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Quality of life in prostate cancer

A comparative study of quality of life in patients with localized prostate cancer treated at a single institution: Stereotactic ablative radiotherapy or external beam + high dose rate brachytherapy boost

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ABSTRACT

Purpose: To compare the quality of life (QOL) in patients treated with stereotactic ablative radiation therapy (SABR) alone or high dose rate (HDR) brachytherapy + hypofractionated external beam radiotherapy (EBRT).

Methods and materials: Patient self-reported QOL was prospectively measured among patients from two sequential phase 2 clinical trials: 1-SABR 35 Gy/5 fractions/5 weeks, 2–15 Gy HDR 1 fraction, followed by EBRT 37.5 Gy/15 fractions/3 weeks. The expanded prostate cancer index composite was assessed at baseline and q6 monthly up to 5 years. Urinary, bowel and sexual domains were analyzed. A minimally clinical important change (MCIC) was defined as 0.5∗standard deviation of the baseline for each domain. Fisher exact test and general linear mixed model were used ($p < 0.05$).

Results: 84 and 123 patients were treated on the SABR and HDR boost studies, with a median follow up of 51 and 61 months respectively. There was a significant difference in MCIC between treatments in the urinary function and bother ($p < 0.0001$), the bowel function ($p = 0.0216$) and the sexual function ($p = 0.0419$) and bother ($p = 0.0290$) domains in favor of the SABR group. Of patients who reported no problem with their sexual function at baseline, 7% and 23% respectively considered it to be a moderate to big problem on follow up ($p = 0.0077$).

Conclusion: Patients treated with HDR-boost reported deterioration of QOL particularly in sexual domains in comparison with SABR.

 Radiotherapy and Oncology 113 (2014) 404–409

In the current paradigm of prostate cancer screening and early detection, prostate cancer is increasingly diagnosed when the tumor remains confined to the prostate gland [1]. Common treatments include watchful waiting (expectant management or active surveillance), radical prostatectomy, external beam radiation therapy (EBRT), interstitial brachytherapy (BT) or combination of these approaches. With the improved effectiveness of our treatment modalities, more patients are cured of their prostate cancer or living with it as a chronic disease and survival rates are more dependent on non-prostate cancer mortality [2]. Treatment goals are to prevent death and disability from prostate cancer, while minimizing treatment-related complications and preserving the quality of life (QOL) in this population of long term survivors.

There is mounting evidence of improved local control and outcomes with higher doses of radiation whether with brachytherapy, external beam radiation or a combination of both [3,4]. Furthermore, based on the assumption of a low α/β ratio of the prostatic adenocarcinoma cells, hypofractionated schedules are thought to be beneficial in prostate cancer to enhance the biological effectiveness that is proportional to the fraction size [5–7]. However, dose escalation is frequently limited by short and long term rectal and urinary toxicity as well as erectile dysfunction. Different dose escalation strategies have demonstrated improved cancer and survival outcomes [4,8–10]. BT provides a means to further boost the local dose without increasing the dose to the surrounding organs, and has been used in an attempt to improve results in men with intermediate and high-risk disease. High biologic effective doses (BED) are achievable with EBRT plus brachytherapy.

On another hand, new high-precision EBRT techniques have allowed for improved RT dose conformality. Moreover, altered

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fractionation with stereotactic ablative radiotherapy (SABR) enables the delivery of higher biological doses to the tumor with biologically similar or lower doses to the adjacent normal tissues, potentially resulting in better tumor control rates with similar treatment morbidities. No consensus has been reached with regard to the best method of dose escalation.

The aim of this single-institution study was to evaluate and compare the change in prostate-specific health-related QOL in patients with localized prostate cancer treated with SABR alone or high dose rate (HDR) BT in combination with hypofractionated EBRT (HDR boost).

Materials and methods

Patient characteristics

Two prospective phase II trials were conducted in our institution and approved by our local Research Ethics Board; the first consisted of a single fraction HDR-BT followed by hypofractionated EBRT [11] and the second of hypofractionated SABR [12]. The patient selection, study design and details of treatment planning and delivery have been documented previously for both clinical trials [11,12]. No androgen deprivation therapy (ADT) was allowed on the HDR-boost trial whereas neoadjuvant ADT was allowed for cytoreduction in the SABR trial. Patient characteristics are summarized in Table 1.

Treatment planning and delivery

HDR boost

As previously described, treatment consisted of a single HDR fraction of 15 Gy, followed by hypofractionated EBRT [11]. Transperineal catheters were inserted under trans-rectal ultrasound (TRUS) guidance and fixed to a template, which was sutured to the perineum. After a first CT simulation, any catheter displacement was corrected and a final CT scan was obtained. Images were transferred to the Nucletron PLATO planning system version 14.3.2 (Nucletron B.V., Veenendaal, The Netherlands). The clinical target volume (CTV) was the prostate. No additional margin was added for Planning Target Volume (PTV). Rectum and urethra were contoured. Dwell time optimization was performed using Inverse Planning with Simulated Annealing (IPSA) [13]. Dose was prescribed as a minimal peripheral dose to the CTV. CT simulation was performed for external beam planning the day following completion of brachytherapy. EBRT began 2 weeks later, and was delivered using a 4-field conformal technique to the prostate and proximal 2 cm of seminal vesicles. Bladder and rectal volumes (from the bottom of the ischium to the sigmoid flexure, typically 11 cm) were contoured as solid organs. The PTV was a uniform 1 cm beyond the CTV and received at least 95% of the prescription dose. 37.5 Gy was prescribed to the isocenter in 15 fractions over 3 weeks. Calculated equivalent dose at 2 Gy per fraction (EQD2) of 115 Gy for an α/β ratio of 1.4 [7].

SABR

The treatment consisted of 35 Gy in 5 fractions delivered weekly over 29 days. Calculated equivalent dose at 2 Gy per fraction (EQD2) of 86 Gy for an α/β ratio of 1.4 [7]. The planning procedure has been detailed previously [12]. All patients had ultrasound guided insertion of 3 fiducial gold seeds transperineally followed by a planning CT scan. Radiotherapy planning scan and treatments were performed in supine position with a comfortably full bladder and empty rectum. A customized vacuum lock bag was used for pelvic immobilization (Vac-Lock, MED-TEC. Inc., Orange City, IA) during simulation and treatment. Prostate was contoured as the CTV. The bladder, penile bulb (PB) and rectum were contoured. A uniform CTV-to-PTV margin of 4 mm was applied [14]. The volume of CTV receiving 35 Gy (V35) was required to be >99% and PTV V33.25 $\geqslant$ 99%. The maximum dose (Dmax) was 105%. The normal tissue DVH constraints were rectal V28 $\leqslant$ 40%, rectal V32 $\leqslant$ 33%, bladder V32 $\leqslant$ 40%, and PB V20 $\leqslant$ 90%. Pinnacle 7.6 h-8.0 d (Philips Medical Systems, Cleveland, OH) inverse planning software was used to generate an optimized IMRT plan. Patients were treated on standard linear accelerators (Siemens Primus, Concord, CA; Elekta Synergy, Stockholm, Sweden) with multi-leaf collimators capable of delivering IMRT plans using a "step and shoot" technique and six MV photons. Patients were setup daily using orthogonal megavoltage electronic portal images of the fiducial markers.

Evaluation

Biochemical, toxicity and pathologic outcomes of both trials were reported previously [11,12]. Patient reported outcomes were

Table 1
Patient characteristics.

	Total (N = 207)		SABR (n = 84)	HDR-BT + RT (n = 123)
Age at baseline (years)				
Median (range)	67 (48–83)		67 (48–82)	66 (45–79)
PSA at baseline				
Median (range)	6.11 (0.83–18.56)		5.31 (0.83–9.93)	6.76 (2.0–18.6)
Prostate size (cm^3)				
Median (range)	33.0 (14.0–90.0)		37.0 (15.0–90.0)	31.0 (14.0–59.0)
IPSS score at baseline				
Median (range)	5.0 (0–25)		5.0 (0–18)	5.0 (0–25)
IPSS >14 at baseline				
$\leqslant$14	188	(90.82%)	79 (94.05%)	109 (88.62%)
>14	19	(9.18%)	5 (5.95%)	14 (11.38%)
Clinical stage				
T1a	1	(0.48%)	1 (1.19%)	0 (0.00%)
T1c	154	(74.40%)	77 (91.67%)	77 (62.60%)
T2	52	(25.12%)	6 (7.14%)	46 (37.40%)
G-Score at baseline				
6	93	(44.93%)	84 (100.00%)	9 (7.32%)
7	114	(55.07%)	0 (0.00%)	114 (92.68%)

measured using the expanded prostate cancer index composite (EPIC) [15]. EPIC is a reliable and validated patient-reported QOL questionnaire that comprises four main domains: urinary, bowel, sexual, and hormonal. Each of these domains includes function, bother, and overall quality subscales. There are a total of 50 questions (12 urinary, 14 bowel, 13 sexual, 11 hormonal). The EPIC questionnaire was completed at baseline and regularly (annually in the HDR boost study and every 6 months in the SABR study) until 5 years.

Statistical analysis

Three domains of EPIC scores and sub-scores were analyzed: urinary (uQOL) (function/bother), bowel (bQOL) (function/bother) and sexual (sQOL) (function/bother). The patient responses to questions were transformed to a scale from 0 to 100, with higher scales indicating better function and less bother.

General linear regression was used to compare baseline EPIC scores and sub-scores between the two treatment groups. To compare dynamic changes over time between two treatment groups, normalized EPIC QOL scores and sub-scores were calculated and general linear mixed model was conducted after assuming individual patient with random effect. A minimally clinical important change (MCIC) was scored if the average EPIC QOL score (months 6–60) was >0.5 standard deviation (SD) of baseline scores for each domain score or sub-score in all patients. In addition, an analysis of specific items in each domain of the questionnaire was done after transforming the item scores into a 5-point Likert scale (0: big problem, 1: moderate problem, 2: small problem, 3: very small, 4: no problem). The proportion of patients who started with no to small problems at baseline and who subsequently developed a moderate to big problem on average over follow-up was calculated. For the sexual QOL, an analysis of the change in the overall sexual domain score was also reported. Sexual domain scores were divided into three categories: <50 (big problem), 50–75 (moderate problem), and 75–100 (no problem). The proportion of patients who started with no problems at baseline and who subsequently developed a moderate to big problem on average over follow-up was calculated. Fisher exact test was used to compare percentage of patients in the two treatment groups. Univariate and multivariate generalized estimating equations (GEEs) analyses were used to investigate the relationship of specific QOL items (moderate to big problem vs. no to small problem) with demographic covariates; age, prostate volume, baseline IPSS score, baseline QOL score. GEEs methodology was applied for such correlated data with repeated measurements over time, binomial distribution and logit link function were used. All analyses were conducted by Statistical analysis Software (SAS for Windows, version 9.3). p-Value <0.05 was considered statistically significant.

Results

One hundred twenty-three and eighty-four patients were treated respectively in the HDR boost and the SABR study. The median follow-up time for the QOL measures was 61.2 months (IQR 54.6–63.2) and 50.8 months (interquartile range [IQR], 44.7–56.3) respectively. Five-year biochemical disease-free survival was >95% in both trials [11,12].

One hundred twenty-one (98%) and eighty-two (97%) patients provided baseline QOL data from each respective trial. The Wilcoxon Signed Rank Test found no significant differences in the bowel ($p = 0.68$) and urinary ($p = 0.56$) domains between baseline and 6-month status in the SABR group whereas a significant difference was found in the sexual domain ($p = 0.001$). We herein used 6 month data as baseline for urinary and bowel domains for the two subjects that did not complete the baseline questionnaire in the SABR group, and excluded them from any sexual domain analysis. Follow-up at month 12 was not used for imputation in the HDR boost analysis. Furthermore, two patients had androgen deprivation therapy in the SABR trial and were excluded from sexual QOL analyses. Adequate follow-up responses on urinary and bowel QOL were obtained for 117 HDR boost and 84 SABR patients whereas sQOL data were obtained from 110 HDR boost and 76 SABR patients. The urinary, bowel and sexual QOL scores at baseline and during follow-up periods are reported in Table 2. There was no significant difference on EPIC domain, function or bother sub-scores at baseline between the two treatment groups ($p > 0.05$).

When comparing QOL changes over time, patients treated in the SABR study had significant higher urinary domain score ($p < 0.0001$) over time compared to patients treated in HDR Boost. However, there was no significant decrease over time for both groups (Fig. 1A). Urinary function ($p = 0.001$) and bother ($p < 0.0001$) scores (i.e., better QOL) were highly significantly different between two treatment groups, but flat over time. Similarly, overall bowel domain score were higher in the SABR group ($p = 0.028$) without a significant decrease over time ($p = 0.099$) (Fig. 1B). Bowel function sub-scores significantly decreased over time in both cohorts ($p = 0.008$) with SABR having higher sub-scores than HDR Boost ($p = 0.030$). There was no significant impact of time ($p = 0.89$) and treatment ($p = 0.072$) for bowel bother sub-score.

To compare the dynamic changes in sexual scores we have excluded patients with erections "very poor" to "not existent" at baseline. Overall 29 patients were excluded from this analysis; 19 from the HDR boost and 10 from the SABR group. The sexual domain score and function sub-score significantly decreased over time ($p < 0.0001$) and patients treated with SABR had higher scores ($p < 0.01$; Fig. 1C). Sexual bother sub-scores significantly decreased over time ($p < 0.0001$) without any significant treatment impact ($p = 0.12$). A subgroup analysis comparing T1c patients only, showed the same patterns of dynamic changes over time. T1c patients treated with SABR had higher sexual domain score and function sub-score ($p < 0.025$), whereas no treatment effect was found in the bother subscore ($p = 0.909$).

The thresholds (0.5*SD) for MCIC scores were 4.4 (3.7/5.8), 4.2(3.6/5.3) and 13.2(13.7/15.9) for the urinary (function/bother), bowel (function/bother), and sexual (function/bother) domains, respectively. The number of patients reporting MCIC in both treatment groups is described in Table 3. A significant difference was found in the urinary function and bother, the bowel function and the sexual bother and function domains in favor of the SABR group. Similarly, when comparing T1c patients in both groups, there was a highly significant difference in the urinary function and bother as well as in the sexual bother domains was found. A trend towards significance was found for the sexual function domain ($p = 0.062$).

The proportion of patients who started with no problems at baseline and who subsequently developed a moderate to big problem on average over follow-up was calculated for specific items of the questionnaire (Table 4). There was a significant difference in favor of SABR on the specific sexual questions. Furthermore sQOL was not a problem at baseline (score 75–100) for 40 (33%) and 27 (32%) patients respectively in the HDR boost and SABR study. Among those, 17 (42%) and 3 (11%) respectively averaged a "big problem" (<50) during follow-up ($p = 0.0075$) (Table 5).

On univariate and multivariate GEEs analyses, patients with baseline IPSS > 14 (OR = 7.20, $p = 0.0012$) or having "moderate" to "big problem" with dripping or leaking urine at baseline (OR = 17.92, $p = 0.0006$) were more likely to have "moderate" to "big problem" with leakage on follow up. While baseline IPSS >14 and worse baseline urinary QOL were predictors of worse overall urinary QOL on follow up on univariate analysis (OR = 2.62,

Table 2
Urinary, bowel and sexual QOL score.

	Urinary		Bowel		Sexual	
Treatment group	HDR-boost	SABR	HDR-boost	SABR	HDR-boost	SABR
Baseline score						
Median	91.0	92.4	98.21	96.4	63.5	66.7
Range	43.7–97.2	59.7–97.2	44.6–100.0	39.3–100.0	0.0–96.1	0.0–98.1
Standard deviation	9.3	8.2	7.1	9.7	25.8	27.5
Average score during follow-up						
Median	83.1	91.7	94.4	94.0	36.1	46.3
Range	43.1–97.3	66.3–97.3	46.4–100.0	66.8–100.0	0.0–85.1	0.0–86.0
Standard deviation	11.5	7.2	10.2	7.3	22.7	23.4

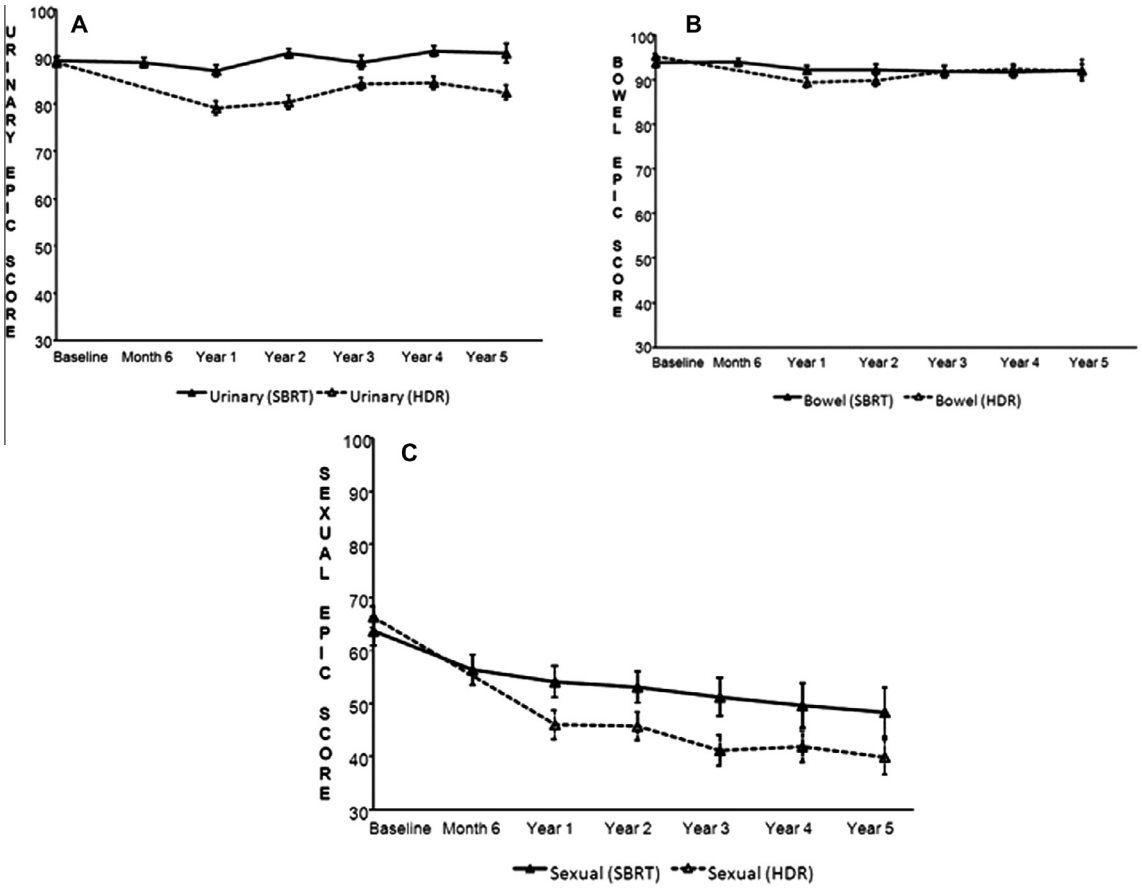

Fig. 1. Mean EPIC score over time for SABR and HDR boost. (A) Mean urinary EPIC score over time. (B) Mean bowel EPIC score over time. (C) Mean sexual EPIC score over time.

Table 3
Patients reporting minimally clinical important change (MCIC) in urinary, bowel and sexual domains and subdomains in both HDR boost and SABR clinical trials.

	Treatment groups			Subanalysis for T1c patients by treatment groups		
	HDR boost *n* (%)	SABR *n* (%)	*p*-Value*	HDR boost *n* (%)	SABR *n* (%)	*p*-Value*
	N = 117	*N* = 84		*N* = 71	*N* = 77	
Urinary	68 (58)	15 (18)	**<0.0001**	44 (62)	12 (16)	**<0.0001**
Urinary function	63 (54)	16 (20)	**<0.0001**	41 (58)	16 (21)	**<0.0001**
Urinary bother	55 (47)	11 (13)	**<0.0001**	36 (51)	8 (10)	**<0.0001**
	N = 117	*N* = 84		*N* = 71	*N* = 77	
Bowel	51 (44)	27 (32)	0.2466	31 (44)	23 (30)	0.0901
Bowel function	43 (37)	26 (31)	**0.0216**	23 (32)	25 (32)	0.9924
Bowel bother	48 (39)	21 (25)	0.0760	29 (41)	19 (25)	0.0527
	N = 110	*N* = 76		*N* = 68	*N* = 71	
Sexual	61 (55)	33 (43)	0.1903	38 (56)	33 (46)	0.3101
Sexual function	58 (53)	26 (34)	0.0290	38 (56)	28 (39)	0.0625
Sexual bother	57 (52)	27 (35)	**0.0419**	36 (53)	25 (35)	**0.0412**

Bolded entries signify *p*-values of statistical significance ($p < 0.05$).
* *p*-Value was obtained from Fisher exact test.

Table 4
Quality of life changes for specific questions.

	HDR BT + RT *n* (%)	SABR *n* (%)	*p*-Value*
Among patients with "no to small problem" at baseline How big a problem on follow up was:			
Urinary			
Dripping or leaking			0.2688
"no" to "small" problem	112 (97)	81 (100)	
"moderate" to "big" problem	3 (3)	0 (0)	
Urinary function			0.4037
"no" to "small" problem	110 (99)	77 (100)	
"moderate" to "big" problem	1 (1)	0 (0)	
Bowel			
Urgency to have a bowel movement			0.5136
"no" to "small" problem	113 (98)	80 (100)	
"moderate" to "big" problem	2 (2)	0 (0)	
Bloody stools			0.4042
"no" to "small" problem	116 (99)	81 (100)	
"moderate" to "big" problem	1 (1)	0 (0)	
Bowel habits			0.5136
"no" to "small" problem	113 (98)	80 (100)	
"moderate" to "big" problem	2 (2)	0 (0)	
Sexual			
Ability to have an erection			<0.0001
"no" to "small" problem	63 (72)	54 (96)	
"moderate" to "big" problem	24 (27)	2 (3)	
Overall sexual function			0.0077
"no" to "small" problem	69 (77)	55 (93)	
"moderate" to "big" problem	21 (23)	4 (7)	
Among patients with fairly good erections at baseline			
Ability to have an erection on follow up			0.0051
"fair" to "very good"	50 (63)	43 (86)	
"poor" to "not existent"	29 (37)	7 (14)	

* *p*-Value was obtained from Fisher exact test.

Table 5
Sexual function among patients with "no problems" at baseline.

Using sexual domain score	Among patients with "no problem" at baseline			
	No change	Moderate problem	Big problem	*p*-Value*
HDR BT + RT ($n = 40$)	3 (7.50%)	20 (50.00%)	17 (42.50%)	**0.0075**
SABR ($n = 27$)	7 (25.93%)	17 (62.96%)	3 (11.11%)	

Bolded entries signify *p*-values of statistical significance ($p < 0.05$).
* *p*-Value was obtained from Fisher exact test.

$p = 0.0185$; and OR = 3.66, $p = 0.0147$), only worse baseline urinary function was significant on multivariate analysis (OR = 3.66, $p = 0.0147$).

No significant predictors of bowel urgency were found. Overall, patients with worse baseline bowel QOL were likely to have a "moderate" to "big" bowel function problem on follow up (OR = 22.8, $p = 0.0008$).

Age and impaired sexual QOL at baseline were correlated with a "poor "to "not existent" erections on follow up on univariate (OR = 1.08, $p < 0.0001$; OR = 12.39, $p < 0.0001$) and multivariate analysis (OR = 1.04, $p = 0.0367$; OR = 10.47, $p < 0.0001$). Age and worse baseline sexual function were predictors of worse overall sQOL on follow up on univariate analysis (OR = 1.03, $p = 0.0272$; OR = 6.93, $p = 0.0001$), however, only baseline sexual function was significant on multivariate analysis (OR = 6.93, $p < 0.0001$).

Discussion

Both SABR and HDR boost were associated with excellent biochemical control rates and low and acceptable toxicities as previously reported [11,12]. With the availability of various treatment options in the setting of localized prostate cancer, patients need information not only on disease control but also about QOL changes associated with these modalities. In our study, patients treated in both groups reported decrease in health-related QOL. However, urinary and sexual QOL appeared significantly better in the SABR group compared to the HDR boost group.

There are a few reports of QOL after SABR or HDR-BT with or without EBRT in the literature. To our knowledge, no direct comparison between the two treatment modalities has been made. We believe that to make any reasonable hypotheses about QOL differences between interventions, it is critical that the same questionnaire and same definition of change has to be used. For example, looking only at the sexual QOL changes that occurred in the SABR group in this study, depending on the definition of change used, the proportion of men having worse QOL post-treatment ranged from 3% (ability to have an erection "poor" or "non-existent") to 43% (minimally clinical important change overall sexual domain). With this caveat in mind, our QOL outcomes are consistent with those reported in the literature for EBRT with HDR-BT boost and SABR.

Potency rates of 53–60% after EBRT with HDR-BT boost, in men without any potency problem before treatment are reported in the literature [16,17]. In our cohort 63% of patients with "fair" to "very good" erections at baseline in the HDR boost, and 86% in the SABR group were able to maintain them on follow-up. Hoskin et al. compared long-term quality of life in patients randomized to EBRT to a dose of 35.75 Gy in 13 fractions followed by a boost of HDR-BT or EBRT alone to at total dose of 55 Gy in 20 fractions, using the functional assessment of cancer therapy-prostate (FACT-P) and FACT-G (General) questionnaires [18]. No difference in FACT-G, FACT-P or Trial Outcome Index (TOI) between treatments arms and no deterioration in QOL scores were found over 10.5 years. However, a higher incidence of erectile dysfunction (ability to maintain an erection) was reported in the HDR-BT group. Local trauma in temporary implantation may have a role in the poor sexual function outcomes after HDR boost, but this remains unproven.

Wiegner and King looked at sexual function of patients treated with SABR at a total dose of 36.25 Gy in 5 fractions of 7.25 Gy [19]. Mean sexual summary score was 67.5 at baseline, and all scores progressively decreased after treatment. Sexual function declined throughout the follow-up period, while sexual bother initially declined and then leveled off at 20 months. Only 40% of patients with erections adequate for intercourse at baseline remained potent at 50 months. Overall 66% of men had erectile dysfunction (inadequate for intercourse) at last follow-up, but only 25% considered their sexual function to be a moderate to big problem. Of patients having no erectile problems at baseline our SABR cohort, 86% of patients remained potent on follow-up and only 7% considered their sexual function to be a moderate to big problem.

The main limitation of this study was its *post hoc* nature. While both studies prospectively collected QOL, the idea for this paper was conceived after each study reached medium maturity. To guard against a "data dredging" exercise, a limited number of *a priori* questions were determined before the QOL data were analyzed. Another limitation is that different biological doses of radiation were prescribed, different volumes were treated, and there were different risk groups in both cohorts. The HDR boost patients were treated to a higher biological dose and the external beam component also included proximal seminal vesicles with a large uniform margin. Daily image guidance was not used. The HDR boost trial included patients with intermediate risk prostate cancer whereas SABR included those with low risk prostate cancer. While this makes it impossible to compare the efficacy of both regimens, we believe the differences in tumor risk category should not interfere with the QOL measures (since both groups have bDFS >95% at 5 years, this minimizes the possibility that tumor

recurrence differences account for some of the changes seen in QOL). In addition, the HDR boost consisted in one fraction of HDR-BT followed by conformal hypofractionated EBRT. It is impossible to distinguish the EBRT toxicity from the HDR toxicity. A more rigorous comparison would have been to compare SABR to HDR monotherapy, where volumes treated and biological dose delivered would be similar.

Our longer-term data found high preservation of health related quality of life in urinary and bowel domains with both treatment regimens. Our data suggest less decrease in the urinary and sexual domains with SABR compared to the HDR/ EBRT combination. The relative contribution of the brachytherapy and external beam components of treatment to this is unknown. These outcomes have to be balanced against relative efficacy and costs of these treatments. We would recommend a randomized study of SABR versus HDR monotherapy in the future. Meanwhile, ongoing phase III randomized studies comparing SABR with standard treatments will provide further information regarding the efficacy and toxicity of SABR (The Prostate Advances in Comparative Evidence (PACE) study (NCT01584258), a multi-center international randomized trial comparing laparoscopic vs. da Vinci prostatectomy vs. cyberknife SABR in low and intermediate risk prostate cancer and the Swedish Hypo-fractional Radiotherapy (HYPO-RT-PC study (ISRCTN45905321), randomizing intermediate- or high-risk patients with PSA <20 between conventional fractionation and seven fractions of 6.1 Gy).

Conflict of interest

There are no conflicts of interest.

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