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Simultaneous Integrated Boost Plan Comparison between Static Intensity-Modulated Radiotherapy and Volumetric-Modulated Arc Therapy for Prostate Fossa and Lymph Node Irradiation

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Abstract

Purpose: The aim of this study was to evaluate the dosimetric differences between Intensity Modulated Radiation Therapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) in regard to target dose conformity, normal tissue and critical structure sparing for Simultaneous Integrated Boost (SIB) treatment plans.

Methods: Ten (n=10) previously treated patients were randomly selected from a pool of patients with high-risk adenocarcinoma of the prostate after laparoscopic radical prostatectomy. The target volumes were defined per RTOG 0534 protocol. The VMAT plans consisted of dual arcs using 6 MV. Nine evenly spaced co-planar beams were used for the IMRT plans. A total of 20 plans were generated; 10 in each technique. The pelvic nodes were treated to 45 Gy in 1.8 Gy daily fractions. The prostatic fossa was simultaneously treated to 62.5 Gy delivered in 2.5 Gy daily fractions. The goal was to deliver the prescription dose to cover 95% of the high dose Planning Target Volume (PTV 62.5). Parameters evaluated included the Conformity Index (CI) at the 100% isodose line, total Monitor Units (MU), critical organ dose, and Normal Tissue Integral Dose (NTID).

Results: Target volume conformity was shown to increase by 4.0% ($p<0.01$) for VMAT over IMRT when delivering SIB adjuvant radiation therapy for postoperative cancer patients. Additionally, normal tissue integral dose data suggest that the dose delivered to non-tumor tissue was lower for VMAT for the 30% ($p<0.01$), 40% ($p<0.01$), and 50% ($p<0.04$) isodose volumes.

Conclusion: For equivalent coverage, VMAT technique provided reduced normal tissue dose and better target conformity. Furthermore, VMAT reduced the MU usage resulting in shorter treatment delivery time.

Keywords: Prostatic fossa; Normal Tissue Integral Dose (NTID); Simultaneous Integrated Boost (SIB); Prostate cancer

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Introduction

Currently prostate cancer is the most common cancer among males in the United States. Based on the stage, the treatment options available to prostate cancer patients include surgery, radiation therapy, hormonal therapy, chemotherapy immunotherapy or a combination of these options. According to the American Cancer Society (ACS), the estimated new prostate cancer cases in 2019 will be 174,650, representing 27.2% of all cancers in men. A total of 31,620 deaths from prostate cancer are projected to occur in the United States in 2019 [1]. Currently, the accepted treatment options include radical prostatectomy, external-beam radiation therapy, brachytherapy, and watchful waiting [2]. Adjuvant radiation therapy is often recommended for high-risk features on surgical pathologic specimen for prostate cancer patients after laparoscopic radical prostatectomy [3]. However, during radiation, non-involved tissue might receive a substantial amount of dose, leading to increased risk of genitourinary and gastrointestinal toxicities as well as small risk of developing radiation-induced malignancies. Presently, modern modifications of treatment solutions deliver better coverage while sparing surrounding normal tissue [4].

Three Dimensional-Conformal Radiation Therapy (3DCRT) was the standard treatment planning technique in clinics around the world until the advent of Intensity Modulated Radiation Therapy (IMRT) in the last 1-2 decades [5]. The latter has been shown to deliver more conformed dose to the targeted treatment area, while providing better sparing of adjacent critical organs. Uysal et al. [6] concluded that IMRT is an effective definitive treatment tool for prostate cancer with improved critical organ sparing and excellent delivery of a more homogenous dose in target organs of the prostate and seminal vesicles. In recent years, the second generation of IMRT known as Volumetric Modulated Arc Therapy (VMAT) has become increasingly the technique of choice for treatment of high-risk prostatectomy patients. Compared to static beam IMRT, rotational VMAT is supposed to decrease the treatment delivery time with at least similar or even better plan quality [7].

In Simultaneous Integrated Boost (SIB) techniques, higher dose is delivered to the primary tumor without increasing the overall treatment delivery time [8]. Furthermore, SIB techniques have been shown to improve plan quality when compared to sequential techniques. In the delivery of SIB plans, the cumulative treatment fractionation is effectively reduced. However, the daily dose to the boost area is higher than normal in sequential treatments. In this study, it was hypothesized that in the delivery of SIB for prostatic fossa and lymph node treatments, VMAT may have superiority over IMRT in terms of both normal tissue integral dose and dose to Organs at Risk (OR).

There is a lack of published literature that examined the dosimetric advantages between VMAT and step-and-shoot IMRT with regard to Normal Tissue Integral Dose (NTID) in SIB delivered treatments for high-risk post prostatectomy patients. The aim of the study was to dosimetrically compare VMAT and IMRT in the delivery of SIB treatments for patients with high-risk adenocarcinoma of the prostate after laparoscopic radical prostatectomy. Specifically, to compare the abilities of the two techniques to spare the normal tissue despite the dose escalation to daily fractions of 2.5 Gy to the prostate bed was evaluated.

Methods and Materials

Patients

Ten (n=10) previously treated patients were randomly selected from a pool of patients with high-risk features of adenocarcinoma of the prostate after laparoscopic radical prostatectomy. All patients received pelvic lymphatic radiation. Based upon RTOG 0534 guidelines, all patients were simulated head-first in the supine position using a CT simulator (GE, Waukesha WI) with 2.5 mm slice thickness and 55 cm Field of View (FOV). The patients were immobilized on the CT table with the aid of a Vac-Lok bag (CIVCO, Iowa City IW). For comfort, the arms of the patients were placed on the chest holding a blue ring. To ensure setup reproducibility, volumetric daily Image Guided Radiation Therapy (IGRT) was used in the form of on-board kV cone-beam CT. IGRT has been shown to improve dose delivery by providing an opportunity to verify the consistency between the planned and actual treatment geometry, minimizing variations in daily setup [9].

Contouring

Target volumes were manually outlined in Velocity ver 3.0.1 fusion software (Varian Medical, Palo Alto CA) before they were exported to Pinnacle ver 9.6 (Philips Medical, Fitchburg WI) Treatment Planning System (TPS) for Organ at Risk (OAR) segmentation and planning [3]. The target volumes were defined per RTOG 0534 protocol [10]. The radiation oncologist outlined the Clinical Target Volumes (CTV) to include the prostatic fossa and the lymphatic nodes. The CTVs were expanded 6 mm posteriorly and 8 mm in all the other directions to form the Planning Target Volumes (PTV). The OAR contoured included the rectum, bladder, sigmoid, penile bulb, small bowel and femoral heads.

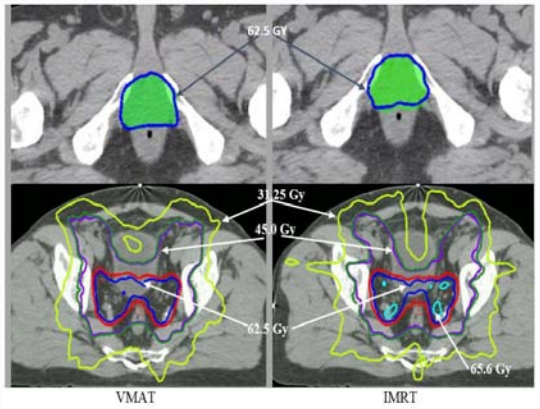

Figure 1: (Top) an axial CT slice of a sample patient showing the prescription isodose line (62.5 Gy) overlaid onto the PTV62.5 (color wash) for VMAT (left) and IMRT (right). (Bottom) An axial CT slice of a sample patient showing a sample treatment plan for VMAT (left) and IMRT (right).

Treatment planning

The prescribed dose to the pelvic nodes was 45 Gy (PTV 45) in 1.8 Gy daily fractions while the prostatic fossa was simultaneously boosted to 62.5 Gy (PTV 62.5) delivered in 2.5 Gy daily fractions. A total of 20 plans were generated-10 VMAT and 10 IMRT. All plans were created for a 6 MV 2100EX linear accelerator equipped with 120 multi-leaf collimator (Varian Medical, Palo Alto CA). In both planning techniques, the calculations were performed with a 3.0 mm isotropic dose grid resolution. VMAT plans consisted of two co-planar arcs with opposite rotation (clockwise and counterclockwise). The path length of each arc was 344° (8°-352°) with the collimator rotated 15° in the first arc and 90° in the counter-clockwise arc to avoid a tongue-and-groove effect. A gantry control point spacing of 4° was applied. Nine evenly spaced coplanar beams were used for the IMRT plans. Both techniques were based from a common isocenter that was placed at the geometrical center of the PTV45. The jaws of each field were extended 10 mm around the edge of PTV45 to compensate for the beam penumbra.

The plans were optimized with appropriate OAR constraints and priority weighting to create suitable plans that met the set criteria. The same constraints and dose requirements for the IMRT plans were also applied in the VMAT plans. In order to achieve the constraints of the small bowel, a secondary target (PTV Optimization) that excluded part of the bowel in the PTV was created. This target structure was used in the plan optimization only. The PTV goal for each plan was to deliver 95% of the prescription dose to cover 100% of the PTV volume, per both RTOG 0534 and the institutional protocols. The objectives used in our institution abide by those quantified in QUANTEC. For comparison purposes, all plans were normalized for 95% of PTV 62.5 to receive 100% of the prescription dose.

Plan comparisons

Plan comparisons were performed using dose Conformity Index

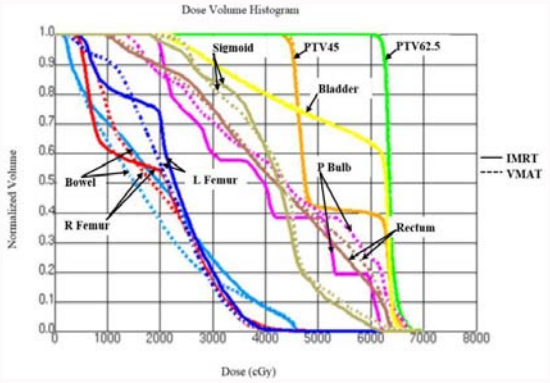

Figure 2: A sample, cumulative, normalized Dose Volume Histogram (DVH) for the CTV, PTV, small bowel, sigmoid, rectum, and right femoral head comparing VMAT (solid lines) and IMRT (dotted lines) for one of the patients.

(CI), Dose Volume Histograms (DVH), Monitor Units (MU), critical structure doses, and NTID. Additionally, the PTV D_{mean} (mean dose), PTV $D_{98\%}$, and PTV $D_{2\%}$ (the dose received by 98% and 2% of the PTV respectively) were evaluated. The isodose distribution of one of the cases is demonstrated in (Figure 1). A DVH for the CTV, PTV, rectum, sigmoid, small- bowel and femoral heads comparing VMAT and IMRT for one of the patients is demonstrated in (Figure 2). The degree of conformity of each treatment technique was evaluated by calculating the CI at the 100% isodose volume. CI is defined as follows:

$$CI_{100\%} = Volume\ of\ 100\%\ isodose\ line / PTV$$

Were the ratio of the volume of total tissue receiving prescription dose to the volume of PTV.

To calculate the NTID, the irradiated non-tumor tissue volume and the mean dose delivered were taken into account. In order to calculate the NTID values, volumes of structures generated from the 10%, 20%, 30%, 40%, 50%, 60% and 70% isodose lines for PTV 62.5 were obtained. The mean dose as well as the mean volume for each isodose structure for the ten patients was computed. NTID was calculated manually and defined as mean dose times the mean volume of the structure. To compare the delivery efficiency between the two techniques, the number of MU per fraction for each plan were recorded and evaluated. OAR doses were evaluated to gauge plan quality. Three critical structures were used (Bladder D_{mean}, V_{60}, and V_{35}; Rectum D_{mean}, V_{60}, and V_{35}; Sigmoid D_{max}). All the comparisons were performed using a paired two-tail t-test with a significance level of $p<0.05$.

Results

All the plans were normalized such that each PTV had a minimum coverage of 95% of the prescribed dose. The statistical dosimetric comparisons for MU and CI for the 20 plans were presented in (Table 1). The results demonstrated that there was a statistically significant difference in the mean CI values between the two techniques ($p<0.02$). A VMAT technique showed improvement in CI of 4.0% over IMRT. The results from the MU mean comparisons showed no statistically significant difference between VMAT and IMRT. Table 2 presented the comparisons for PTV D_{mean}, PTV $D_{98\%}$, and PTV $D_{2\%}$ for the two techniques. Equivalence between both PTV D_{mean} and PTV $D_{2\%}$ were observed ($p=0.27$ and $p=0.56$ respectively). However, there was a significant reduction of PTV $D_{98\%}$ dose ($p<0.02$) in the IMRT plans.

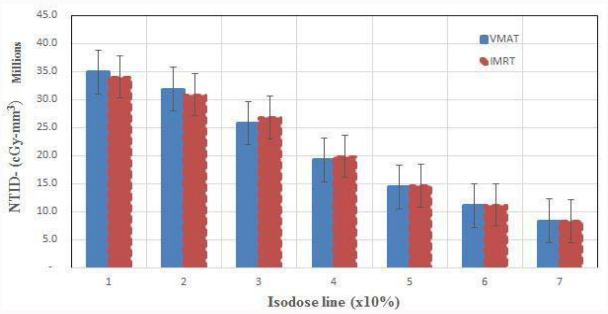

Figure 3: A graphical comparison of the normal tissue integral dose.

Table 1: Conformity index monitor unit parameters, and t-test comparisons between the two treatment techniques.

Parameter	VMAT	IMRT	t-test (p-value)
Conformity index			
Mean	1.02	0.99	0.02
Range	1.08 to 1.23	1.03 to 1.19	
MU per fraction			
Mean	901	959	0.11
Range	805 to 998	755 to 1073	

Table 2: PTV D_{mean}, PTV D98%, PTV D2%, and t-test comparisons between the two treatment techniques.

Parameter	VMAT	IMRT	t-test (p-value)
PTV D_{mean} (cGy)			
Mean	6405.9	9424.4	0.27
Range	6377.5 to 6462.6	6367 to 6517.5	
PTV $D_{98\%}$			
Mean	6199.8	6174.4	0.02
Range	6143 to 6237	6114 to 6230	
PTV $D_{2\%}$			
Mean	6603.6	6620.6	0.56
Range	6472 to 6724	6480 to 6781	

Table 3: Mean NTID in cGy-mm3 and t-test comparisons between the two treatment techniques.

Isodose line	VMAT	IMRT	t-test (p-value)
10%	34.89	33.00	0.06
20%	31.85	30.88	Not significant
30%	25.79	26.79	0.01
40%	19.27	19.84	0.01
50%	14.38	14.61	0.04
60%	11.08	11.18	0.06
70%	8.31	8.29	Not significant

NTID was evaluated by comparing the product of the mean volumes generated for 10%, 20%, 30%, 40%, 50%, 60% and 70% isodose lines and their mean doses. Table 3 listed a comparison of NTID. Whereas the 20% and 70% isodose lines showed no significant difference between the two techniques, there was significant decrease in NTID at the 30% ($p<0.01$), 40% ($p<0.01$), and 50% ($p<0.04$) isodose lines for VMAT plans. Overall, the OR dose comparisons showed no significant sparing differences between VMAT and IMRT. However, the highest percent difference favoring the VMAT plans was recorded

Table 4: Organs at Risk (OR) mean DVH parameters, and t-test com.

Parameter	VMAT	IMRT	% mean difference
Bladder			
$D_{mean\ (cGy)}$	5,569	5,596	-0.48
$V_{60\ (\%)}$	60.5	59.9	0.88
$V_{35\ (\%)}$	91.8	93.6	-1.98
Rectum			
$D_{mean\ (cGy)}$	3,999	4,115	-2.89
$V_{60\ (\%)}$	18.7	17.9	3.91
$V_{35\ (\%)}$	59.9	65.2	-8.88
Sigmoid			
$D_{max\ (cGy)}$	5,583	5,528	0.98

in the rectal mean and V_{35} doses at 3% and 9%, respectively.

Discussion

This study examined normal tissue sparing in VMAT treatments when compared to IMRT for radiation of 10 post-prostatectomy patients. Results in Table 1 demonstrate the VMAT technique provided superior plans in conformity compared to IMRT plans. The quality of VMAT plans is also supported by the tight isodose lines as presented in (Figure 1). This is further supported by the PTV $D_{98\%}$ comparison results that showed there is significant reduction of dose to the 98% of the PTV volume for the IMRT plans. However, the difference is small in absolute values. Delivery efficiency was found to be similar in the two techniques. Other studies have shown that VMAT plans generate fewer MU than IMRT plans. Recent reports have demonstrated that VMAT technique was able to reduce treatment time and doses to the OR as compared to static-gantry IMRT for the treatment of prostate alone, prostate plus seminal vesicles, and postoperative prostate bed [11-14]. Although the current study demonstrated that there is no statistically significant MU difference between the two techniques, an average for all ten patients showed that VMAT required 6.4% fewer monitor units than IMRT (901 *vs.* 959) for delivery of 2.5 Gy per fraction. In order to definitively demonstrate that VMAT allows better delivery efficiency, a larger patient sample for this study might be necessary. In addition, comparison between plans was done using three OR, namely: the bladder, rectum, and sigmoid. Table 4 presented the OR mean DVH parameters and percent difference comparisons. The results showed that both techniques achieved similar results with regard to critical structure sparing. However, in regard to the rectal dose, VMAT demonstrated a 3% advantage for the mean rectal dose and a 9% advantage for the V35 dose.

There is concern that high NTID as a result of multiple beam radiotherapy presents a potential risk to the patient of developing late occurrences of radiation-induced malignancies [15]. The large number of beamlets and MU generated in both VMAT and IMRT are believed to lead to an increase in NTID [16]. Table 3 presents the mean NTID and t-test comparisons between the two treatment techniques. The results suggest that between the 30% and 50% isodose lines, IMRT plans tend to deposit more doses to normal tissue. Figure 5 showed a graphical comparison of the NTID among the 10 patients. The greatest significant difference occurred at the 30% isodose line. Further research is necessary to validate these results.

Conclusion

This study compared VMAT *vs.* IMRT in the delivery of SIB adjuvant radiation therapy for high-risk prostatectomy patients. The study demonstrated that VMAT, when compared to static IMRT, provides overall better target dose conformity, reduced normal tissue dose and MU, for equivalent target coverage. The VMAT plans required an average of 6.4% less MU than the IMRT plans to deliver a daily dose of 2.5 Gy per fraction. Although VMAT produced more conformal plans, on average the DVHs demonstrated similar target coverage for both techniques. Further research is necessary to investigate why the NTID results suggest that the greatest significant difference occurred at the 30% isodose line.

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