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CLINICAL INVESTIGATION **Genitourinary Cancer**

STEREOTACTIC BODY RADIOTHERAPY AS MONOTHERAPY OR POST–EXTERNAL BEAM RADIOTHERAPY BOOST FOR PROSTATE CANCER: TECHNIQUE, EARLY TOXICITY, AND PSA RESPONSE

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Purpose: High dose rate (HDR) brachytherapy has been established as an excellent monotherapy or after external-beam radiotherapy (EBRT) boost treatment for prostate cancer (PCa). Recently, dosimetric studies have demonstrated the potential for achieving similar dosimetry with stereotactic body radiotherapy (SBRT) compared with HDR brachytherapy. Here, we report our technique, PSA nadir, and acute and late toxicity with SBRT as monotherapy and post-EBRT boost for PCa using HDR brachytherapy fractionation.

Patients and Methods: To date, 38 patients have been treated with SBRT at the University of California—San Francisco with a minimum follow-up of 12 months. Twenty of 38 patients were treated with SBRT monotherapy (9.5 Gy × 4 fractions), and 18 were treated with SBRT boost (9.5 Gy × 2 fractions) post-EBRT and androgen deprivation therapy. PSA nadir to date for 44 HDR brachytherapy boost patients with disease characteristics similar to the SBRT boost cohort was also analyzed as a descriptive comparison.

Results: SBRT was well tolerated. With a median follow-up of 18.3 months (range, 12.6–43.5), 42% and 11% of patients had acute Grade 2 gastrourinary and gastrointestinal toxicity, respectively, with no Grade 3 or higher acute toxicity to date. Two patients experienced late Grade 3 GU toxicity. All patients are without evidence of biochemical or clinical progression to date, and favorably low PSA nadirs have been observed with a current median PSA nadir of 0.35 ng/mL (range, <0.01–2.1) for all patients (0.47 ng/mL, range, 0.2–2.1 for the monotherapy cohort; 0.10 ng/mL, range, 0.01–0.5 for the boost cohort). With a median follow-up of 48.6 months (range, 16.4–87.8), the comparable HDR brachytherapy boost cohort has achieved a median PSA nadir of 0.09 ng/mL (range, 0.0–3.3).

Conclusions: Early results with SBRT monotherapy and post-EBRT boost for PCa demonstrate acceptable PSA response and minimal toxicity. PSA nadir with SBRT boost appears comparable to those achieved with HDR brachytherapy boost. © **2012 Elsevier Inc.**

Prostate cancer, PSA nadir, Stereotactic body radiotherapy.

INTRODUCTION

A controversial paradigm shift may be under way in the radiotherapeutic management of localized prostate cancer (PCa). With accumulating evidence for a low α/β ratio for this disease (1–5), hypofractionated external-beam radiotherapy (EBRT) is emerging as a safe and effective alternative for definitive treatment (6–13). Analogously, hypofractionation with brachytherapy using high dose rate (HDR) brachytherapy has demonstrated excellent efficacy and toxicity profiles as both monotherapy and post-EBRT boost for localized PCa (14–26). The University of California—San Francisco (UCSF) has recently reported its HDR brachytherapy boost experience in mostly intermediate to high-risk disease, achieving 5-year bNED rates of 93% with minimal toxicity (24). A randomized Phase III trial has reported superior biochemical no evidence of disease (bNED) rates with HDR brachytherapy boost compared with EBRT alone (25), and a recent systematic review of the world literature has concluded that the combination of EBRT and HDR brachytherapy results in superior bNED and overall survival (OS) compared with EBRT alone or EBRT plus permanent prostate seed implant (PPI) boost (21). Others

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have also reported equivalent disease control and improved toxicity and quality of life (QOL) measures with HDR brachy-monotherapy compared with PPI monotherapy (16).

Despite such excellent results, HDR brachytherapy has been slow to achieve widespread adoption because of its relatively invasive nature, the need for hospitalization, operating room time, and anesthesia, as well as the significant time, resources, and technical expertise required in planning and delivery. However, as demonstrated by investigators at UCSF (27) and by Fuller *et al.* (28), stereotactic body radiotherapy (SBRT) can be used to replicate HDR brachytherapy's dosimetry in the treatment of localized PCa. Theoretically, such an SBRT approach using HDR brachytherapy dose/fractionation could achieve the excellent therapeutic profile of HDR brachytherapy while eliminating the risks of an invasive procedure, anesthesia, and prolonged bed rest, as well as the resource and technical challenges unique to HDR brachytherapy. SBRT is also likely to be more cost-effective compared with HDR brachytherapy, given that operating room time, monitored anesthetic use, and hospital admission are not necessary. Here, we report UCSF's early Committee on Human Research (CHR)-approved experience with SBRT using HDR brachytherapy dosing and fractionation as both monotherapy and post-EBRT boost for localized PCa.

PATIENTS AND METHODS

At the time of this analysis, 52 patients had been treated with SBRT at UCSF with CHR approval for primary localized PCa using the Cyberknife robotic radiosurgery/SBRT system (Accuray Incorporated, Sunnyvale, CA). The choice of treatment modality was made by the patients after extensive discussion of various treatment and modality options, including surgery, brachytherapy with permanent prostate seed implants, HDR brachytherapy, and IMRT with dose escalation. Thirty-eight patients in this cohort (median age of 65.9 years [range, 54.0–82.4], performance status 0–1, mean prostate volume 47 cc [range, 20–119]) had a minimum follow-up of 12 months and were included in this report (Table 1a). Twenty of 38 patients with mostly low or low-intermediate risk disease (including one patient with low-risk characteristics except for a pretreatment prostate-specific antigen [pPSA] of 21 and prostate size of 119 cc and a second patient with Gleason score 6, cT2C and pPSA 12 disease) were treated with SBRT monotherapy using UCSF's HDR brachy-monotherapy dose/fractionation of 9.5 Gy × 4 fractions. Eighteen of 38 patients with intermediate to high-risk disease were treated with SBRT boost post whole-pelvis intensity-modulated radiotherapy (IMRT) to 45–50 Gy and short to long-term androgen deprivation therapy (ADT), similar to the current UCSF and the Radiation Therapy Oncology Group's (RTOG) HDR brachytherapy boost protocols (24, 26). Among the entire study cohort, 5 of 14 intermediate risk and 13 of 15 high-risk patients received ADT; ADT was not administered to any low-risk patients. The D'Amico risk classification was used for risk group definition. Combined ADT was used, consisting of an antiandrogen and an luteinizing hormone releasing hormone (LHRH) agonist.

Because the SBRT boost protocol used a dose/fractionation scheme identical to UCSF's HDR brachytherapy boost protocol, PSA nadir (post-ADT completion) for 44 HDR brachytherapy boost patients with disease characteristics similar to the SBRT boost cohort were analyzed, and results for this cohort are also presented as a descriptive comparison (Table 1b).

Table 1a. Patient and treatment characteristics: SBRT (monotherapy and boost)

Median age (range)	65.9 years (54.0–82.4)
T Stage	
T1c	13 (34%)
T2a, b, c	17 (45%)
T3a, b	8 (21%)
Gleason sum	
6	16 (42%)
7	15 (40%)
8–9	7 (18%)
pPSA	
Median (range)	7.5 ng/mL (3.6–37.1)
No. >20 ng/mL	2 patients
SBRT protocol	
Monotherapy (38Gy)	20 (53%)
Post-EBRT boost with ADT	18 (47%)
EBRT 45 Gy	9
EBRT 50 Gy	9
PTV expansion	
0 mm	15 (39%)
2 mm	23 (61%)
Median follow-up (months)	18.3
Range	12.6–43.5
No. >24 months	14
Duration ADT, months	
0	20 (53%)
3–4	7 (18%)
6–9	8 (21%)
Long term	3 (8%)
Risk category	
Low: pPSA <10, GS 6, T1c, 2a	9 (24%)
Intermediate:	
pPSA 10–<20, GS 7 *or* T2b	14 (37%)
High: at least 1 feature:	
pPSA >20, GS 8, *or* T2c, T3	15 (39%)
Risk category by SBRT cohort	
Monotherapy	
Low	9
Intermediate	9
High	2*
Boost post-EBRT + ADT	
Low	0
Intermediate	5
High	13

*One high-risk patient due to T1c, GS = 6, PSA = 21; one high-risk patient due to T2c, GS = 6, PSA=12.

SBRT technique

Three prostate fiducial markers were placed into the prostate gland a minimum of 1 week before simulation for SBRT and/or EBRT. A CT scan was obtained as the primary treatment-planning imaging modality. A 3T pelvic magnetic resonance imaging (MRI) using 3-mm thickness T1 and T2 sequences without gadolinium contrast enhancement was also obtained for optimal target and organ at risk (OAR) delineation and fused to the planning CT using the implanted fiducial markers. The use of an endorectal coil during MRI acquisition and/or indwelling Foley catheter (for the purposes of urethral delineation) during any portion of simulation or treatment was prohibited to prevent prostate gland deformation. Using CT-MRI fusion, the prostate gland ± the seminal vesicles (SV) was carefully delineated. The delineation and extent

Table 1b. Patient and treatment characteristics: HDR-brachytherapy boost

Median age (range)	65.0 years (49.2–78.8)
T Stage	
T1c	4 (9%)
T2	18 (41%)
T3	22 (50%)
Gleason sum	
7	36 (82%)
8–9	8 (18%)
pPSA	
Median (range)	9.1 ng/mL (1.4–99.3)
No. >20 ng/mL	2 patients
Median follow-up, months	48.6
Range	16.4–87.8
No. >24 months	41 patients
Duration of ADT, months	
3–4	37 (84%)
6–9	5 (16%)
Long term	2 (4.5%)
Risk	
Low: pPSA <10, GS 6, T1c, 2a	0
Intermediate: pPSA 10–<20, GS7 *or* T2b	12 (27%)
High: at least 1 feature:	
pPSA >20, GS 8, *or* T2c, T3	32 (73%)

Abbreviations: ADT = androgen deprivation therapy; EBRT = external-beam radiotherapy; GS = Gleason score; HDR = high dose rate; pPSA = pretreatment prostate-specific antigen; PTV = planning target volume; SBRT = stereotactic body radiotherapy.

of SV involvement included in the clinical target volume (CTV) was determined on a case-by-case basis depending on disease characteristics and risk of SV involvement. The urethra was also outlined using CT-MRI fusion as an avoidance structure. The initial 15 patients treated with SBRT were planned without an expansion of the CTV for most conservative sparing of critical structures such as rectum and bladder. A planning target volume (PTV) margin expansion of +2 mm beyond the CTV in all directions (with the exception of posteriorly where no overlap with the rectum was allowed) was used in the latter 23 patients of this cohort. Treatment planning was carried out with dosimetric constraints comparable to UCSF's inverse-planned HDR brachytherapy technique, achieving similarly strict target-volume coverage, dose heterogeneity, and normal tissue sparing parameters. Approved treatment plans mimicked HDR brachytherapy conformality with a heterogeneous dose distribution similar to that reported by Fuller *et al.* (28). The resulting prescription isodose lines (IDL) were in the 60%–80% range. UCSF's technique and results for HDR brachytherapy boost treatment of intermediate to high-risk PCa have been described previously (17, 24, 29). Four patients in this SBRT cohort also received a simultaneous integrated boost of 1 Gy/fraction to a dominant intraprostatic lesion visible on planning MRI, as under formal investigation in a UCSF magnetic resonance spectroscopy (MRS) and HDR brachytherapy prospective protocol. The majority of patients were treated on consecutive working days, without a specific requirement for daily vs. every-other-day treatment and/or weekend breaks in the treatment schedule. During treatment delivery, real-time tracking of implanted fiducials with automatic beam adjustment for intrafraction prostate motion was carried out by the Cyberknife device's tracking system. Posttreatment, patients were followed every 3–4 months for PSA response, testosterone levels (until normalization post-ADT), and physician-assessed and patient-reported acute (<6 months) and late toxicity using the Common Terminology Criteria for Adverse Events (CTCAE) v.3.

Table 2a. Maximum acute GU and GI toxicity for all SBRT patients

Acute Treatment Toxicity	*n* (%)
(Max.) Grade acute GU	
0	11 (29%)
1	11 (29%)
2	16 (42%)
(Max.) Grade acute GI	
0	26 (68%)
1	8 (21%)
2	4 (11%)

Statistical analysis

Descriptive statistics have been calculated to characterize the patients, treatment parameters, and PSA nadir outcomes. The frequency of acute gastrointestinal (GI) and genitourinary (GU) toxicity observed during the minimum follow-up period of 12 months or longer post-SBRT was compared between the monotherapy and boost subsets using Fisher's exact test.

RESULTS

With a median follow-up of 18.3 months (range, 12.6–43.5), SBRT monotherapy or boost for newly diagnosed localized PCa was well tolerated, with 42% and 11% of the 38 study patients reporting acute Grade 2 GU and GI toxicity, respectively, and no Grade 3 or higher acute toxicity (Table 2a). No difference in acute toxicity has been detected with respect to monotherapy vs. boost cohorts (Table 2b). To date, the majority of patients have had no late toxicity, although two patients experienced late Grade 3 GU toxicity (Table 3). One patient aged 78 years at time of SBRT with a pretreatment American Urological Association (AUA) urinary symptom score of 13 developed urinary urge incontinence requiring condom catheter placement at 24 months post-SBRT boost, which resolved to no urinary symptoms by 34.5 months posttreatment. One patient aged 59 years at the time of SBRT who had a pretreatment AUA urinary symptom score of 13 required intraurethral injections of steroids and intermittent self-catheterization for urinary irritative symptoms at 16.1 months post-SBRT monotherapy.

PSA response as defined by PSA nadir to date has been excellent (Fig. 1). With a median follow-up of 18.3 months (range, 12.6–43.5) and a median of five posttreatment PSA

Table 2b. Maximum acute GU and GI toxicity by monotherapy vs. boost SBRT cohort

	Boost	Monotherapy
Acute GU		
0/1	61%	55%
2	39%	45% ($p = 0.75$)
Acute GI		
0/1	83%	95%
2	17%	5% ($p = 0.33$)

Abbreviations: GI = gastrointestinal; GU = gastrourinary.

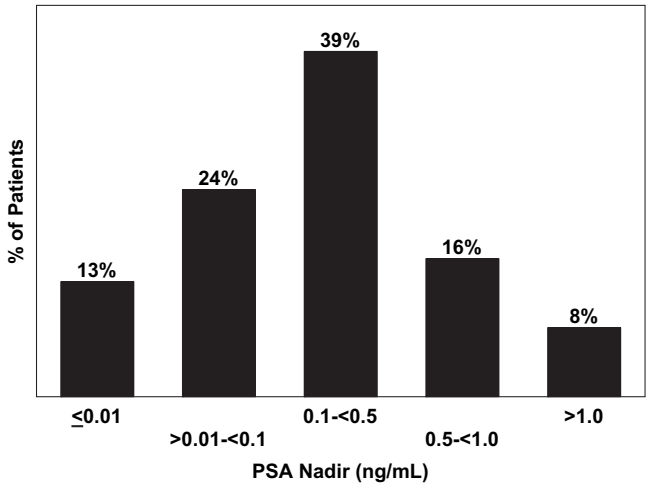

Fig. 1. Prostate-specific antigen (PSA) nadir to date (as measured after androgen deprivation therapy cessation and/or testosterone recovery) for the entire cohort.

measurements (range, 3–10), the entire cohort has achieved a median PSA nadir of 0.35 ng/mL (range, <0.01–2.1). The monotherapy cohort has achieved a current median PSA nadir of 0.47 ng/mL (range, 0.2–2.1) with a median follow-up of 18.1 months (range, 12.9–43.5) and a median of five posttreatment PSA measurements (range, 3–10). The SBRT boost patients achieved a current median PSA nadir of 0.10 ng/mL (range, 0.01–0.5; after documented androgen recovery in cases of ADT) with a median follow-up of 23.5 months (range, 12.6–34.5) and a median of 5.5 posttreatment PSA measurements (range, 3–8). A typical dose distribution for a SBRT boost plan is shown in figure 3. Absolute PSA nadir has likely not yet been reached for the majority of patients, and all patients are clinically and biochemically without evidence of disease progression at last follow-up.

Forty-four patients treated with HDR brachytherapy boost at UCSF with disease characteristics similar to the SBRT boost cohort were also analyzed with respect to PSA nadir

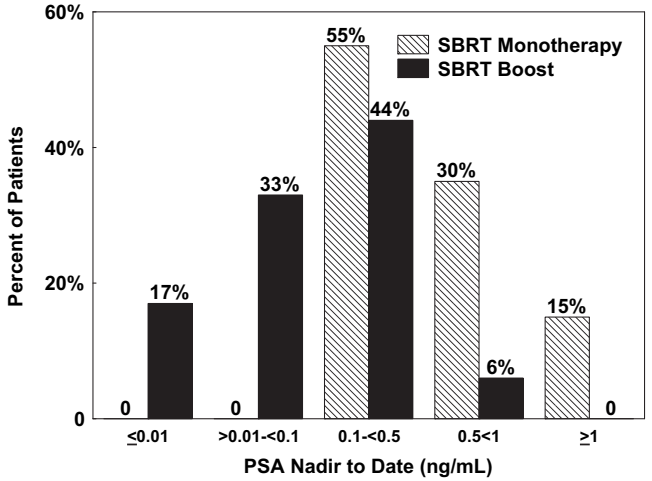

Fig. 2. Prostate-specific antigen (PSA) nadir to date (as measured after androgen deprivation therapy cessation and/or testosterone recovery) by boost vs. monotherapy cohorts.

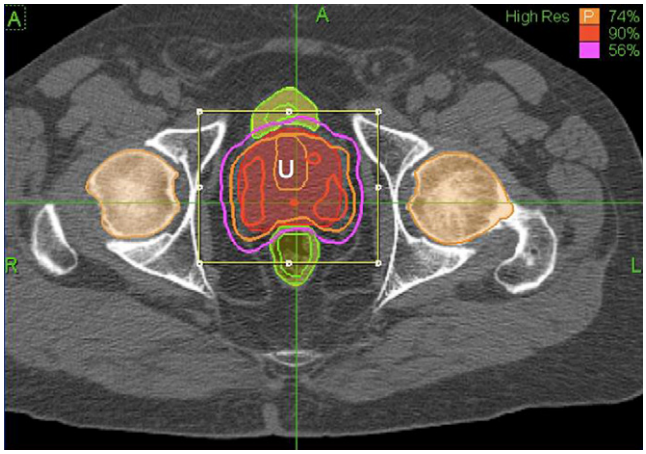

Fig. 3. Sample stereotactic body radiotherapy (SBRT) dosimetric plan. The dose delivered for SBRT boost was 19 Gy in 2 fractions prescribed to the 74% isodose line. The 90% isodose line represent 120% of the prescription dose (22.8 Gy), and the 56% isodose line represents 75% of the prescription dose (14.25 Gy). The urethra (U) was defined by T2 axial MRI images on a 3T scanner. The V75% for bladder and rectum was <2 cc. The V120% for the urethra was <10%.

as a descriptive comparison. With a median follow-up of 48.6 months (range, 20.0–87.8), the comparable HDR brachytherapy boost cohort achieved a median PSA nadir of 0.09 ng/mL (0.0–3.33) after completion of ADT (only one patient achieved PSA nadir >1.0).

DISCUSSION

This report examines UCSF's technique, early PSA response, and toxicity with SBRT using HDR brachytherapy dose/fractionation for localized PCa. To date, 38 patients with a minimum follow-up of 1 year (median, 18.3 months) have been treated under CHR approval with SBRT monotherapy or post-EBRT boost, achieving excellent PSA nadirs (Figs. 1 and 2) comparable to results of a similar HDR brachytherapy boost cohort, as well as to historical PSA nadir results achieved with PPI and EBRT (30–33). Although PSA nadir has been shown to predict long-term bNED, distant metastasis–free survival, and OS (30–33), absolute (final) PSA nadir has likely not been reached in this SBRT cohort, and longer follow-up is necessary for adequate evaluation of this outcome. Similarly, although no

Table 3. Maximum late GU and GI toxicity for all SBRT patients

Max. reported late GU toxicity	
0	32 (84%)
1	1 (3%)
2	3 (8%)
3	2 (5%)
Max. reported late GI toxicity	
0	35 (92%)
1	2 (5%)
2	1 (3%)

Abbreviations: GI = gastrointestinal; GU = gastrourinary; SBRT = stereotactic body radiotherapy.

patient has experienced biochemical or clinical disease progression in this SBRT cohort, the assessment of durable bNED rates with SBRT for localized PCa requires further study, as does the feasibility of salvage therapies such as cryotherapy, high-intensity focused ultrasound brachytherapy, or surgery in cases of post-SBRT local failure.

Although the frequency and severity of toxicity in this cohort has been minimal to date, further accrual and follow-up are required for the true assessment of late effects with SBRT for localized PCa. The critical importance of long-term follow-up in the assessment of late toxicity and as a function of fraction size is highlighted by the recently published toxicity results of the RTOG 9406 Phase I/II dose escalation study (34), in which patients receiving 78 Gy at 2 Gy per fraction more than doubled their rate of moderately severe late GU or GI toxicity compared with those receiving 79.2 Gy at 1.8 Gy per fraction. Importantly, this significant difference in toxicity was reported after a median of 6.1–12.1 years follow-up. It should also be noted, however, that patients enrolled on RTOG 9406 were treated with three-dimensional conformal EBRT (3D-CRT) techniques, but contemporary studies using IMRT have resulted in lower GU and GI toxicity than 3D-CRT (35, 36) and the toxicity rates reported in RTOG 9406. Although we echo the concerns of the RTOG investigators, who cautioned that "large (external beam) fraction sizes are currently not a standard of care (and) radical changes in dose/fraction. . . should be conducted in the context of a clinical trial," hypofractionated radiotherapy/SBRT may play a role in select patients seeking appropriate study enrollment for an abbreviated and noninvasive course of therapy.

Early results of SBRT as monotherapy for localized PCa have recently been published by other investigators (37–40), although this study is the first to our knowledge to report the use of SBRT boost post-EBRT for patients with intermediate to high-risk disease. King *et al.* (37) at Stanford University recently published their experience with SBRT for the monotherapy of low-risk PCa, reporting similarly excellent PSA response and low overall toxicity in a cohort of 41 patients and a median follow-up of 33 months. All patients in the Stanford study used gold fiducial markers for tracking. Interestingly, in the Stanford study, 38% of the patients in the "consecutive daily treatments" cohort reported a "moderate" or "big" rectal problem based on any item score of 4–5 on the Expanded Prostate Cancer Index Composite (EPIC) vs. 0% in the "every-other-day treatment" cohort ($p = 0.0035$), leading King *et al.* to hypothesize that consecutive-day treatment may result in higher toxicity rates than every-other-day treatment. No such pattern was observed in UCSF's monotherapy cohort, however, in which both consecutive and nonconsecutive daily treatments were employed. Keeping in mind the limited sample size and short follow-up of both studies, it is possible that the Stanford investigators' finding of rectal toxicity dependence on daily vs. every-other-day fractionation is due to the use of a quality of life instrument other than that used at UCSF (EPIC vs. Common Terminology Criteria for Adverse Events—v.3) (41, 42). Alternatively, such discordant findings could be due to a "learning-curve" phenomenon, because the daily schedule was used in the Stanford group's early experience, with a later shift to every-other-day treatment.

A novel fractionation schedule of 7.25 Gy × 5 fractions was used by Stanford University (and 7–7.25 Gy per fraction in other recently published SBRT studies) (37–40). UCSF's protocol, however, uses the extensively published HDR brachytherapy fractionation of 9.5 Gy × 4 fractions for the low-risk monotherapy cohort, and 9.5 Gy × 2 fractions after 45–50 Gy of whole-pelvis EBRT for the intermediate- to high-risk cohort. This dose/fractionation scheme has been determined as optimal by a Phase I/II HDR brachytherapy dose escalation study (22) and has demonstrated excellent clinical outcomes in various reports from UCSF, other institutions, and a published ongoing RTOG Phase II trial (14, 16, 22–24, 26). This approach thus minimizes the inherent risks of utilizing a novel dose/fractionation scheme, such as the occurrence of unacceptably high failure rates with longer follow-up due to an overestimation of the biological dose delivered to the tumor or the occurrence of a high proportion of late toxicities caused by an underestimation of the normal tissue biological dose. This concern is highlighted by uncertainties in the true α/β ratio of PCa (1–5). UCSF's monotherapy cohort's low occurrence of rectal toxicity to date regardless of treatment schedule is consistent with the low rectal toxicity results reported with the previously cited HDR brachytherapy fractionation schedule in which daily or twice-daily fractionation is consistently employed (14, 16, 17, 22–24, 26). Alternatively, variations in target and OAR volume delineation (MRI vs. CT) and treatment planning may have led to differing toxicity profiles observed in the UCSF and Stanford PCa SBRT protocols. Unfortunately, CT has been shown to overestimate prostate gland volume by 25%–35% vs. MRI, which, when combined with the Stanford protocol's larger PTV expansion (5 mm, except 3 mm posteriorly vs. 0–2 mm used at UCSF), may lead to increased dose to OAR (43, 44). Similarly, whereas King *et al.*'s dosimetric goals for rectal volume included <20% of rectal volume receiving 80% of the prescribed dose, UCSF's rectal dose constraints sought to replicate the sharper dose falloff of HDR brachytherapy, limiting no more than 2 cc of rectal volume to 75% of the prescription dose.

A further distinction in our technique vs. those of the investigators at Stanford pertains to the degree of dose heterogeneity achieved in each SBRT plan. As previously stated, UCSF's treatment planning protocol seeks to replicate HDR brachytherapy's dosimetry in terms not only of target coverage and outside-of-target OAR sparing (*e.g.,* bladder, rectum, penile bulb), but also HDR brachytherapy's significant intratarget dose-heterogeneity and intratarget OAR (urethra) sparing from high-dose regions. For example, a SBRT plan at UCSF is prescribed to the 60%–80% IDL, resulting in regions of high dose within the target (while sparing the urethra) with heterogeneities of up to 40% above the

prescription dose, as seen in modern HDR brachytherapy. Such intrinsic dose heterogeneity may contribute to the excellent therapeutic profile of HDR brachytherapy and should be adhered to in SBRT protocols seeking to duplicate HDR brachytherapy dosimetry and fractionation. Conversely, the Stanford SBRT protocol required normalization to the 89%–90% IDL, resulting in much lower intratarget dose heterogeneities and fundamentally dissimilar biological dose delivery to the tumor compared with HDR brachytherapy. The impact of these issues on long-term disease control and toxicity are unknown and require further study.

A final point regarding UCSF's technique for PCa SBRT requires discussion. Given our protocol's goal of simulating the sharp dose falloff and normal tissue sparing of HDR brachytherapy, no PTV expansion was initially used in treatment planning. The latter 23 patients in this cohort, however, were planned with a 2-mm nonuniform PTV expansion (0–2 mm posteriorly, excluding rectum) after a UCSF intrafraction prostate motion study using the Cyberknife's online tracking system documented the utility of such an expansion (45). This system's real-time tracking of implanted fiducials with automatic intrafraction beam-adjustment allows for such minimal PTV expansions while minimizing the risk of a geographic miss due to interfraction and intrafraction prostate motion (46, 47). Although promising results have been published with linac-based SBRT platforms for other nonprostate sites, including lung, liver, and spine, the prostate gland's unpredictable intrafractional motion and the minimal PTV expansions required for safe HDR brachytherapy–like dosimetry may preclude the use of linac-based systems for prostate SBRT without a real-time target tracking and beam-correction system to account for intrafraction motion. Further study is thus warranted to document the safety of large-dose per fraction SBRT for PCa with or without the use of real-time intrafraction target tracking and the impact of other factors such as the length of treatment delivery and patient dietary instruction in reducing prostate motion (48, 49).

CONCLUSION

Early results from UCSF's CHR-approved experience with SBRT using HDR-like dose/fractionation for monotherapy or post-EBRT boost of localized PCa demonstrate feasibility, promising PSA nadirs, and low acute and late toxicity. Although SBRT may be an attractive option in terms of patient convenience, caution is urged because additional accrual and follow-up are required before widespread adoption, as is establishment of durable bNED and acceptable late toxicity. Furthermore, similar to the extensive experience necessary for the safe and effective practice of HDR brachytherapy, similar expertise is required to reproduce HDR brachytherapy–like dosimetry using SBRT. MRI-guided target volume delineation and intrafraction prostate motion tracking with real-time beam adjustment are also critical for safe high dose per fraction prostate SBRT.

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