 1% for the rectum with the 6 MV FF beam compared to the 10 MV FF beam. This difference for OARs sparing depended on the beam energy. However, the doses were similar for the left and right femoral heads. The overall dose differences for the OARs were not significant for all four plans.

Our results have shown that using the 10 MV FF and 10 MV FFF plans reduced integral dose compared with 6 MV FF and 6 MV FFF plans.

High energy photons (10 MV FF, 10 MV FFF) have lower MUs than low energy photons (6 MV FF, 6 MV FFF). Lower MUs reduce the head scatter and leakage radiation. Lower MUs reduced the head scatter and leakage radiation and the risk of secondary malignancy [3-5].

If target coverage and normal tissue sparing are comparable between different treatment techniques, the risk of secondary malignancy should be an important factor in beam energy selection.

Multiple field radiation tends to decrease the volume receiving high radiation dose and increase the volume receiving low-dose radiation. The relationship between integral doses of low energies and high energies is significant, although there is no significant relationship between $V_{5\%}$ doses of all energies.

In comparison with different treatment plans, we showed that $V_{5\%}$ alone did not provide enough information for possible secondary cancer risk calculation.

Conflicts of interest*: *Declared none.

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