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*research article*

# The dosimetric significance of using 10 MV photons for volumetric modulated arc therapy for post-prostatectomy irradiation of the prostate bed

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**Background.** The purpose of the study was to analyse the dosimetric differences when using 10 MV instead of 6 MV for VMAT treatment plans for post-prostatectomy irradiation of the prostate bed.

**Methods and materials.** Ten post-prostatectomy prostate bed irradiation cases previously treated using 6 MV with volumetric modulated arc therapy (VMAT) were re-planned using 10 MV with VMAT. Prescription dose was 66.6 Gy with 1.8 Gy per fraction for 37 daily fractions. The same structure set, number of arcs, field sizes, and minimum dose to the Planning Target Volume (PTV) were used for both 6 MV and 10 MV plans. Results were collected for dose to Organs at Risk (OAR) constraints, dose to the target structures, number of monitor units for each arc, Body $V_5$, Conformity Index, and Integral Dose. The mean values were used to compare the 6 MV and 10 MV results. To determine the statistical significance of the results, a paired Student t test and power analysis was performed.

**Results.** Statistically significant lower mean values were observed for the OAR dose constraints for the rectum, bladder-Clinical Target Volume (bladder-CTV), left femoral head, and right femoral head. Also, statistically significant lower mean values were observed for the Body $V_5$, Conformity Index, and Integral Dose.

**Conclusions.** Several dosimetric benefits were observed when using 10 MV instead of 6 MV for VMAT based treatment plans. Benefits include sparing more dose from the OAR while still maintaining the same dose coverage to the PTV. Other benefits include lower Body $V_5$, Conformity Index, and Integral Dose.

Key words: volumetric modulated arc therapy (VMAT); prostate bed; 10 MV; 6 MV; radiation therapy

## Introduction

In radiation therapy, high energy photons are used to deliver x-rays to a tumor target. It is known that as the energy of the photons is increased, they will penetrate deeper into tissue resulting in more radiation dose being delivered to the tumor target. This has been observed when treating prostate cancer with three dimensional conformal radiation therapy (3DCRT).[1]

However, as the photon energy is increased, two issues arise: an increase in the penumbra and the production of secondary neutrons from the head of the linac when using photon energies greater than or equal to 10 MV.[2-4] As the technology of radiation therapy has changed, 3DCRT has given way to Intensity Modulated Radiation Therapy (IMRT), with 6 MV being the most commonly used beam energy in IMRT treatment planning. IMRT allows more dose to be delivered to the tumor target with less dose being deposited to adjacent organs at risk (OAR), as seen in two studies of prostate cancer.[5,6] For treatment plans using IMRT, numerous studies have been conducted about the impact of differ-

ent photons energies in treating prostate cancer.[7-14] Some of these studies show no clear benefit to using higher energy photons.

Volumetric Modulated Arc Therapy (VMAT) has now begun to replace IMRT for treating prostate cancer, and numerous studies show that using VMAT instead of IMRT for prostate cancer results in dosimetric benefits, such as reduced treatment time and more dose sparing to OAR.[15-20] Therefore, it is relevant to investigate if using higher energy photons has greater potency than using the traditional 6 MV for VMAT. To deal with the issue of neutron contamination, 10 MV photons were used for this work since the issue of neutron production for higher photon energies is negligible at that energy.[21]

When deciding which cancer type would be appropriate for conducting this study, we chose prostate cancer patients who were undergoing post-prostatectomy irradiation of the prostate bed. The reason for this selection is two-fold. The first reason is that we wanted a location with a deep seated target volume. This would ensure that using photon beam energies higher than 6 MV would result in x-rays that would penetrate into the target; photon beam energies greater than 6 MV would not be useful for a shallower target. The second reason is due to there being no requirement for additional boost plans. This allows the same plan to be used during the entire course of patient treatment, requires less treatment planning time per patient, and reduces the complexity of the plan.

## Materials and methods

Ten cases of prostate cancer patients who had undergone a prostatectomy and received irradiation of the prostate bed using 6 MV photons with VMAT at Roswell Park Cancer Institute were selected for a retrospective study. These cases were re-planned using 10 MV photons with VMAT, and were compared to the clinically used 6 MV plans. The prescription dose was kept the same at 66.6 Gy for all ten cases for both beam energies, with 1.8 Gy per fraction in 37 daily fractions. Treatment plans were created with the Varian Eclipse version 11 treatment planning system (Varian Medical Systems, Inc., Palo Alto, CA, USA). The Varian implementation of VMAT is known as RapidArc and used Anisotropic Analytical Algorithm version 10 and Progressive Resolution Optimizer version 10. Two complete arcs were used for all ten cases for both beam energies. For each patient, the field sizes for the 10 MV plan were kept the same as the corresponding 6 MV plan. Structure sets containing regions of interest were generated using CT based contouring, and the same structure set was used for both sets of treatment plans for dose measurement purposes. For each patient, the same minimum dose to the planning target volume (PTV) structure that existed for each 6 MV plan was used for the corresponding 10 MV plan. This was done as a baseline to compare the 6 MV and 10 MV plans for each patient. It should be noted that this study was performed using only a treatment planning system. There was no actual treatment plan verification of dose delivery by the linear accelerator.

Plan evaluation was based on the OAR dose constraint categories provided in Radiation Therapy Oncology Group (RTOG) protocol 0534.[22] Based on this protocol, values were collected for the following OAR dose constraint categories: Bladder-Clinical Target Volume (Bladder-CTV) $D_{50}$, Bladder-CTV $D_{70}$, Rectum $D_{35}$, Rectum $D_{55}$, Right Femoral Head $D_{10}$, and Left Femoral Head $D_{10}$. Bladder-CTV was created by cropping out the part of the bladder that overlaps with the CTV structure. For each plan, the cumulative dose volume histogram was used to collect these values. We also collected the minimum dose, maximum dose, and mean dose for the CTV and PTV, and the volume percentages of the CTV and the PTV that receives 95% of the prescription dose of 66.6 Gy. We also collected values for the Body $V_5$, the number of monitor units for the first and second arcs, the Conformity Index, and the Integral Dose. The Body $V_5$ provided a measurement of low dose exposure to the Body as contoured in the treatment planning system. The International Committee for Radiation Units (ICRU) report 62 defined the Conformity Index as the ratio between the treated volume receiving a selected dose and the PTV volume receiving a selected dose.[23] Based on ICRU report 62, we defined the Conformity Index in our study as the ratio between the Body volume receiving 66.6 Gy and the PTV volume receiving 66.6 Gy. We defined the Integral Dose as the volume of the Body-PTV structure multiplied by the mean dose to the Body-PTV. The Body-PTV structure was created by cropping out the section of the Body structure that overlapped with the PTV. For each category of interest, the results collected for both energies were used to generate a mean along with a standard deviation of the mean for 6 MV and 10 MV. To determine the statistical significance of our results, a paired Student t test and power analysis was conducted using the R statistical software package version 3.2.3.[24] The OAR dose constraint limits were adapted from RTOG protocol 0534, and

are presented in Table 1. We did not want the dose to the OAR to exceed these limits.

Additional optimization structures were used for the 10 MV treatment plans in order to spare dose to the OAR and increase dose to the PTV. These structures were labeled PTVx, Bladder-PTVx, Rectum-PTVx, Penile Bulb-PTVx, Rectum 7 mm, and Rectum Mid. The PTVx is created from the PTV with a margin expansion of 1 mm in all directions. The Bladder-PTVx structure is created by cropping out the portion of the bladder that overlaps with the PTVx with a 3 mm separation between the new structure and the PTVx. The Rectum-PTVx structure is created by cropping out the portion of the rectum that overlaps with the PTVx with a 3 mm separation between the new structure and the PTVx. The Penile Bulb-PTVx structure is created by cropping out the portion of the penile bulb that overlaps with the PTVx with a 3 mm separation between the new structure and the PTVx. Not every plan had this structure due to the possibility that the penile bulb completely overlaps with the PTVx. The Rectum 7 mm structure was created through several steps. First, the Rectum-PTVx structure is created with no additional separation. Then, this structure is expanded by 5 mm on all sides. This new structure is cropped out from the PTVx with an additional margin of 7 mm. Any instances of the Rectum 7 mm structure on slices where the PTVx structure did not exist were erased. The Rectum Mid structure was created through several steps. First, the Rectum-PTVx structure is created with no additional separation. This structure is expanded the margin by 5 mm on all sides. Then, using a Boolean operation, this structure is cropped from the Rectum 7 mm structure. This new structure is then cropped from the PTVx structure with an additional separation of 3 mm. Any instances of the Rectum Mid structure on CT slices where the PTVx structure did not exist were erased. These two structures Rectum Mid and Rectum 7 mm were created to move the 50% isodose line away from the posterior portion of the rectum. This is due to a study that showed an increased complication risk if the 50% isodose line falls outside the rectum.[25] Additionally, we want the 90% isodose line to fall at half the width posteriorly in the rectum and the 50% isodose line should fall at less than half the full width posteriorly in the rectum.

**TABLE 1.** Dose constraint limits adapted from RTOG protocol 0534

| Category | Dose Constraint |
|---|---|
| Bladder-CTV $D_{50}$ | 65 Gy |
| Bladder-CTV $D_{70}$ | 40 Gy |
| Rectum $D_{35}$ | 65 Gy |
| Rectum $D_{55}$ | 40 Gy |
| Right Femoral Head $D_{10}$ | 50 Gy |
| Left Femoral Head $D_{10}$ | 50 Gy |

CTV = Clinical Target Volume

## Results

For each category in Table 2, the mean, standard deviation of the mean (SDOM), the percent increase, the *p*-value, and the power of the statistical test are presented below. The percent increase is the increase (or decrease) when transitioning from the 6 MV mean to the corresponding 10 MV mean. A negative sign in the percent increase column indicates a percent decrease going from 6 MV to 10 MV. A *p*-value less than or equal to 0.05 is considered statistically significant.

Looking at Table 2, we see that all the values for the OAR dose constraint categories show a lower dose when using 10 MV in place of 6 MV. We also see more than 10% reduction in the mean dose for the categories Bladder-CTV $D_{70}$, Right Femoral Head $D_{10}$, and Left Femoral Head $D_{10}$. Note that the 6 MV and 10 MV results for all OAR dose constraint categories were much lower than the dose limits set by the RTOG 0534 protocol displayed in Table 1.

For the two categories CTV Percent Volume Covered by the 95% Isodose Line and PTV Percent Volume Covered by the 95% Isodose Line, we observed that 100% of the respective target structure received 95% of the prescription dose of 66.6 Gy for all ten patients for both 6 MV and 10 MV. Therefore, there is no standard deviation of the mean and no *p*-value to be found for these two categories.

Looking at the *p*-values less than or equal to 0.05 in Table 2, we see that the 10 MV results are statistically significant for the following categories: Bladder-CTV $D_{50}$, Bladder-CTV $D_{70}$, Rectum $D_{35}$, Rectum $D_{55}$, Right Femoral Head $D_{10}$, Left Femoral Head $D_{10}$, CTV Mean Dose, Body $V_5$, Conformity Index, and Integral Dose. The following categories had a *p*-value greater than 0.05, and therefore are not statistically significant: CTV Min Dose, CTV Max Dose, PTV Min Dose, PTV Max Dose, PTV Mean Dose, Global Max Dose, Arc 1 Monitor Units, and Arc 2 Monitor Units. It should be noted that for the number of MU for the first arc, eight of the ten

**TABLE 2.** Mean, standard deviation of the mean, percent increase, *p*-value, and power for both 6 MV and 10 MV are displayed

| Category | 6 MV Mean ± SDOM | 10 MV Mean ± SDOM | Percent Increase | *p*-value | Power |
|---|---|---|---|---|---|
| Bladder-CTV $D_{50}$ | 32.5 ± 4.3 Gy | 29.7 ± 3.9 Gy | -8.62% | 0.013 | 0.79 |
| Bladder-CTV $D_{70}$ | 18.5 ± 3.7 Gy | 16.2 ± 3.2 Gy | -12.4% | 0.011 | 0.81 |
| Rectum $D_{35}$ | 49.5 ± 3.3 Gy | 46.8 ± 3.9 Gy | -5.45% | $6.6 \times 10^{-3}$ | 0.88 |
| Rectum $D_{55}$ | 28.5 ± 2.7 Gy | 26.7 ± 2.7 Gy | -6.32% | 0.023 | 0.68 |
| Right Femoral Head $D_{10}$ | 34.12 ± 0.86 Gy | 29.80 ± 0.99 Gy | -12.66% | $1.2 \times 10^{-4}$ | 1.0 |
| Left Femoral Head $D_{10}$ | 32.74 ± 0.94 Gy | 29.4 ± 1.1 Gy | -10.20% | $8.3 \times 10^{-5}$ | 1.0 |
| CTV Min Dose | 65.53 ± 0.38 Gy | 65.29 ± 0.21 Gy | -0.3662% | 0.41 | 0.12 |
| CTV Max Dose | 71.01 ± 0.37 Gy | 70.53 ± 0.31 Gy | -0.6760% | 0.10 | 0.37 |
| CTV Mean Dose | 68.30 ± 0.29 Gy | 67.68 ± 0.27 Gy | -0.9078% | 0.019 | 0.72 |
| CTV Percent Volume Covered by the 95% Isodose Line | 100% | 100% | 0% | N/A | N/A |
| PTV Min Dose | 64.42 ± 0.29 Gy | 64.42 ± 0.29 Gy | 0% | 0.10 | 0.37 |
| PTV Max Dose | 71.78 ± 0.29 Gy | 71.76 ± 0.33 Gy | -0.02786% | 0.94 | 0.051 |
| PTV Mean Dose | 68.39 ± 0.38 Gy | 67.94 ± 0.28 Gy | -0.6580% | 0.063 | 0.47 |
| PTV Percent Volume Covered by the 95% Isodose Line | 100% | 100% | 0% | N/A | N/A |
| Body $V_5$ | (27.0 ± 1.0)% | (26.5 ± 1.0)% | -1.85% | $2.2 \times 10^{-3}$ | 0.96 |
| Global Max Dose | 71.80 ± 0.38 Gy | 71.76 ± 0.33 Gy | -0.05571% | 0.89 | 0.052 |
| Arc 1 Monitor Units | 325 ± 17 MU | 311.8 ± 9.8 MU | -4.06% | 0.41 | 0.12 |
| Arc 2 Monitor Units | 330 ± 15 MU | 312 ± 10 MU | -5.5% | 0.19 | 0.24 |
| Conformity Index | 1.127 ± 0.013 | 1.091 ± 0.015 | -3.194% | $6.8 \times 10^{-4}$ | 0.99 |
| Integral Dose | 207 ± 12 Gy·L | 191 ± 11 Gy·L | -7.73% | $1.1 \times 10^{-5}$ | 1.0 |

CTV = Clinical Target Volume; N/A = not applicable for that category; PTV = Planning Target Volume

cases had lower MU when using 10 MV, and for the number of MU for the second arc, eight of the ten cases had lower MU when using 10 MV. For the Global Max Dose, six of the ten cases had lower Global Max Dose when using 10 MV. Further analysis of our power results are presented in the Discussion section below.

## Discussion

Our results have shown that using 10 MV photons instead of 6 MV photons for irradiation of the prostate bed will result in statistically significant lower values for the OAR dose constraint categories, Body $V_5$, Conformity Index, and Integral Dose. We also observed that using 10 MV results in 95% of the prescription dose of 66.6 Gy covering 100% of the CTV and PTV volumes for all ten patients; this is the same coverage as using 6 MV for all ten patients. This is important because OAR dose sparing should not occur at the expense of tumor target coverage.

It should be noted that the mean results for both 6 MV and 10 MV plans were well below the dose constraints outlined in the RTOG 0534 protocol and posted in Table 1 above. RTOG 0534 was developed as a phase 3 trial for androgen deprivation with pelvic lymph node or prostate bed only radiation therapy after a prostatectomy. We used this protocol for our study because it is used at Roswell Park Cancer Institute for plan evaluation when using 6 MV for post-prostatectomy prostate bed irradiation.

For our study, we used a sample size of ten cases. Even though this is a small sample size, there is no minimum size requirement in using a paired Student t test. Research in the methodology of statistical testing has shown that a possible limitation for using a small sample size exists in the power of the statistical test that was performed.[26,27] However, it has also been shown that this limitation regarding small sample sizes does not exist for experiments where there is a large effect size present.[28] For our study, the null hypothesis is that for each category listed above in Table 2, the difference

between the respective means for 6 MV and 10 MV are 0. The alternative hypothesis is that there is a difference between the respective means for 6 MV and 10 MV. The probability of committing a Type II error is the probability of failing to reject a false null hypothesis, and is denoted by β. The probability of rejecting a false null hypothesis is known as the power of the statistical test, and is denoted by 1–β. Looking at our power results in Table 2, we see that for the categories where the *p*-values are statistically significant, there is a high probability that we will reject a false null hypothesis, and therefore will not commit a Type II error. Another issue is the possibility of committing a Type I error. The probability of committing a Type I error is the probability of rejecting a true null hypothesis, and is denoted by α. By setting $\alpha = 0.05$, and obtaining a *p*-value less than or equal to 0.05 means that there is a high probability (greater than or equal to 95%) that we will not commit a Type I error.

In making a comparison between the 6 MV and 10 MV plans used for this study, it should be noted that the 6 MV and 10 MV cases were created by different planners. The 6 MV cases were created by an experienced dosimetrist, while the 10 MV cases were created by a non-experienced planner. This can introduce some biases regarding the 10 MV plan outcomes. However, looking at the 10 MV results, we argue that if the same 6 MV planner had worked on the 10 MV plans, the same or better results could be obtained due to planner experience. The 6 MV plans were created with time constraints imposed by real-world clinical conditions; this was not the case for the 10 MV plans. However, it can be argued that 10 MV plans with the same or better outcomes could be created by an experienced dosimetrist using the same time constraints as the 6 MV plans.

Our results for OAR dose sparing contrast with other studies of IMRT treatment plans using higher photon beam energies for intact prostate where there is no improvement in dose reduction to OAR and no better Conformity Index.[9,11,13] Work done by Pirzkall *et al.* has shown that when the number of IMRT static fields are increased, the effects of using higher photon energy are downplayed.[13] This same study wondered if higher photon energies would play less of a role in rotational IMRT, *i.e.* VMAT. Studies performed by Pasler *et al.*[12] and Ost *et al.*[29] looked at VMAT planning for prostate cancer for ten and twelve patients, respectively. The study by Pasler *et al.* found that using photon energies of 10 MV and 15 MV versus 6 MV resulted in a statistically significant lower Integral Dose; however, monitor units were not investigated in that study. The study by Ost *et al.* found that using 18 MV instead of 6 MV resulted in statistically significant lower monitor units; however, Integral Dose was not investigated in that study.

Furthermore, a recent study by Mattes *et al.* using 6 MV and 10 MV with VMAT to treat intact prostate cancer also found a lower Conformity Index, lower Integral Dose, and lower monitor units, while having minimal dose sparing to the OAR.[30] However, that VMAT study purposely uses the same optimization constraints for both 6 MV and 10 MV treatment plans, thereby not allowing the optimizer to make full use of the 10 MV photons. It can be argued that using 10 MV may allow the optimizer in the Eclipse treatment planning system more leeway to shift more dose from the OAR. Therefore, setting higher dose constraints on the optimization structures may prove useful. In that same study, 10 MV resulted in a more than 16% decrease in maximum dose to the skin structure. While our work did not measure dose to the skin, the possibility of lower skin dose would be another benefit to using 10 MV photons due to the greater penetrating power and longer dose build-up of 10 MV. Skin sparing effects have been noted in a study by Chow *et al.* of prostate irradiation using IMRT.[31] This topic could be investigated in a future work.

For our study, most of the OAR dose constraint categories that exhibited the largest dose reduction of more than 10% were to the shallow OAR, *i.e.* the left and right femoral heads. It stands to reason that using 10 MV photons can result in large dose reductions to OAR that are shallowly located relative to the tumor target. Other cancer sites that one may wish to investigate should possess deep seated target volumes. This ensures that much of the dose is deposited into the target, and not to adjacent healthy tissue. Therefore, cancers located in the pelvic or abdominal regions should be investigated into whether using 10 MV photons provide similar benefits.

Another possible benefit for using 10 MV rather than 6 MV could be the reduced chance of a patient having a secondary cancer malignancy. Work done by Kry *et al.* has shown that the lifetime risk of developing a fatal secondary cancer is 39% higher when using 6 MV compared to 10 MV for IMRT.[32] It is possible that this finding carries over into VMAT when using 10 MV instead of 6 MV. A system that tracks future occurrences of cancer in patients treated with prostate bed irradiation may prove useful for future studies.

## Conclusions

In this retrospective study of treatment plans comparing 6 MV to 10 MV for post-prostatectomy irradiation of the prostate bed, we have shown that using 10 MV photons can result in statistically significant better outcomes for our OAR dose constraints, Body $V_5$, Conformity Index, and Integral Dose. We also have shown that 10 MV can be used in our treatment plans without compromising dose coverage to the CTV and PTV. In addition, neutron contamination from the linac head is not a major concern when choosing 10 MV over 6 MV. From these observations, it can be argued that using 10 MV rather than 6 MV can result in better treatment plans for patients undergoing prostate bed irradiation after a prostatectomy.

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