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Reduced acute toxicity associated with the use of volumetric modulated arc therapy for the treatment of adenocarcinoma of the prostate

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Abstract

Purpose: Novel techniques to deliver intensity modulated radiation therapy (IMRT) have resulted in improved treatment efficiency and dosimetric endpoints. We aimed to compare acute gastrointestinal (GI) and genitourinary (GU) toxicity in patients treated for adenocarcinoma of the prostate (ACP) using volumetric modulated arc therapy (VMAT).

Methods and Materials: A total of 122 (71 IMRT and 51 VMAT) ACP patients treated from 2004 to 2011 with definitive external beam radiation therapy were analyzed. Dose-volume histogram endpoints (V40, V65, V70, and V75 of the bladder and rectum) were collected for each patient. Median follow-up for patients treated with VMAT was 269 days versus IMRT was 1121 days. Acute Common Toxicity Criteria for Adverse Events (CTCAE) GI and GU toxicity scores, obtained during each weekly treatment check, were compared across cohorts. The univariate (UV) association between the covariates and outcomes was assessed and multivariable (MV) cumulative logit models were fit for each outcome.

Results: Median patient age was 68 years and median prostate-specific antigen was 8.3. Both bladder and rectal V40, V65, V70, and V75 were all higher in the IMRT group versus the VMAT group (P b .05), which was likely influenced by larger planning target volumes in the IMRT group. The VMAT group had significantly lower rates of acute GU and acute GI CTCAE toxicity on UV association analysis. On MV analysis, VMAT remained independently associated with acute GU (odds ratio [OR], 0.18; 95% confidence interval [CI], 0.07−0.44; P b .001) and GI (OR, 0.16; 95% CI, 0.07−0.41; P b .001) toxicity.

Conclusions: VMAT appears to be independently associated with lower rates of acute GI and GU toxicity when compared with traditional IMRT. Further exploration of toxicity improvements associated with VMAT use in the definitive treatment of ACP is needed.

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Introduction

Adenocarcinoma of the prostate (ACP) is a very common malignancy, and as our population ages the incidence of ACP is likely to increase.[1] There are several options available for definitive treatment of ACP, one of which is external beam radiation therapy (EBRT).[2] As technology has advanced, the delivery of EBRT has moved beyond conventional 3-dimensional conformal radiation therapy (3DCRT) and into an era of highly conformal intensity modulated radiation therapy (IMRT). IMRT has improved outcomes by minimizing toxicity and increasing the delivered dose to the target volume.[3,4] Traditional IMRT is achieved using multiple fixed gantry positions and multileaf collimators that moved during the beam on time. This method results in increased number of monitor units, and significantly longer treatment times than 3DCRT.[5] In an attempt to improve the efficiency and quality of IMRT, this delivery modality was modified into an arc-based system known as intensity modulated arc therapy (IMAT). IMAT delivers IMRT over continuous arcs allowing more degrees of freedom, reduced dose to normal tissues, and shorter overall treatment times.[6] This delivery modality has been modified and improved since its conception into a similar system known as volumetric modulated arc therapy (VMAT).[7] Simultaneously with the evolution of IMRT and VMAT, image guided radiation therapy (IGRT) has substantially progressed over the past 10 years and has integrated computed tomographic (CT) imaging into treatment delivery.[8]

It has been shown in several prior studies[5,9–12] that VMAT can improve treatment efficiency in prostate cancer, along with improve dosimetric endpoints. Despite the simulated evidence of dose-volume histogram (DVH) improvements there are few publications examining the clinically measureable benefits (such as improvements in acute gastrointestinal [GI] or genitourinary [GU] toxicity) of this technology.

The initial hypothesis for this study asked whether improvements in dosimetric endpoints and improved treatment efficiency result in clinically measureable reductions in acute GI and GU toxicity. Furthermore, a recently published analysis[13] demonstrated that the use of VMAT in ACP treatment was associated with a reduction in prostate motion. If VMAT results in shorter overall treatment time (and consequently less intrafraction prostate movement), does this translate to reduced acute treatment toxicity independent of improvements in dosimetric endpoints? This hypothesis was also supported by other studies examining the dosimetric consequences of intrafraction prostate motion.[14] To date, despite the evidence demonstrating improvements in DVH measurements, there are little published data describing the clinically measureable benefits (such as improvements in acute GI or GU toxicity) of this technology.

We hypothesized that improvements in dosimetric endpoints and treatment efficiency associated with VMAT would result in clinically measureable reductions in acute GI and GU toxicity compared with IMRT. Accordingly, we designed and conducted a study to examine the acute GI and GU toxicity in a cohort of patients treated with VMAT compared with a cohort treated with conventional IMRT.

Methods and materials

Patients

The charts of 184 consecutive patients treated between the years 2004–2011 with definitive EBRT using either IMRT or VMAT in the Emory University Hospital Network were retrospectively reviewed. A gradual transition was made in the Emory University network of hospital systems from treating patients with traditional IMRT to VMAT from 2004 to 2011, which enabled this comparative analysis. Patients were excluded who had the following: (1) brachytherapy; (2) cryotherapy; (3) surgery as any component of their treatment; (4) patients receiving IMRT or VMAT for only a portion of their treatment (ie, IMRT or VMAT boost); and (5) patients who had less than 40 days of follow-up available; (6) patients who did not have complete acute GI and GU toxicity data available; or (7) those patients without detailed dosimetric data available for review. This resulted in 122 (71 IMRT and 51 VMAT) ACP patients who met the final study inclusion criteria.

Simulation CT scans were done in the supine position with either a custom immobilization device consisting of a Vac-Lok pelvic cushion (Civco Medical Solutions, Kalona, IA) or no immobilization device, depending on the treating physician. The CT simulation data sets were used to design the treatment plans for each of the patients with either a VMAT or IMRT technique. Some patients were treated with either gold marker fiducials or Calypso Beacons (Calypso, Seattle, WA). All patients not treated with Calypso had on-board imaging done daily. The prostate, seminal vesicles, pelvic lymph nodes, and normal structures were manually contoured on the planning CT using Radiation Therapy Oncology Group guidelines.[15]

The initial clinical target volume (CTV1) was defined as the prostate, seminal vesicles, and pelvic lymph nodes (when treated). This CTV1 was expanded by a range of margins of 0.3–1 cm to define the planning target volume (PTV1), which was treated to 45.0–50.4 Gy in 1.8 Gy per fraction. This was followed by a boost treatment to the prostate alone to a total of 25.2–36 Gy; this resulted in cumulative RT doses ranging between 70 and 81 Gy. The vast majority of patients were treated with conventionally fractionated RT consisting of 1.8 Gy per fraction. A total of 5 patients in the VMAT cohort were treated with hypofractionated RT to the prostate alone; this consisted of 70 Gy over 28 fractions. The VMAT plans were designed using the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA). A Varian 23EX linear accelerator (Varian Medical Systems) was used to deliver the VMAT treatment plan, which was commercially referred to as RapidArc treatment. This technique has been previously described.[7] Either a single or double coplanar arc treatment plan was used. The Eclipse treatment planning system was also used for the IMRT treatment planning. This planning system uses an inverse planning algorithm for creating segmented multileaf collimator patterns that are delivered using the sliding-windows dynamic multileaf collimator delivery technique. Patients were treated with either 5-field or 7-field IMRT treatment plans.

Hormone therapy was typically administered for patients with adverse prognostic factors and consisted of a combination of testosterone receptor antagonist (flutamide or bicalutamide) and a GnRH agonist (leuprolide or goserelin); duration of hormone therapy ranged from 6

months to 2 years. The presence or absence of hormone therapy use was known for each patient included in the study.

Acute GI and GU toxicity scores were also collected from the individual weekly treatment check notes, charted according to Common Terminology Criteria for Adverse Events (CTCAE, version 3.0)[16] grading. These scores were compared across cohorts. The CTCAE acute toxicity scores are part of the standard weekly treatment check notes and follow-up notes at Emory University and were not retrospectively assigned. In addition the V40, V65, V70, and V75 DVH parameters for each of the patients were collected from the individual treatment plans. All toxicity assessments included in the analysis took place during treatment or at the first 1 month of follow-up visit. No toxicity scores that occurred beyond the 1-month follow-up were included in the analysis.

Statistical analysis

Statistical analysis was conducted using SAS, version 9.3 (SAS Institute, Cary, NC). Univariate (UV) associations between the covariates and treatment, and covariates and toxicity outcomes were assessed using the χ^2 or the Fisher exact test for categoric covariates, depending on sample sizes; and analysis of variance for numeric covariates. Multivariable cumulative logit models were fit for each outcome. Treatment, PTV, region treated, V40, V65, and V70 (either rectum or bladder as appropriate depending on the outcome), were forced in the models. The remaining covariates, race, T stage, Gleason score, hormone use, localization, MRI, length of follow-up, age, prostate specific antigen (PSA), and dose, were entered subject to a backward variable selection method with an alpha = .20 removal criteria. Height, weight, and prostate volume were excluded from the models due to the large number of missing values. Risk group was excluded as it was based on T stage, PSA, and Gleason score. V75 could not be included in the models due to the high correlation with V70 resulting in high multicollinearity. The correlation between V70 and V75 for the bladder was 0.95 (P b .0001) and for the rectum was .91 (P b .0001).

Results

The patient characteristics can be seen in Table 1. The median follow-up for patients treated with VMAT was 269 days and for those treated with IMRT was 1121 days. The use of IGRT, including both gold seeds and Calypso localization, was more frequent in patients treated with VMAT. Additionally, mean follow-up time, utilization of MRI, V40, V65, V70, and V75 of the rectum and bladder were statistically different between the cohorts. The UV associations of several treatment factors and the acute toxicity endpoints can be seen in Table 2. Several UV associations with acute GI and GU toxicity were insignificant and were not reported in Table 2. Those nonsignificant covariates consisted of race, Gleason score, hormone therapy use, age, height, weight, prostate volume, PSA, and prescribed RT dose. It can be seen in Table 2 that on UV analysis, treatment modality with either VMAT or IMRT, T stage, region treated, and MRI use all had significant associations with either acute GI or GU toxicity. Treatment modality used had a significant association with both acute GI and GU toxicity with VMAT having significantly lower rates of both. The results of the multivariate (MV) analysis for acute GU toxicity can be seen in Table 3. The

only factor that was found to be significantly associated with acute GU toxicity on MV analysis was the treatment modality (either IMRT or VMAT). Notably, the IMRT treatment modality was associated with higher acute GU toxicity, independent of the V40, V65, and V70 for the bladder. Additionally, the results of the MV analysis for acute GI toxicity can be seen in Table 4. As illustrated in Table 4, the IMRT treatment modality was independently associated with higher acute GI toxicity.

Discussion

As technology advances for the delivery of EBRT, it is important that the perceived benefits of this technology are confirmed using meaningful clinical endpoints. VMAT has been shown in devoted dosimetric studies to deliver lower RT doses to the bladder and rectum, which is consistent with our results.[5,9–12] The intent of this series was to examine toxicity differences associated with VMAT rather than perform another dosimetric comparison of the VMAT modality with IMRT. Furthermore, a robust dosimetric study would be difficult in this cohort given differences in IMRT and VMAT PTV volumes. Unique to this analysis is a statistically significant reduction in acute GI and GU toxicity associated with the use of VMAT as compared with IMRT.

During the early evaluation of IMRT use for the definitive treatment of ACP, several publications focused on the measureable acute toxicity advantages of IMRT.[17,18] As VMAT gains additional prevalence in the definitive management of ACP, there is a growing need for the evaluation of its measureable clinical benefits, including acute GI and GU toxicity.

Overall, the improvements in dosimetric endpoints in our series are similar to those that have previously been published, with some exceptions. A recent series by Wolff et al[5] demonstrated that the use of VMAT reduced the mean dose to the rectum by approximately 3.0% to 7.5%, which is similar to the dose reduction seen for our mean V40 (6.3%) and mean V65 (6.59%) dosimetric endpoints. A second series by Aznar et al[9] demonstrated a reduction in the V50 of the rectum of approximately 10% to 11%, which is slightly higher than the dose reduction we have demonstrated for the V40 and V65. Furthermore, Ost et al[11] demonstrated a range of improvements in dosimetric measurements to the rectum, with the V65 falling between 8% and 14%. Notably, the average improvement in the V40s seen in the Ost et al series is higher than the VMAT dose reduction demonstrated in the current series. Additionally it should be noted that in the series by Ost et al there was not a dosimetric improvement seen to the bladder when comparing 7-field IMRT with VMAT, which is inconsistent with the current series. It is likely that, in the current series, the differences in the total PTV volume between the IMRT and VMAT cohorts contributed to these conflicting dosimetric findings. The dosimetric improvements demonstrated in the current series cannot be attributed to VMAT alone given the differences in PTV volume.

An important question remains. Can a reduction in the total PTV volume and dose to bladder or rectum of 6% single handedly explain the differences in the acute toxicity? Several historic dosimetric studies comparing 3DCRT and IMRT have shown a large range in the reduction in mean dose to the rectum of approximately 20% to 40% when IMRT was used in place of 3DCRT.[5,19] This dosimetric improvement is substantially higher

than published dosimetric improvements measured with the use of VMAT in place of IMRT.[5,12] This reduction is also considerably higher than the dose reductions presented in the current series. The acute toxicity benefits of IMRT versus 3DCRT are similar in magnitude to those demonstrated in the current series; therefore, it appears apparent that the improvements in acute GI and GU toxicity with VMAT may be attributable to more than dosimetric improvements alone.[17] Furthermore, the differences in PTV volume between the cohorts should not be underestimated and may have contributed to the measured toxicity differences; however, it is unclear if this difference is enough to explain the substantial toxicity improvements seen with VMAT.

In an attempt to answer this question, the PTV volumes and dosimetric improvements were included in the MV analysis and the results support a contributing factor beyond these differences. It can be seen that VMAT emerges as a highly statistically significant predictor of acute GI and GU toxicity. Treatment with VMAT appears to be resulting in some reduction in acute toxicity independent of reduced dose to the bladder, rectum, and smaller PTVs. Numerous other variables were included and analyzed when creating the MV analysis including MRI use. However, the use of VMAT remained independently associated with reduced toxicity. Furthermore, several interesting findings emerge in our analysis outside of acute toxicity improvements associated with the use of VMAT. We have confirmed that MRI use appears to be associated with improvements in acute toxicity, which has been previously reported.[20] This finding is likely secondary to reduced margins associated with those patients' treatment plans as this toxicity difference did not remain significant independent of dosimetric endpoints on the MV analysis.

It is well established that the average treatment times for patients with VMAT are significantly shorter than with IMRT.[6,11,13] In some series,[5,10] the demonstrated difference has been up to approximately 8 minutes, with treatments delivered in less than half the time using VMAT compared with IMRT. Furthermore, there is evidence in multiple disease sites (including ACP) that intrafraction movement increases as the treatment time is prolonged.[13,14] Given this fact, it would stand to reason that the prostate and normal tissues' intrafraction movement increase when patients are treated with IMRT as compared with VMAT. This finding has been specifically confirmed in a series by Shelton et al[13] in which the use of VMAT was demonstrated to substantially reduce intrafraction prostate motion. The impact of this additional movement on the dose to normal tissues (including the bladder and rectum) is more difficult to model and is poorly understood.[14] We therefore hypothesize that some of the toxicity differences observed in this analysis could be secondary to differences in normal organ movement.

There are several limitations of the current series that merit discussion. Important statistically significant differences between the treatment groups existed (Table 1). We have attempted to examine each of these differences and account for them whenever possible. It should also be noted that there exists the possibility for confounding variables that are not accounted for in the analysis. An obvious example of this can be seen in Table 2 with the "region treated variable." There exists a paradoxical relationship between acute toxicity and the region treated, with the large treatment area having a small, albeit statistically significant, reduction in acute GU toxicity. Given that pelvic nodal RT is often controversial, it tends

to be preferentially administered by either a select institution or physician with the Emory University network of hospitals. It is likely that this bias was not accounted for, which introduced this paradoxical relationship. It is unlikely that a bias was present that influenced the toxicity comparison of VMAT versus IMRT as there was nearly uniform adoption of the VMAT system for treating prostate cancer in the Emory University network of hospitals after 2009. Furthermore, there are conflicting results regarding the dosimetric improvements in this series as compared with others, which is likely attributable to differences in PTV volumes among the cohorts. Finally, the overall number of patients included in this series is relatively small and this analysis requires validation in larger cohorts.

Conclusions

Meaningful clinical endpoints are essential for validating the benefits of any new technology. We have demonstrated, in a cohort of 122 patients, a significant improvement in acute GU and GI CTCAE toxicity endpoints associated with the use of VMAT for the definitive treatment of ACP. Interestingly, VMAT emerged on MV analysis as a predictor of acute GU and GI toxicity independent of improvements in dosimetric endpoints, or other variables known to predict acute toxicity. This hypothesis generating finding suggests that the improved treatment efficiency of VMAT could potentially contribute to the reduction in acute toxicity observed in our series. However, these findings require further validation in larger patient cohorts. Finally, as longer follow-up of the VMAT patients is accumulated, further analysis of our data will be necessary to evaluate differences in late toxicity endpoints.

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Table 1

Patient characteristics

Demographics	All patients N = 122 (%)	IMRT n = 71 (%)	VMAT n = 51 (%)	*P* value[a,b]
Age (y), mean (range)	68 (52–82)	67	68	.773[a]
Race				.624[a]
White	63 (52)	38 (54)	25 (49)	
Other	59 (48)	33 (47)	26 (51)	
Height (cm), mean (range)	178 (161–194)	179 (161–194)	177 (165.1–188)	.402[a]
Weight (kg), mean (range)	91 (58–127)	91 (61.8–125.4)	92 (57.8–126.8)	.800[a]
Prostate volume (cc), mean (range)	44 (13–105)	46 (12.5–105)	43 (19.5–85)	.637[a]
Disease characteristics				
PSA, mean (range)	12 (1–109)	11 (1.01–66.1)	13 (1.53–108.7)	.417[a]
T-stage				
T1	78 (64)	50 (70)	28 (55)	.078[a]
T2/T3	44 (36)	21 (30)	23 (45)	
Gleason score				.053[a]
6	24 (20)	19 (27)	5 (10)	
7	67 (55)	34 (48)	33 (65)	
8+	31 (25)	18 (25)	13 (25)	
Risk group				.05[a]
Low	15 (12)	13 (18)	2 (4)	
Intermediate	64 (53)	36 (51)	28 (55)	
High	43 (35)	22 (31)	21 (41)	
Treatment characteristics				
Hormone use				.298[a]
Yes	65 (53)	35 (49)	30 (59)	
No	57 (47)	36 (51)	21 (41)	
Region treated				.139[a]

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Demographics	All patients N = 122 (%)	IMRT n = 71 (%)	VMAT n = 51 (%)	*P* value[a,b]
Prostate only	74 (61)	47 (66)	27 (53)	
Prostate + LNs	48 (39)	24 (34)	24 (47)	
Localization				< .001[b]
Daily OBI	89 (73)	61 (86)	28 (55)	
Gold seeds	25 (21)	9 (13)	16 (31)	
Calypso	8 (7)	1 (1)	7 (14)	
MRI used for RT planning				< .001[a]
No	90 (74)	65 (92)	25 (49)	
Yes	32 (26)	6 (8)	26 (51)	
Prescribed RT dose (Gy),				.097[a]
mean (range)	77.74 (70–81)	78.06 (75.6–81)	77.29 (70–79.2)	
Dose per fraction (Gy)				.011[b]
1.8	117 (96)	71 (100)	46 (90)	
>1.8	5 (4)	0 (0)	5 (10)	
PTV volume (cc),				<.001[a]
mean (range)	210 (75.47–420)	238.5 (117.2–420.4)	170.11 (75.5–306.5)	
V40 rectum (%), mean	54.45	57.09	50.77	.007[a]
V65 rectum (%), mean	19.89	23.67	14.62	<.001[a]
V70 rectum (%), mean	13.74	15.94	10.68	<.001[a]
V75 rectum (%), mean	8.83	10.44	6.59	<.001[a]
V40 bladder (%), mean	56.63	59.8	52.2	.034[a]
V65 bladder (%), mean	25.23	30.15	18.38	<.001[a]
V70 bladder (%), mean	19.11	22.53	14.34	<.001[a]
V75 bladder (%), mean	14.35	17.3	10.25	<.001[a]
Follow-up (days), mean	814	1167	324	<.001[a]

IMRT, intensity modulated radiation therapy; LN, lymph nodes; MRI, magnetic resonance imaging; OBI, on-board imaging; PSA, prostate specific antigen; PTV, planning target volume; RT, radiation therapy; VMAT, volumetric modulated arc therapy.

[a] *P* value was calculated by analysis of variance for numeric covariates and the χ^2 test for categoric co-covariates.

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[b] P value was calculated by the Fisher exact test.

Table 2

Univariate associations with acute toxicity

Covariate	Acute GU			*P* value[a,b]	Acute GI			*P* value[a,b]
	0 n = 22 (%)	**1 n = 40 (%)**	**2 n = 60 (%)**		**0 n = 44 (%)**	**1 n = 39 (%)**	**2 n = 39 (%)**	
Treatment				<.001[a]				<.001[a]
IMRT	6 (9)	18 (25)	47 (66)		13 (18.3)	26 (36.6)	32 (45.1)	
VMAT	16 (31)	22 (43)	13 (25)		31 (60.8)	13 (25.5)	7 (13.7)	
T stage				.036[a]				.457[a]
T1	9 (11.5)	26 (33.4)	43 (55.1)		25 (32)	27 (34.6)	26 (33.4)	
T2/T3	13 (29.5)	14 (31.8)	17 (38.6)		19 (43.2)	12 (27.4)	13 (29.6)	
Region treated				.006[a]				.787[a]
Prostate only	7 (9.5)	29 (39.2)	38 (51.4)		25 (33.8)	25 (33.8)	24 (32.4)	
Prostate + LNs	15 (31)	11 (22.9)	22 (45.8)		19 (39.6)	14 (29.2)	15 (31.3)	
Risk group				.434[b]				.905[b]
Low	1 (6.7)	4 (26.7)	10 (66.7)		5 (33.3)	5 (33.3)	5 (33.3)	
Intermediate	10 (15.6)	23 (35.9)	31 (48.4)		21 (32.8)	21 (32.8)	22 (34.4)	
High	11 (25.6)	13 (30.2)	19 (44.2)		18 (41.9)	13 (30.2)	12 (27.9)	
MRI use				.003[a]				.049[a]
No	17 (18.9)	22 (24.4)	51 (56.7)		28 (31.1)	28 (31.1)	34 (37.8)	
Yes	5 (15.6)	18 (56.3)	9 (28.13)		16 (50)	11 (34.38)	5 (15.6)	
PTV volume (cc),				.308[a]				.204[a]
mean	187.8	216.8	213.4		193.8	220.5	217.5	
Dose per fraction (Gy)				.322[b]				.620[b]
1.8	21 (17.95)	37 (31.62)	59 (50.43)		41 (35.0)	38 (32.5)	38 (32.5)	
>1.8	1 (20)	3 (60)	1 (20)		3 (60.0)	1 (20)	1 (20)	
Localization				.466[b]				.106[b]
None	18 (20.2)	25 (28.1)	46 (51.7)		28 (31.5)	27 (30.3)	34 (38.2)	
Gold seeds	3 (12)	11 (44)	11 (44)		13 (52)	9 (36)	3 (12)	
Calypso	1 (12.5)	4 (50)	3 (37.5)		3 (38)	3 (38)	2 (25)	

Covariate	Acute GU			*P* value[a,b]	Acute GI			*P* value[a,b]
	0 **n = 22 (%)**	**1** **n = 40 (%)**	**2** **n = 60 (%)**		**0** **n = 44 (%)**	**1** **n = 39 (%)**	**2** **n = 39 (%)**	
Prescribed RT dose (Gy),				.119				.193[a]
mean	77.01	77.45	78.19		77.38	77.53	78.34	
V40 bladder (%),				.461[a]	N/A	N/A	N/A	
mean	54.84	54.23	58.87					
V65 bladder (%),				.077[a]	N/A	N/A	N/A	
mean	19.01	24.07	28.28					
V70 bladder (%),				.179[a]	N/A	N/A	N/A	
mean	14.83	19.85	20.18					
V75 bladder (%),				.163[a]	N/A	N/A	N/A	
mean	10.94	14.11	15.77					
V40 rectum (%),	N/A	N/A	N/A					.059[a]
mean					51.0	55.17	57.62	
V65 rectum (%),	N/A	N/A	N/A					.072[a]
mean					16.34	21.08	22.59	
V70 rectum (%),	N/A	N/A	N/A					.431[a]
mean					12.7	14.75	13.9	
V75 rectum (%),	N/A	N/A	N/A					.736[a]
mean					8.31	9.23	9.03	

GI, gastrointestinal; GU, genitourinary; IMRT, intensity modulated radiation therapy; MRI, magnetic resonance imaging; N/A, not applicable; PTV, planning target volume; RT, radiation therapy; VMAT, volumetric modulated arc therapy.

[a]The *P* value was calculated by analysis of variance for numeric covariates and the χ^2 test for categoric co-covariates.

[b]The *P* value was calculated by the Fisher exact test.

Table 3

Multivariate analysis predicting acute genitourinary toxicity (n = 122)

Covariate	OR	95% CI	OR *P* value[a]
Treatment			
VMAT	0.18	0.07–0.44	<.001
IMRT (ref)	—	—	—
V40 bladder	1.00	0.97–1.03	.934
V65 bladder	1.05	1.00–1.10	.076
V70 bladder	0.96	0.90–1.01	.135
Region treated			
Prostate + LNs	0.49	0.18–1.34	.166
Prostate only (ref)	—	—	—
T stage			
T1	1.91	0.86–4.27	.113
T2/3 (ref)	—	—	—
Gleason score:			
6	0.29	0.08–1.10	.069
7	0.38	0.13–1.08	.07
8 + (ref)	—	—	—
Prescribed RT dose (Gy)	1.14	0.96–1.34	.131
PTV volume (cc)	1.00	0.99–1.00	.217

CI, confidence interval; IMRT, intensity modulated radiation therapy; LNs, lymph nodes; OR, odds ratio; ref, reference; PTV, planning target volume; RT, radiation therapy; VMAT, volumetric modulated arc therapy.

[a]The probability of having more toxicity is modeled.

Table 4

Multivariate analysis predicting acute gastrointestinal toxicity (n = 122)

Covariate	OR	95% CI	OR *P* value[a]
Treatment			
VMAT	0.16	0.07–0.41	<.001
IMRT (ref)	—	—	—
V40 rectum	1.03	0.99–1.08	.108
V65 rectum	1.02	0.97–1.07	.462
V70 rectum	0.93	0.86–1.00	.050
Region treated			
Prostate + LNs	0.93	0.43–2.02	.863
Prostate only (ref)	—	—	—
Localization			
Calypso	1.89	0.43–8.29	.398
Gold	0.47	0.18–1.20	.113
Daily OBI (ref)	—	—	—
Prescribed RT dose (Gy)	1.12	0.96–1.30	.147
PTV volume (cc)	1.00	0.99–1.01	.956

CI, confidence interval; IMRT, intensity modulated radiation therapy; LNs, lymph nodes; OBI, on-board imaging; OR, odds ratio; RT, radiation therapy; VMAT, volumetric modulated arc therapy.

[a]The probability of having more toxicity is modeled.