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ORIGINAL ARTICLE

Low-dose rate brachytherapy with I-125 seeds has an excellent 5-year outcome with few side effects in patients with low-risk prostate cancer

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ABSTRACT

Background: Low-dose rate brachytherapy (LDR-BT) has been used in Sweden for more than a decade for treatment of low-risk prostate cancer. This study presents the outcome for patients treated with LDR-BT at a single institution with focus on the association between dose and biochemical failure-free survival (BFFS).

Methods: In total 195 patients were treated with LDR-BT between 2004 and 2008. The patients were followed systematically for side effects for at least one year. PSA levels were followed regularly from three months and for at least five years. Outcome was analyzed in relation to clinical variables at baseline and to radiotherapy data.

Results: Kaplan-Meier estimated BFFS at five years was 95.7%. Dose to the prostate in terms of $D_{90\%}$ was significantly associated with BFFS [HR 0.90 (95%CI 0.83−0.96), p = 0.002].

Conclusion: Out data confirmed that absorbed dose is a predictive factor for BFFS for low-risk patients without androgen deprivation therapy. With our treatment routines and dosimetry, a $D_{90\%}$ in the range of 170−180 Gy gives excellent outcomes with acceptable toxicity for patients with low-risk prostate cancer.

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Low-dose rate brachytherapy (LDR-BT) is one way to administer radiotherapy, and it has been used in Sweden for more than a decade for low- and intermediate-risk prostate cancer. Iodine-125 or palladium-103 is used as permanent LDR implants. The volume of irradiated tissue is relatively small compared with external beam radiotherapy (EBRT), which makes dose escalation feasible.

Data on long-term biochemical outcome and survival after LDR-BT have been reported by several institutions. For low-risk patients the reported 5- and 10-year biochemical control rates are within the range of 90−98% and 81−95%, respectively [1–4]. One randomized controlled trial and several retrospective studies compared treatment results after radical retro-pubic prostatectomy (RRP) versus LDR-BT. None of the studies showed any significant difference in efficacy in patients with low-risk prostate cancer [3,4]. Patients treated with LDR-BT had significantly greater and longer lasting urinary urgency and dysuria but had better erective function than patients treated with RRP [3]. Other retrospective studies support the same conclusion when comparing LDR-BT and EBRT. LDR-BT results in less erectile dysfunction and less rectal morbidity and in addition might lead to fewer secondary cancers [4,5].

The standard alternative in Sweden today for most patients with low-risk prostate cancer is active surveillance, preferably in a prospective study, which should reduce the risk for overtreatment. According to the Swedish health care program for prostate cancer (2015) the most important factors that speak in favor of definitive treatment for these patients is high PSA density, large prostate or anterior cancer (difficult to monitor), anorectal diseases (difficult with repeated biopsies), low ratio free/protein bound PSA, patients with high heredity of deadly prostate cancer, patients with anxiety or expected difficulties of compliance to the surveillance program or a health care unit unable to offer the recommended control program. Additionally, about 25% of the patients in active surveillance program needs active treatment in five years and almost half of them in 15 years because of reclassification or PSA kinetics [6,7]. It is therefore still important to find a treatment alternative with low toxicity for the patients that needs treatment, especially as the expected survival is long.

A dose-response relationship for biochemical control has been found in a number of retrospective LDR-studies, the first one from Mount Sinai in 1998 [8] which suggested a $D_{90\%}$ range of 140−160 Gy using AAPM TG43 guidelines [9]. Later works from the same center and others support a dose-response relationship between $D_{90\%}$ and biochemical failure-free survival (BFFS). Some of these studies reports $D_{90\%}$ in terms of BED with $\alpha/\beta = 2$ Gy and repair half time $T_{½}$=0.5 h. Some of the studies support an association between BED and post-treatment biopsy results and indicate that higher BED

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doses (180−200 Gy) are required [10–14]. In a large study on 1006 patients by Morris et al. [15], $D_{90\%}$ was not found to be predictive of disease-free survival for the whole cohort. However, for the subset of low-risk patients without androgen deprivation therapy (ADT), increasing dose was associated with disease-free survival [2,15,16].

In this report we present long-term follow-up of prostate LDR-BT results from our department with focus on the relationships between dose and BFFS.

This study was carried out at the Department of Oncology at Skåne University Hospital in Malmö and Lund, Sweden and approved by the Central Research Ethics committee in Sweden.

Material and methods

Patient selection

All patients treated with LDR-BT at the Skåne University Hospital with at least a five-year follow-up were included in the study. In total 195 patients met the requirements and they were all treated during 2004−2008. The majority of patients (90%) had low-risk prostate cancer while the remainders had intermediate disease. Low-risk prostate cancer was defined as patients presenting with PSA $\leq$10 ng/ml, Gleason score $\leq 3+3$ and $\leq$ T2a disease. We aimed to include patients with a maximum International Prostate Symptom Score (IPSS) of 8, a maximum prostate volume of 50 cm^3, a maximum urine flow rate of >10 ml/s and residual urine <100 ml. None of the patients received ADT.

For patients' baseline characteristics, see Table 1.

Table 1. Patient baseline characteristics (n = 195).

Variable		%
Age at diagnosis (years)		
Median	64 (50–77)	
Gleason score		
<6	41	21.0
6	153	78.5
>6	1	0.5
PSA		
<4	40	20.5
4–7	91	46.7
7–10	53	27.2
>10	11	5.6
T stage		
1	135	69.2
2	50	25.6
Unknown	10	5.1
Treatment year		
2000–2003		
2004	25	12.8
2005	58	29.7
2006	50	25.6
2007	53	27.2
2008	9	4.6
Treatment parameters	Mean (SD)	
Prostate volume, cm^3	31.1 (7.6)	
No. of needles	25.6 (3.9)	
No. of seeds	64.0 (8.5)	
$D_{90\%}$, Gy	173.9 (6.9)	
$V_{100\%}$, %	97.8 (1.2)	
$V_{150\%}$, %	61.2 (5.0)	
Urethra $D_{30\%}$, %	125.5 (7.7)	
Rectum, D_{2cc}, Gy	72.8 (13.0)	
Rectum V_{70Gy}, cm	0.59 (0.54)	
Total administered activity, mCi	26.3 (4.2)	

Implantation of seeds was performed with the patient in anesthesia. An average of 64 (39−82) seeds was used per treatment. The dose prescribed to the prostate was 145 Gy (=100% isodose). The pre-treatment dosimetry aimed for at least 98% of the prostate to receive 100% ($V_{100\%}$>98%) and less than 65% to receive 150% ($V_{150\%}$<65%). The mean $D_{90\%}$ was 174 Gy with a range of 155−190 Gy. The planning system used was VariSeed 7.1 (Varian Medical Systems, Inc., Palo Alto, CA, USA). The seeds were RAPID Strand™ (Oncura, Inc., Plymouth Meeting, PA). Post-implant computed tomography (CT)-based dosimetry was made for the first patients but was then excluded from standard procedure as a minor clinical benefit was not considered to justify the additional work load. For further information about treatment and dosimetry, see Table 1.

Follow-up

The patients treated with LDR-BT were followed systematically with phone calls or visits to the doctor's office after three, six and nine months and an office visit at 12 months. At each time point the patients were questioned about side effects: urinary urgency, urinary incontinence, feces inconvenience and erectile dysfunction. PSA blood samples were taken in close connection with the checkups. Patients-reported IPSS and urine bother scores were collected before treatment, after three months, and after 12 months for most of the patients. For some of the patients maximum urine flow rate was also measured at these visits. After 12 months the patients were referred to their urologist for further follow-up according to local routines with PSA regularly, and clinical visit if needed, up to 10 years after treatment.

Biochemical failure was defined according to the Phoenix definition, i.e. nadir +2 ng/ml. Bounce was defined as a temporary PSA increase of more than 0.2 ng/ml above nadir with a subsequent return to the pre-bounce level, or to below 0.5 ng/ml.

Statistical analysis

Time to biochemical failure and duration of follow-up was calculated from the date of implant. The Kaplan-Meier method was used to estimate BFFS. Cox regression analysis was used for univariate and multivariate analyses to identify and assess predictive clinical and treatment-related factors of BFFS. Multivariate analyses were made with only two covariates considering the limited number of events. The combination of $D_{90\%}$ and PSA was chosen based on presumed causality and the results from univariate analyses. $D_{90\%}$ was entered as a continuous variable. Spearman's correlation was used for studying the correlation between side effects and treatment-related factors. A p-value <0.05 was considered as significant. All statistical analyses were performed using IBM Statistical Package for Social Sciences (SPSS), version 22.

Results

Kaplan–Meier estimated median follow-up time for the LDR-BT patients was 6.2 years. Eight of the patients were lost to

follow-up before five years and nine died during the follow-up period, whereof two from prostate cancer.

Biochemical failure-free survival and dose

At five years, according to the Phoenix definition, 23 patients had biochemical recurrence but 14 of these patients were classified as bounce, leaving nine patients with true recurrence of disease (4.6%), 191 patients free from disease (91.2%) and eight patients lost to follow-up (4.1%). Two of the relapsed patients had generalized disease diagnosed 2.5 and 3 years after treatment, respectively. At last follow-up 17 patients had relapsed (8.7%) with a median follow-up time of six years. Kaplan–Meier estimated BFFS at five years was 95.7%.

The patients with recurrences were treated with cryotherapy, hormonal therapy or watchful waiting (Table 2).

$D_{90\%}$ was a significant predictor of BFFS [HR =0.90 (95% CI 0.83−0.96), p = 0.002]. The only variable that contributed significantly in addition to $D_{90\%}$ in a multivariate analysis was PSA before treatment; the higher the PSA the higher the risk of relapse. With BFFS as dependent variable, the estimated HR for $D_{90\%}$ was 0.89 (95% CI 0.83−0.96, p = 0.002) after adjustments for PSA before treatment [HR = 1.20 (95% CI 1.00−1.44), p = 0.049]. ROC curve analysis as well as Cox proportional hazard analysis of the most significant split between the BFFS curves suggested an optimal cutoff level of 167 Gy. As an illustration a Kaplan-Meier plot of BFFS for patients with $D_{90\%}$ above and below this cutoff value is shown in Figure 1.

In 58 patients PSA bounced on average 1.4 years after treatment. None of the patients with a PSA bounce had recurrence of disease during the follow-up period.

There was a tendency in the material towards better outcome in the patients treated during the last treatment years (Figure 2).

Table 2. Status for LDR-BT patients at 5 years and at last follow-up (n = 195).

Variable	5 years	Last follow-up (0.7–8.9 years)
ANED	173 (88.7%)	165 (84.6%)
DNED	5	5
AWD	8	13
DO/WD	1	4
Lost to follow-up	8	8
Disease-free (ANED + DNED)	178 (91.2%)	170 (87.2%)
Biochemical recurrence (AWD + DO/WD)	9 (4.6%)	17 (8.7%)
BCR-PD[a]	23	
Bounce[b]	58	
Bounce-PD[c]	14	
Biochemical recurrence	9	

[a]BCR-PD: Biochemical recurrence according to Phenix definition, PSA-nadir +2;
[b]Bounce: Post-treatment PSA raise of ≥0.2 + nadir followed by spontaneous return to the pre-bounce levels or <0.5 without intervention;
[c]Bounce-PD: PSA Bounce that also met Phenix definition of biochemical recurrence.

Urinary side effects

The patient's mean self-scored IPSS and urinary bother increased at three months and then decreased at one year without reaching the pre-treatment level. Large individual variations were seen. The same tendency was seen for maximal urinary flow rate.

Significant correlations between ΔIPSS at three months and total administered activity and prostate volume were found. Δ-urine flow at one year correlated significantly to total activity and prostate volume.

Almost half of the patients reported urinary urgency after three months. This number decreased to 20% after one year. Urinary incontinence was rare.

There was no correlation between $D_{90\%}$ or urethra $D_{30\%}$ and urinary side effects (Tables 3 and 4 and Figure 3).

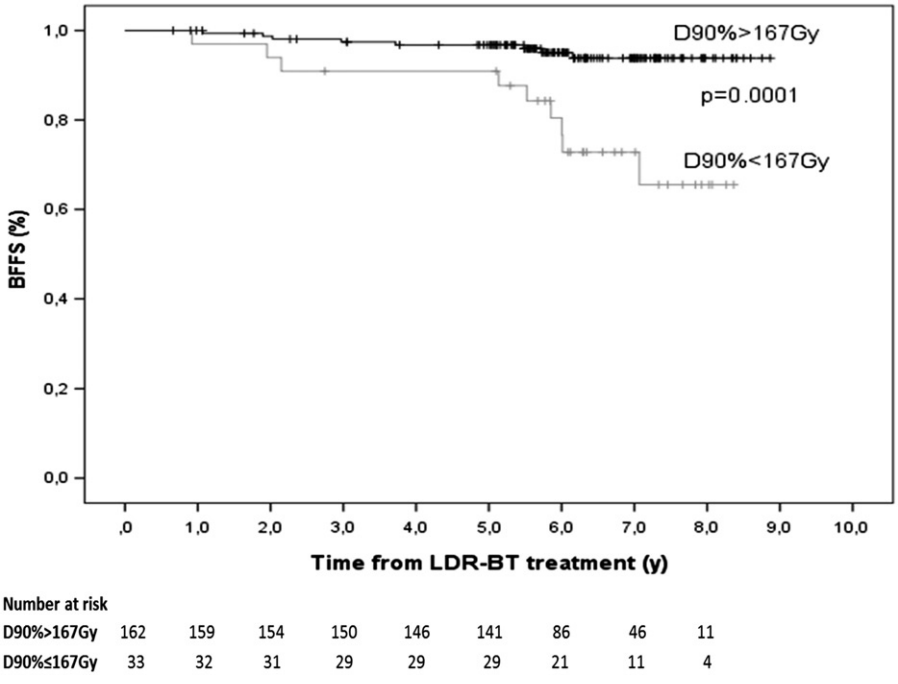

Figure 1. Kaplan–Meier survival plot of BFFS with a cutoff value of $D_{90\%}$=167 Gy.

Fecal side effects

About 10% of the patients treated with LDR-BT reported fecal inconvenience after three months without further specification. This problem also decreased at the one-year follow-up. There were no statistical significant correlations between $D_{90\%}$, rectum $V_{70\%}$, rectum $V_{100\%}$ or rectum D_{2cc} and fecal side effects (Tables 3).

Erectile dysfunction

There was a tendency towards increased incidence of erectile dysfunction with time after treatment. In spite of this, 88 patients (45%) had no ED after one year in the LDR-BT group. Of the 83 patients that were reported as potent before treatment 61% were still potent at the one-year follow-up.

There was no correlation between $D_{90\%}$ and ED (Table 3).

Discussion

LDR-BT without hormonal therapy for patients with low-risk prostate cancer is a safe treatment with excellent results. Even though the treatment has been used in many centers for more than two decades the question of dose-response still remains an issue for discussion at least for patients treated with LDT-BT in combination with ADT [2]. There is also a lack of consensus regarding the optimal dose level [10,11,13,15]. Differences in treatment routines, e.g. margins and extra prostatic seeds, might to some extent explain this ambiguity.

The vast majority of the patients in the present study had low-risk prostate cancer. No hormones were used and patients with high IPSS score or large prostate volumes were excluded from treatment.

In this material we found a significant association between dose and tumor control. The strongest predictor for BFFS was $D_{90\%}$ which also remained significant in multivariate analysis.

With our routines and with $D_{90\%}$ measured with pre-implant techniques, a $D_{90\%}$ in the range of 170−180 Gy gives excellent results concerning BFFS. This dose is higher than the suggested 140–160 Gy in the first paper from Mount Sinai

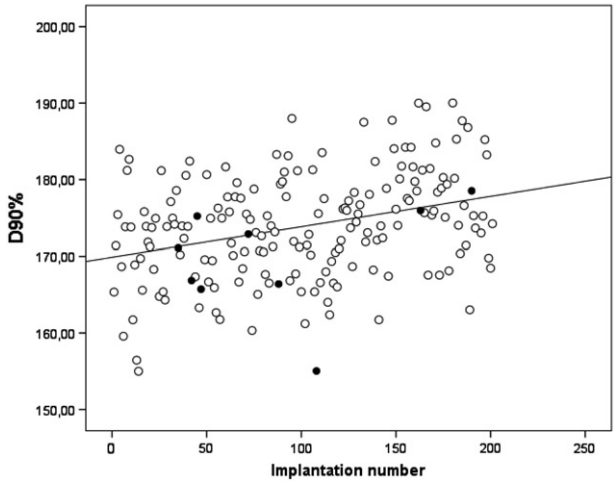

Figure 2. $D_{90\%}$ variation with implantation number. Biochemical recurrence in 5 years is indicated with filled circles.

Table 3. Side effects for LDR-BT (n = 195).

Variable	Before treatment	3 months	1 year
IPSS			
Patients (n)	178	161	153
Mean (SD)	4.5 (3.8)	13.4 (7.2)	7.9 (5.6)
Bother			
Patients (n)	173	158	152
Mean (SD)	0.8 (1.1)	2.3 (1.4)	1.4 (1.2)
Max. urinary flow			
Patients (n)	52	39	61
Mean (SD)	16.1 (6.3)	10.6 (4.9)	14.6 (6.6)
Erectile dysfunction, n (%)			
ED	31 (15.9)	50 (25.6)	64 (32.8)
No ED	83 (42.6)	96 (49.2)	88 (45.1)
Unknown	81 (41.5)	49 (25.1)	43 (22.0)
Urinary urgency, n (%)			
Yes		95 (48.7)	38 (19.5)
No		86 (44.1)	140 (71.8)
Unknown		14 (7.2)	17 (8.7)
Urinary incontinence, n (%)			
Yes		4 (2.1)	2 (1.0)
No		177 (90.8)	181 (92.8)
Unknown		14 (7.2)	12 (6.2)
Fecal inconvenience, n (%)			
Yes		20 (10.3)	8 (4.1)
No		162 (83.1)	170 (87.2)
Unknown		13 (6.7)	17 (8.7)

IPSS: International Prostate Symptom Score.

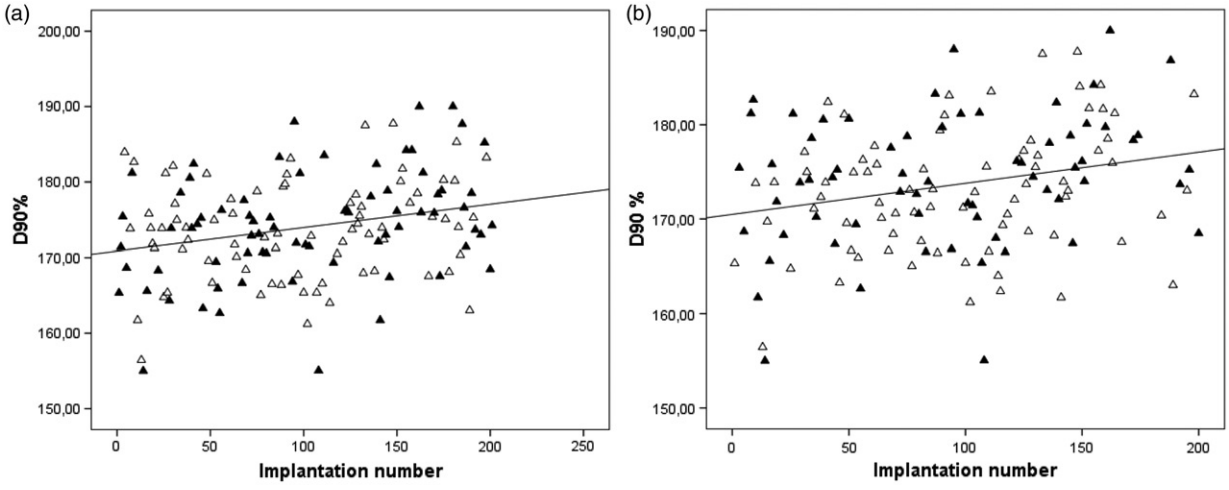

Figure 3. (a) $D_{90\%}$ variation with implantation number. Delta IPSS at 3 months >8 is indicated with filled triangles. (b) $D_{90\%}$ variation with implantation number. Delta IPSS at 1 year >3 is indicated with filled triangles.

Table 4. Univariate and multivariate analyses of patient, disease and treatment characteristics versus BFFS and side effects for LDR-BT patients.

Outcome	Variable	HR (95% CI)	p-Value	Analysis
BFFS				
Patient characteristics	Age (years)	1.01 (0.92;1.11)	0.83	Cox-UA
Disease characteristics	Gleason score	0.84 (0.40;1.77)	0.64	Cox-UA
	PSA (ng/ml)	1.17 (0.99;1.39)	0.071	Cox-UA
	T stage	0.95 (0.33;2.69)	0.92	Cox-UA
	Prostate volume (cm^3)	0.93 (0.87;1.00)	**0.046**	Cox-UA
Treatment characteristics	Treatment year	0.84 (0.52;1.34)	0.46	Cox-UA
	No. of seeds	0.97 (0.92;1.02)	0.21	Cox-UA
	Prostate volume-T (cm^3)	0.95 (0.89;1.01)	0.10	Cox-UA
	Total activity (mCi)	0.92 (0.83;1.02)	0.13	Cox-UA
	$D_{90\%}$ (Gy)	0.90 (0.83;0.96)	**0.002**	Cox-UA
Multivariate analysis	$D_{90\%}$ (Gy)	0.89 (0.83;0.96)	**0.002**	Cox-MA
	PSA (ng/ml)	1.20 (1.00;1.44)	**0.049**	Cox-MA
Side effects				
Δ IPSS 3 months	Total activity (mCi)	$r = 0.22$	**0.008**	Spearman's correlation
	Prostate volume-T (cm^3)	$r = 0.18$	**0.030**	Spearman's correlation
	$D_{90\%}$	$r = 0.06$	0.493	Spearman's correlation
ΔUrineflow, 1 year	Total activity (mCi)	$r = 0.34$	**0.016**	Spearman's correlation
	Prostate volume-T (cm^3)	$r = 0.34$	**0.027**	Spearman's correlation
	$D_{90\%}$	$r = 0.24$	0.087	Spearman's correlation

Significant value ($p<0.05$) are presented in bold.
BFFS: biochemical failure-free survival; IPSS: International Prostate Symptom Score; MA: multivariate analysis; UA: univariate analysis.

[8] or the median dose of 152 Gy reported by Morris et al. at Vancouver Cancer center [16] but quite in line with results from Shiratishi et al. 130 − 180 Gy [11]. The later papers from Mount Sinai also support higher doses, up to 200 Gy reported as BED [12,14]. A $D_{90\%}$ of 170−180 Gy corresponds to a BED of 180−191 Gy using $\alpha/\beta = 2$ Gy and a repair half time of 1 h, as used in these papers from Mount Sinai. In theory dose reporting in BED is advantageous when comparing, e.g. different treatment methods but there is not yet a clear consensus on the numerical values on the radiobiological parameters to be used in the BED calculations. If we apply $\alpha/\beta = 1.5$ Gy and a slightly longer repair half time of 1.5 h as suggested in other papers [17–19] our preferred $D_{90\%}$ interval correspond to BED in the range of 190−200 Gy.

It should be noted that during the treatment period for this study, including the startup, we had a significant trend towards better results concerning BFFS. This might be considered as a learning effect, and it is probably mostly dosimetric, as the trend for $D_{90\%}$ also increased. Such a dosimetric learning curve has been described earlier [16].

The incidence rates of acute genitourinary (GU) toxicity after LDR-BT are reported to be high but mostly mild. The most common toxicity is frequency/urgency which affects a majority of the patients. Several studies show that long-term GU toxicity is low [20–22]. The International Prostate Symptom Score (IPSS) before seed implantation, higher $D_{90\%}$, larger prostate size, $V_{100\%}$ and age have all shown to predict GU toxicity [20]. Time to IPSS resolution is reported to be 6−24 months, usually about 12 months. Higher prostate $D_{90\%}$, maximal post-implant IPSS and urinary retention slowed down the IPSS resolution time. In our material the most reliable follow-up information comes from the measurements of IPSS and urine bother as those parameters are well established and patient reported. There is an increase in urine side effects at three months after LDR-BT but these side effects improve at one year and approach but do not reach the pre-treatment levels.

The risk of post-treatment urinary incontinence and bowel dysfunction is low. Rectal volume receiving 100% of the prescribed dose ($V_{100\%}$) has been described as a significant parameter for acute gastrointestinal toxicity [21–23]. In our material no such correlation could be identified.

Concerning erectile dysfunction after treatment large variations have been reported. A long-term study concerning potency preservation after brachytherapy with 1063 patients found 75% potency rate after five years without ADT. In that study dose, reported as BED, did not have an impact on potency [24]. Other studies demonstrate 33−86% likelihood of preserved erectile function 1−6 years after implant [23,25]. A poorer erectile function has been reported in patients treated with I-125 and $D_{90\%}>160$ Gy [23]. We found no significant correlation between dose and ED in our material.

For the studied side effects no correlation to $D_{90\%}$, Urethra $D_{30\%}$, Rectum $V_{70\%}$, Rectum $V_{100\%}$ or Rectum dose to 2 cm^3 were found in the studied range of 155−190 Gy.

For the selected group of patients with low-risk disease it is reasonable to consider if treatment is really necessary or if active surveillance could be an alternative, as is the standard of care today to low-risk patients. This is supported by the fact that patients with early prostate cancer include patients with an indolent cancer that will not be needed treatment even in long term. At the time when these patients were treated they were considered suitable for treatment.

Anyhow, as previously mentioned in the introduction a fraction of low-risk patients will need definitive therapy at the time of diagnosis and almost half of the patients in active surveillance are treated within long-term follow-up [6].

If treatment is considered, LDR-BT is a strong alternative to radical prostatectomy and the treatment of choice if radiotherapy is used in low and possibly intermediate-risk prostate cancer because of excellent cancer control and low toxicity, not least higher chance of preserving the erectile function. More prospective studies remain to be done.

Conclusion

Tumor response is significantly associated with absorbed dose ($D_{90\%}$). With our treatment routines and dosimetry a

$D_{90\%}$ in the range of 170−180 Gy gives excellent outcome with acceptable toxicity for selected patients with low-risk prostate cancer.

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Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Hinnen KA, Battermann JJ, van Roermund JG, Moerland MA, Jurgenliemk-Schulz IM, Frank SJ, et al. Long-term biochemical and survival outcome of 921 patients treated with I-125 permanent prostate brachytherapy. Int J Radiat Oncol Biol Phys 2010;76:1433–8.
2. Morris WJ, Keyes M, Spadinger I, Kwan W, Liu M, McKenzie M, et al. Population-based 10-year oncologic outcomes after low-dose-rate brachytherapy for low-risk and intermediate-risk prostate cancer. Cancer 2013;119:1537–46.
3. Giberti C, Chiono L, Gallo F, Schenone M, Gastaldi E. Radical retropubic prostatectomy versus brachytherapy for low-risk prostatic cancer: a prospective study. World J Urol 2009;27:607–12.
4. Rodrigues G, Yao X, Loblaw DA, Brundage M, Chin JL. Evidence-based guideline recommendations on low-dose rate brachytherapy in patients with low- or intermediate-risk prostate cancer. Canadian Urological Assoc J = Journal De L'Association Des Urologues Du Canada 2013;7:E411–16.
5. Peinemann F, Grouven U, Bartel C, Sauerland S, Borchers H, Pinkawa M, et al. Permanent interstitial low-dose-rate brachytherapy for patients with localised prostate cancer: a systematic review of randomised and nonrandomised controlled clinical trials. Eur Urol 2011;60:881–93.
6. Klotz L, Vesprini D, Sethukavalan P, Jethava V, Zhang L, Jain S, et al. Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. J Clin Oncol 2015;33:272–7.
7. Bul M, Zhu X, Valdagni R, Pickles T, Kakehi Y, Rannikko A, et al. Active surveillance for low-risk prostate cancer worldwide: the PRIAS study. Eur Urol 2013;63:597–603.
8. Stock RG, Stone NN, Tabert A, Iannuzzi C, DeWyngaert JK. A dose-response study for I-125 prostate implants. Int J Radiat Oncol Biol Phys 1998;41:101–8.
9. Nath R, Anderson LL, Luxton G, Weaver KA, Williamson JF, Meigooni AS. Dosimetry of interstitial brachytherapy sources: recommendations of the AAPM Radiation Therapy Committee Task Group No. 43. American Association of Physicists in Medicine. Medical Phys 1995;22:209–34.
10. Ash D, Al-Qaisieh B, Bottomley D, Carey B, Joseph J. The correlation between D90 and outcome for I-125 seed implant monotherapy for localised prostate cancer. Radiother Oncol J Eur Soc Therap Radiol Oncol 2006;79:185–9.
11. Shiraishi Y, Yorozu A, Ohashi T, Toya K, Saito S, Nishiyama T, et al. A dose-response analysis of biochemical control outcomes after (125)I monotherapy for patients with favorable-risk prostate cancer. Int J Radiat Oncol Biol Phys 2014;90:1069–75.
12. Stock RG, Stone NN, Cesaretti JA, Rosenstein BS. Biologically effective dose values for prostate brachytherapy: effects on PSA failure and posttreatment biopsy results. Int J Radiat Oncol Biol Phys 2006;64:527–33.
13. Stone NN, Potters L, Davis BJ, Ciezki JP, Zelefsky MJ, Roach M, et al. Customized dose prescription for permanent prostate brachytherapy: insights from a multicenter analysis of dosimetry outcomes. Int J Radiat Oncol Biol Phys 2007;69:1472–7.
14. Stone NN, Stock RG, Cesaretti JA, Unger P. Local control following permanent prostate brachytherapy: effect of high biologically effective dose on biopsy results and oncologic outcomes. Int J Radiat Oncol Biol Phys 2010;76:355–60.
15. Morris WJ, Spadinger I, Keyes M, Hamm J, McKenzie M, Pickles T. Whole prostate D90 and V100: a dose-response analysis of 2000 consecutive (125)I monotherapy patients. Brachytherapy 2014;13:32–41.
16. Morris WJ, Keyes M, Palma D, McKenzie M, Spadinger I, Agranovich A, et al. Evaluation of dosimetric parameters and disease response after 125 iodine transperineal brachytherapy for low- and intermediate-risk prostate cancer. Int J Radiat Oncol Biol Phys 2009;73:1432–8.
17. Dasu A, Toma-Dasu I. Prostate alpha/beta revisited – an analysis of clinical results from 14 168 patients. Acta Oncology 2012;51:963–74.
18. Nickers P, Hermesse J, Deneufbourg J-M, Vanbelle S, Lartigau E. Which α/β ratio and half-time of repair are useful for predicting outcomes in prostate cancer? Radiother Oncol 2010;97:462–6.
19. Fowler J, Chappell R, Ritter M. Is α/β for prostate tumors really low? Int J Radiat Oncol Biol Phys 2001;50:1021–31.
20. Keyes M, Miller S, Pickles T, Halperin R, Kwan W, Lapointe V, et al. Late urinary side effects 10 years after low-dose-rate prostate brachytherapy: population-based results from a multiphysician practice treating with a standardized protocol and uniform dosimetric goals. Int J Radiat Oncol Biol Phys 2014;90:570–8.
21. Emara AM, Chadwick E, Nobes JP, Abdelbaky AM, Laing RW, Langley SE. Long-term toxicity and quality of life up to 10 years after low-dose rate brachytherapy for prostate cancer. BJU Int 2012;109:994–1000.
22. Bottomley D, Ash D, Al-Qaisieh B, Carey B, Joseph J, St Clair S, et al. Side effects of permanent I125 prostate seed implants in 667 patients treated in Leeds. Radiother Oncol J Eur Soc Therap Radiol Oncol 2007;82:46–9.
23. Machtens S, Baumann R, Hagemann J, Warszawski A, Meyer A, Karstens JH, et al. Long-term results of interstitial brachytherapy (LDR-Brachytherapy) in the treatment of patients with prostate cancer. World J Urol 2006;24:289–95.
24. Snyder KM, Stock RG, Buckstein M, Stone NN. Long-term potency preservation following brachytherapy for prostate cancer. BJU Int 2012;110:221–5.
25. Matsushima M, Kikuchi E, Maeda T, Nakashima J, Sugawara A, Ando T, et al. A prospective longitudinal survey of erectile dysfunction in patients with localized prostate cancer treated with permanent prostate brachytherapy. J Urol 2013;189:1014–18.