Hypofractionated Versus Standard Fractionated Proton-beam Therapy for Low-risk Prostate Cancer

Interim Results of a Randomized Trial PCG GU 002

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Objective: To identify differences in terms of quality of life, the American Urological Association Symptom Index (AUA), or adverse events (AEs) among patients with prostate cancer treated with either standard fractionation or hypofractionation proton-beam therapy.

Materials and Methods: Patients were prospectively randomized to receive 38 Gy relative biological effectiveness (RBE) in 5 treatments (n = 49) or 79.2 Gy RBE in 44 treatments (n = 33). All patients had low-risk prostate cancer and were treated with proton therapy using fiducial markers and daily image guidance.

Results: Median follow-up for both groups was 18 months; 33 patients had follow-up of 2 years or longer. Baseline median (range) AUA was 4.7 (0 to 13) for the 38 Gy RBE arm and 4.8 (0 to 17) for the 79.2 Gy RBE arm. We observed no difference between the groups regarding the Expanded Prostate Index Composite urinary, bowel, or sexual function scores at 3, 6, 12, 18, or 24 months after treatment. The only significant difference was the AUA score at 12 months (8 for the 38 Gy RBE arm vs. 5 for the 79.2 Gy RBE arm; $P = 0.04$); AUA scores otherwise were similar between groups. No grade 3 or higher AEs occurred in either arm.

Conclusions: Patients treated with proton therapy in this randomized trial tolerated treatment well, with excellent quality-of-life scores, persistent low AUA, and no grade 3 or higher AEs on either arm. We showed no apparent clinical difference in outcomes with hypofractionated proton-beam therapy compared with standard fractionation on the basis of this interim analysis.

Key Words: adverse events, EPIC, outcomes, stereotactic body radiation therapy, toxicity

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Different approaches are used in the treatment of low-risk prostate cancer.[1–5] For patients undergoing image-guided proton radiation or intensity-modulated radiation therapy with standard doses, daily treatments for 8 to 9 weeks are typical. However, patients who are ideal candidates for external radiation may choose alternative modalities with shorter treatment times. Proton therapy, another treatment approach, uses particles to deliver high doses of radiation with high accuracy to the tumor and low doses to the surrounding healthy tissue; treatment duration is 1 to 2 weeks.

The prostate is a mobile organ in the pelvis. It is subject to movement with respect to pelvic bones due to changes in rectal distention, bladder filling, and abdominal pressure. Multiple studies have shown movements exceeding 5 mm in >15% of cases, especially with a full rectum.[6–8] The use of prostate fiducial markers improves prostate positioning and decreases necessary margins for treatment. Image guidance approaches improve prostate targeting, thereby improving cancer control rates while decreasing toxicity. The rationale for the image-guidance approach for proton therapy has been reviewed.[8,9] Previous literature provides the framework for the margins used in this protocol.

We used a protocol that combines a hypofractionated approach that benefits from the low α/β ratio of prostate cancer and the conformality achieved with proton therapy to deliver an abbreviated course of therapy for patients with low-risk prostate cancer.[1,3,4,10,11] We hypothesized that the hypofractionated and standard fractionated image-guided proton therapy regimens would result in similarly low adverse event (AE) rates. The results reported here correspond to the first interim analysis. The main objective was to evaluate initial rectal and bladder toxicity and quality-of-life (QOL) metrics.

MATERIALS AND METHODS

This study was approved by the Western Institutional Review Board (protocol 20101536). All patients provided written, informed consent. This trial was registered at Clinicaltrials.gov (NCT01230866).

Study Power

We defined estimates for our trial design on the basis of previously reported data regarding freedom from treatment failure for patients with low-risk prostate cancer treated with standard fractionation or hypofractionation. We expected that a sample size of 174 patients would be able to determine equivalence in both arms in terms of freedom from treatment failure at 5 years. We anticipated that the difference between study arms would be 10% or less. This trial makes use of blocked stratified sampling, using a total of 16 possible strata, with 8 strata per study arm. This study was designed to detect noninferiority of 10% or less between the 2 study arms, with a significance level of $\alpha = 0.0417$ and a statistical power of 0.80.

Patients

Patients were enrolled from July 18, 2011, through August 20, 2014. They were stratified by preenrollment values

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for prostate-specific antigen (<4 vs. ≥4 to <10 ng/mL), number of positive needle biopsy cores (1 to 4 vs. ≥5), and cancer stage (T1 vs. T2). All patients were required to have a Gleason score of 6, cancer stage T1 to T2, and prostate-specific antigen levels <10 ng/mL.

We limited inclusion to patients with an American Urological Association Symptom Index (AUA) score of 17 or less to establish a more homogenous cohort with only mild to moderate urinary bother. The AUA scale has 7 questions that measure different aspects of the urinary process. Each question has a scale from 0 to 5 (maximum total score, 35 points), with higher scores indicating worsening urinary symptoms. Although prostate stereotactic body radiation therapy can be used to treat patients with higher AUA scores, we defined our cohort in this manner to decrease heterogeneity and better define differences between study arms.

Radiotherapy

Briefly, planning for proton therapy involved the fusion of 1.5 to 3 T magnetic resonance images to computed tomographic scan images. Patients were in the supine position. The clinical target volume included the prostate only. The planning target volumes were 2 mm posteriorly and 3 mm elsewhere. The proton planning target volume was constructed to include 5 mm in the beam direction distally and proximally. Proton-specific expansion was used to accommodate changes in dose deposition and improve treatment delivery robustness. The proton beams were oriented laterally left and right and the expansions accordingly were in the lateral direction only. Because changes in prostate position are seen between the computed tomographic and magnetic resonance images, soft tissue registration of the T2 turbo spin-echo images and the computed tomographic images was performed. Excellent agreement could be achieved for most cases, even with differences in normal tissue anatomy (Fig. 1).

Patients were treated with either 79.2 Gy relative biological effectiveness (RBE) or 38 Gy RBE. All patients had the same volume definitions, margins, immobilization, and setup. Dose volume constraints were proportionally scaled down for the 38 Gy RBE arm. We assumed it was safe to define the α/β ratio for healthy tissue on the basis of the available literature and to define the dose such that rectal isotoxicity was achieved between the 2 arms.[12–14] In this manner, 38 Gy RBE in 5 treatments was equivalent to 79.2 Gy RBE in 44 treatments for a rectal α/β ratio of 3.5 Gy (Table 1). The dose to the target was 38 Gy RBE. If the α/β ratio of the prostate was lower than 3.5 Gy RBE, the resulting biological equivalent dose would be higher than 79.2 Gy RBE in 44 treatments.

Daily kV imaging with coil gold fiducials was performed before delivery of each beam. Rectal balloons were used for all cases. Margins were determined on the basis of prior publications,[8,15] which indicated that margins of about 2 mm are necessary when using a rectal balloon and taking images before beam delivery.

A prepopulated block randomization sheet was used for study arm assignment by the protocol research office. The randomized patient allocation scheme was 1:1 for the first 37 patients; subsequently, it was adjusted to 2:1 by request of the collaborating institutions. The randomized patient allocation scheme was 2:1 favoring the 38 Gy RBE arm.

Toxicity Assessment

Protocol toxicity was measured using the Common Terminology Criteria for Adverse Events (CTCAE), version 4.0. Statistical calculations for toxicity used a double-sided $\alpha < 0.05$ threshold for significance. AEs were evaluated for 3 years.

The use of CTCAE grading for urinary toxicity might be misleading. Patients are commonly prescribed tamsulosin as a measure to decrease urinary frequency and urgency, but most patients will not have urinary retention or any threatening complication if the medication is not used. Other publications have modified the CTCAE grading of grade 2 AEs to accommodate this inconsistency.[4] Here, we used the strictest definition, that is, any use of a prescription or over-the-counter medication over baseline was considered a grade 2 AE.

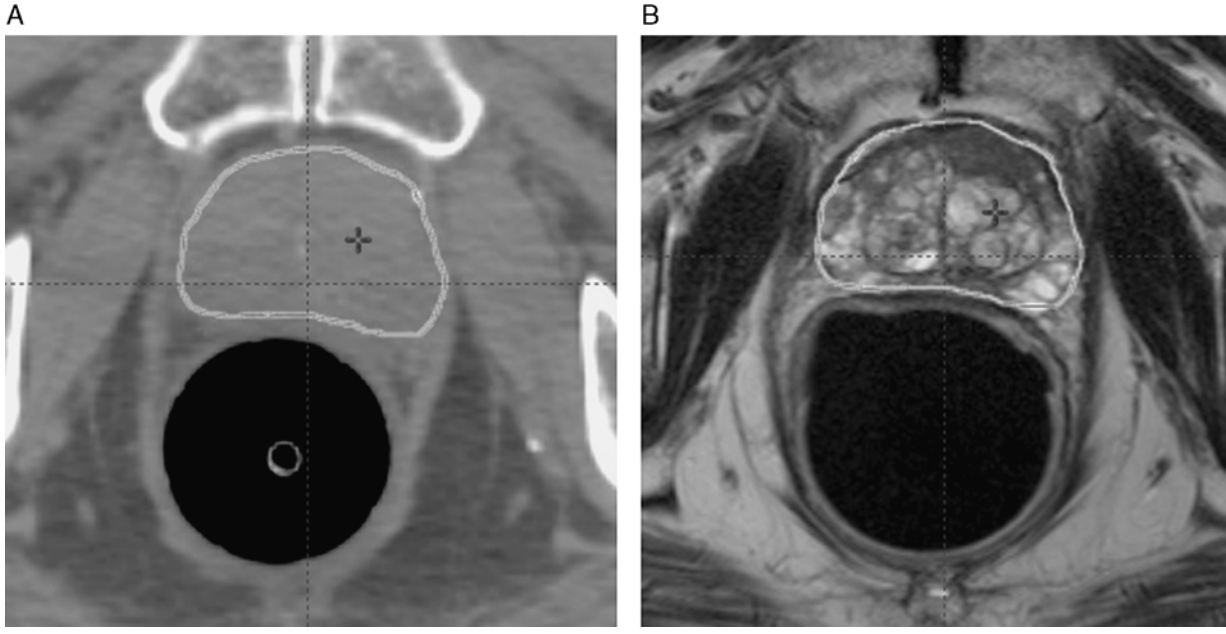

FIGURE 1. Magnetic resonance (A) and computed tomographic (B) registration with the prostate contour showing agreement (thin white outline).

TABLE 1. Dose Constraints for the 79.2 Gy RBE Standard Fractionation Arm and the 38 Gy RBE Hypofractionation Arm

Structure	Goal	Minor Deviation	Major Deviation
79.2 Gy RBE (arm I)			
Rectum (%)	V50 < 35	V50 < 40	V50 ≥ 40
	V70 < 10	V70 < 20	V70 ≥ 20
Bladder (cm^3)	V80 < 8	V80 < 12	V79.2 ≥ 12
Femoral heads (cm^3)	V45 < 1	V45 < 2	V45 ≥ 2
PTV	Minimum-dose PTV	99.5% > 75.24 Gy	—
PTV evaluation	PTV coverage	95% to 79.2 Gy	—
38 Gy RBE (arm II)			
Rectum (%)	V24 < 35	V24 < 40	V24 ≥ 40
	V33.6 < 10	V33.6 < 20	V33.6 ≥ 20
Bladder (cm^3)	V39 < 8	V39 < 12	V39 ≥ 12
Femoral heads (cm^3)	V23 < 1	V23 < 2	V23 ≥ 2
PTV	Minimum-dose PTV	99.5% > 36.1 Gy	—
PTV evaluation	PTV coverage	95% to 38 Gy	—

PTV indicates planning tumor volume; RBE, relative biological effectiveness; V, volume.

QOL Measures

Patients completed the Expanded Prostate Index Composite (EPIC)[16] and AUA[17] before treatment and during routine follow-up visits at 3, 6, 12, 18, and 24 months after completion of treatment. As described by Bhattasali et al,[18] EPIC is a validated instrument that measures urinary, bowel, and sexual function and bother.[16] To statistically evaluate change over time, responses were grouped by physiological domains and assigned a numeric score. The difference in mean scores was assessed with the *t* test. Multi-item scale scores were transformed linearly to a 0 to 100 scale, following scoring instructions for the EPIC. Lower numbers corresponded to worsening function and increased bother. To assess changes in health-related QOL from baseline, a clinically significant difference was defined as half a SD.[19] A clinically significant change in AUA scores was defined as a change of 5 points or more.[17]

TABLE 2. Patient Characteristics (N = 82)

Characteristics	38 Gy RBE in 5 Fractions (n = 49)	79.2 Gy RBE in 44 Fractions (n = 33)	*P*
T stage (N [%])			0.75
T1c	41 (84)	29 (88)	
T2a	8 (16)	4 (12)	
Prostate-specific antigen (ng/mL) (N [%])			0.79
0-4	11 (22)	9 (27)	
>4-10	38 (78)	24 (73)	
Age (median [range]) (y)	65 (52-75)	65 (49-80)	0.89
American Urological Association Symptom Index			0.71
Score of 0-10 (N [%])	45 (92)	29 (88)	
Score of 11-17 (N [%])	4 (8)	4 (12)	
Score (median [range])	4.69 (0-13)	4.76 (0-17)	

RBE indicates relative biological effectiveness.

Statistical Analysis

The primary endpoint of this study was the cumulative incidence of AEs that were grade 3 or higher. Gastrointestinal and urinary tract AEs were analyzed by incidence and prevalence. Prevalence was calculated at 3, 6, 12, 18, and 24 months after radiotherapy. For incidence, we considered grade 2 or higher AEs occurring for each arm for 3 years. All analyses were conducted in the intention-to-treat population using Fisher exact tests and 2-sided 0.05 significance levels. An interim analysis was scheduled at an accrual goal of 80 patients. The primary objective of the trial was a similar freedom from failure in both arms. The α for rejection of the null hypothesis (H_0) was 0.000005, based on a critical value (*z*-statistic) for rejection of H_0 of 4.555. Data and safety monitoring board reports, which included AEs, failures, and accrual goals, were submitted every 6 months.

RESULTS

Patients

We enrolled 85 patients in the study. Three patients withdrew consent; the remaining 82 were assessable, with 49 randomly assigned to receive 38 Gy RBE and 33 to receive 79.2 Gy RBE. No major violations of the study protocol were seen for any patient. Table 2 shows the similar patient characteristics for both study arms.

Median follow-up for both arms was 18 months, and 33 patients had follow-up for 2 years or longer (range, 3 mo to 3 y). Long-term outcomes could not be extrapolated from the available follow-up data. However, as of manuscript preparation, no patients had treatment failure, and no deaths related or unrelated to treatment have occurred. Accrual is still ongoing.

AEs

Table 3 shows grade 2 AEs for the urinary and gastrointestinal tracts. No grade 3 or higher toxicity was seen in either arm. Patients tolerated treatment well, and only some needed medication (for bowel symptoms, 6 from the 38 Gy RBE arm and 3 from the 79.2 Gy RBE arm; for urinary symptoms, 17 and 11 from the 2 study arms, respectively). Overall, the incidence of urinary or gastrointestinal tract grade 2 AEs at any point during the first 3 years were similar for both arms.

The most common urinary symptoms were frequency and urgency, affecting 14 patients overall. A small difference in medication use for urinary symptoms was seen at 6 months, with 7 patients using additional medications over baseline for the 38 Gy RBE arm versus none for the 79.2 Gy RBE arm ($P = 0.04$). No other difference was seen at any other timepoint.

Gastrointestinal AEs were minimal. The most common concern was blood in the stool, which could not be definitively attributed to treatment. We did not observe any difference in grade 2 AEs at any timepoint between arms.

American Urological Association Symptom Index

No difference was seen between study arms at different endpoints, with the exception of AUA scores at 12 months, when the score in the 38 Gy RBE arm was slightly higher. The absolute difference was 3 points, smaller than the 5-point difference needed to show clinical relevance (Table 4).

TABLE 3. Urinary and Gastrointestinal Tract Grade 2 Adverse Events

Time of Grade 2 Adverse Events	38 Gy RBE in 5 Fractions (Arm I)	79.2 Gy RBE in 44 Fractions (Arm II)	*P*
Urinary tract			
Before radiotherapy (n/N [%])	7/46 (15.2)	5/27 (18.5)	0.76
During treatment (n/N [%])	9/46 (19.6)	7/27 (25.9)	0.77
After treatment (n/N [%])			
3 mo	4/40 (10.0)	0 (0)	0.29
6 mo	7/40 (17.5)	0 (0)	0.04
1 y	7/31 (22.6)	2/17 (11.8)	0.46
2 y	2/16 (12.5)	5/16 (31.3)	0.39
Overall (n/N [%])	17/46 (37.0)	11/27 (40.7)	0.48
Gastrointestinal tract			
Before radiotherapy (n/N [%])	0 (0)	0 (0)	>0.99
During treatment (n/N [%])	2/49 (4.1)	0 (0)	0.53
After treatment (n/N [%])			
3 mo	1/40 (2.5)	0 (0)	0.99
6 mo	3/40 (7.5)	1/26 (3.8)	0.99
1 y	1/31 (3.2)	3/17 (17.6)	0.12
2 y	1/16 (6.3)	1/17 (5.9)	0.77
Overall (n/N [%])	6/46 (13.0)	3/27 (11.1)	0.99

RBE indicates relative biological effectiveness.

TABLE 4. Quality-of-Life Survey Outcomes, Stratified by Treatment Arm

	Mean (SD)		
Time of Survey	38 Gy RBE in 5 Fractions (Arm I)	79.2 Gy RBE in 44 Fractions (Arm II)	*P*
American Urological Association Symptom Index			
Baseline	4.82 (3.92)	4.55 (4.02)	0.76
3 mo	6.25 (4.06)	4.54 (3.49)	0.07
6 mo	6.13 (5.63)	5.04 (4.18)	0.40
12 mo	7.68 (5.39)	4.59 (3.45)	0.04
18 mo	7.95 (7.97)	4.81 (4.59)	0.17
24 mo	6.69 (4.71)	4.47 (5.94)	0.25
EPIC—urinary score			
Baseline	91.27 (8.19)	92.13 (8.03)	0.64
3 mo	87.00 (11.12)	91.70 (9.51)	0.08
6 mo	88.69 (12.44)	90.15 (11.02)	0.63
12 mo	85.91 (12.55)	91.51 (8.87)	0.11
18 mo	84.01 (15.61)	91.97 (11.89)	0.10
24 mo	90.92 (7.30)	91.31 (13.11)	0.92
EPIC—bowel score			
Baseline	96.39 (4.29)	95.73 (5.19)	0.53
3 mo	91.85 (9.50)	94.10 (6.56)	0.28
6 mo	87.60 (15.86)	91.05 (11.65)	0.34
12 mo	87.52 (14.00)	92.44 (6.84)	0.18
18 mo	90.48 (11.19)	91.74 (9.26)	0.72
24 mo	89.24 (13.67)	93.28 (6.67)	0.29
EPIC—erectile function score			
Baseline	59.98 (22.75)	61.33 (21.89)	0.79
3 mo	57.16 (24.57)	58.49 (20.18)	0.81
6 mo	55.88 (27.47)	56.54 (19.79)	0.92
12 mo	52.12 (25.33)	57.43 (20.46)	0.48
18 mo	47.90 (25.87)	55.44 (24.62)	0.38
24 mo	46.55 (25.62)	60.35 (22.04)	0.12

EPIC indicates Expanded Prostate Index Composite; RBE, relative biological effectiveness.

Expanded Prostate Index Composite

Urinary scores did not vary between study arms over time (Table 4). Scores declined slightly for the 38 Gy RBE arm for the first 18 months before returning to baseline at 2 years. The largest difference was seen at 12 months, with an absolute difference of 8 points between arms ($P = 0.10$) and a half-SD change of 7.8 points. The difference between groups was not statistically significant and not associated with a change in grade 2 AE between arms.

We reviewed specific questions within the urinary domain. Each question was compared independently between arms at baseline and at 3, 6, 12, 18, and 24 months. A small difference was seen between the 2 arms in specific questions of the urinary domain at 3 months. Patients treated in the 38 Gy RBE arm indicated slightly more urinary symptoms or bother at 3 months, including a weaker urinary stream, more bother waking up to urinate at night, overall urinary bother, and within the irritative and obstructive subscale. The symptoms subsequently improved, although patients continued to mention a small difference in terms of overall urinary bother that improved a year after treatment. Although the difference was statistically significant, the half-SD overlapped between arms.

Bowel scores similarly did not vary between arms over time (Table 4). The maximum difference between arms was 5 points ($P = 0.18$), with a half-SD of 7 points at 12 months' follow-up. Bowel urgency was slightly increased at 3 months in both arms but was back to baseline thereafter. Overall gastrointestinal bother was slightly increased at 3 and 6 months but subsequently returned to baseline in both arms.

We reviewed specific questions within the bowel domain. Each question was compared independently between arms at baseline and at 3, 6, 12, 18, and 24 months. No difference was seen for any other individual question at any timepoint within the gastrointestinal domain, nor were differences seen for the subdomains of frequency, fecal incontinence, bloody stools, or rectal pain.

Sexual domain scores also did not vary between arms over time (Table 4). The largest difference between the 2 arms was 14 points at 2 years, but the change was not statistically significant. No difference was seen for any individual question within the domain at any endpoint.

Relationship Between Baseline and Posttreatment Symptoms

A strong relationship between AUA and EPIC urinary scores was seen (Fig. 2). Baseline symptoms were strongly associated with posttreatment symptoms as well. Pretreatment and 3-month AUA outcomes were significantly related ($P = 0.02$), particularly for all urinary questions and urinary subdomain questions ($P < 0.001$). Baseline and 3-month EPIC urinary scores were strongly associated with each other and the AUA as well. Baseline EPIC urinary scores were associated with all individual questions and urinary subdomains at 3 months ($P < 0.01$), with a few exceptions: urinary leakage, blood, pain, dripping, and burning were not related to baseline EPIC scores.

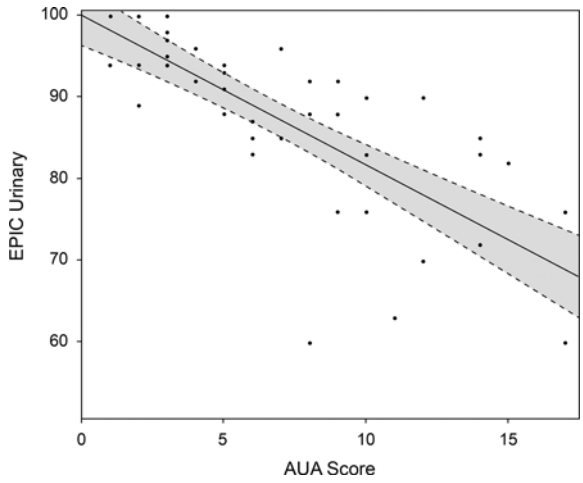

FIGURE 2. One-year American Urological Association Symptom Index (AUA) and Expanded Prostate Index Composite (EPIC) urinary scores. The regression line and fit curves are shown.

DISCUSSION

Interest in hypofractionated radiation approaches is growing.[1–4,10,12,20] Stereotactic body radiation therapy has shown excellent results for different tumor sites, including prostate cancer.[1–3,20] Hypofractionation has several advantages for the patient in terms of convenience with regard to transportation, time off work, and duration of treatment. Economic advantages are evident and savings to the health care system potentially may be realized.[21]

If the α/β ratio of prostate cancer is lower than the healthy tissue at risk, clinical gains are possible.[4,10,12] Higher biological doses could improve cancer control. Alternatively, similar biological doses can be administered to the target while lowering the biological dose to healthy tissue, thereby decreasing the risk of AE. The exact α/β ratio of prostate cancer is debatable. However, it is generally believed to be lower than that of the rectum and bladder. Our design was based on data published with high-dose-rate brachytherapy for prostate cancer and the published α/β ratios for healthy tissue.[10,12,13,22,23] Assuming that long-term AEs for the rectum and bladder are similar between the 2 arms, then the α/β ratio for both structures is close to 3.5 Gy, as previously published.[13]

In the current study, we saw no difference in gastrointestinal AEs between the 2 arms for the first 3 years or within shorter intervals. In addition, no grade 3 or higher AEs were reported. Although the gastrointestinal AE rate may continue to increase with time, we currently have no reason to anticipate a difference between study arms. The treatment was shown to be safe in both arms, with a low rate of gastrointestinal AE.

Urinary toxicity was relatively more difficult to evaluate. Changes in urination may be due to bladder irritation and to obstructive changes arising from the treatment of the prostate itself. Few papers have shown a difference in urinary toxicity with different dose volume histogram endpoints.[24] The most important predictor of late urinary toxicity likely is the baseline urinary function, as seen in our study and others.[17,24] No grade 3 or higher AEs occurred, and grade 2 AE rates were similar overall. Again, grade 2 events included the use of any medication, including over-the-counter medications or tamsulosin for mild urinary changes. Because no difference was seen overall for AUA scores or for the overall genitourinary domain, the α/β ratio potentially is close to 3.5, as hypothesized previously.[13]

No difference was seen for the EPIC urinary, gastrointestinal, or sexual domain scores at any point during follow-up. Only a small, temporary difference was seen between arms in individual urinary questions, but the half-SD values overlapped.[19] Similarly, at 6 months, a larger proportion of patients used medications over baseline for urinary bother, but this difference later disappeared. However, the overall incidence of urinary grade 2 AE was similar between arms. Patients treated with 38 Gy RBE had slightly more acute urinary bother, especially in the irritative/obstructive subdomain at 3 months, but this later improved. These data were consistent with our understanding of hypofractionated treatment, that is, patients may have slightly more acute urinary symptoms with a 38 Gy RBE than with more protracted treatment regimens.[25] However, for late AE, no differences should be apparent; this prediction also was supported by our data. A small deterioration in genitourinary function was noted in patients in the hypofractionated arm, but they were not statistically or clinically significant when compared with patients in the 79.2 Gy RBE arm. Because we saw no difference between study arms for the overall urinary domain (half-SDs overlapped for all individual questions and urinary subdomains) and the overall incidence of urinary AE, the clinical relevance of temporary acute urinary changes remains controversial.

Previous experience with hypofractionated photon radiation has shown excellent results.[2,3,18,26] Similar to our current trial, long-term toxicity (grade 3 or higher) has been infrequent, and no evidence suggests that toxicity rates in our trial will change suddenly. Furthermore, this early study was not designed to define absolute long-term AE rates; rather, it was intended to compare treatment arms. Even if AE rates increased with time, we believe the relative numbers between arms would still be similar to those reported here. However, given the lower α/β ratio of prostate cancer cells compared with the surrounding tissues, larger fraction sizes may have therapeutic benefit.[10,12,27,28] Potentially lower toxicity rates therefore are still possible for the hypofractionated treatment arm compared with the standard treatment arm. However, most AEs occur within 3 years, and a median time of 2 years or shorter can be expected.[2,4,29] Thus, greater differences between the arms are unlikely with longer follow-up. Interestingly, QOL data show that bowel or urinary changes generally occur within the first year after treatment and improve thereafter. For treatment-related QOL, most AEs likely will be noted relatively soon after treatment.[2,18,30] Erectile dysfunction is multifactorial and time related. Because most men eventually will not have erections (with or without treatment), long-term interpretation of erectile dysfunction should be evaluated with caution.

A potential shortcoming of this study includes the relative short duration of follow-up, which prevented estimation of late AE rates. However, the SDs of the samples should not change with larger estimates or longer follow-up, and comparison between arms thus should remain unchanged. For low-risk patients, survival is generally high, so comparison of AE and QOL metrics are even more important. A second shortcoming relates to the exclusive use of proton therapy in our trial. However, the same overall concept should apply in a trial that includes intensity-modulated radiation therapy in both study arms. A third component relates to the potentially limited generalizability of our findings because of our use of fiducial markers for all patients as well as magnetic resonance imaging for registration. A trial not requiring this type of guidance or registration may potentially show differences not apparent in

our trial due to lower overall guidance accuracies or lack of adequate target definition. Low-risk patients can potentially be managed with watchful waiting, with treatment deferred until progression is apparent. With this in mind, the trial was designed to achieve similar freedom from failure between the 38 Gy RBE and 79.2 Gy RBE arms. It is important to consider watchful waiting for this patient population.

CONCLUSIONS

No grade 3 urinary or gastrointestinal tract AEs occurred in either study arm. No difference was seen for the EPIC urinary, gastrointestinal, or sexual domains, nor did we observe any overall difference for AUA scores. In this interim analysis, hypofractionated proton-beam therapy for patients with low-risk prostate cancer has a similar (low) toxicity profile compared with standard fractionated treatment.

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