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FULL PAPER

Low dose rate brachytherapy (LDR-BT) as monotherapy for early stage prostate cancer in Italy: practice and outcome analysis in a series of 2237 patients from 11 institutions

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Objective: Low-dose-rate brachytherapy (LDR-BT) in localized prostate cancer is available since 15 years in Italy. We realized the first national multicentre and multidisciplinary data collection to evaluate LDR-BT practice, given as monotherapy, and outcome in terms of biochemical failure.
Methods: Between May 1998 and December 2011, 2237 patients with early-stage prostate cancer from 11 Italian community and academic hospitals were treated with iodine-125 (^{125}I) or palladium-103 LDR-BT as monotherapy and followed up for at least 2 years. ^{125}I seeds were implanted in 97.7% of the patients: the mean dose received by 90% of target volume was 145 Gy; the mean target volume receiving 100% of prescribed dose (V_{100}) was 91.1%. Biochemical failure-free survival (BFFS), disease-specific survival (DSS) and overall survival (OS) were estimated using Kaplan–Meier method. Log-rank test and multivariable Cox regression were used to evaluate the relationship of covariates with outcomes.
Results: Median follow-up time was 65 months. 5- and 7-year DSS, OS and BFFS were 99 and 98%, 94 and 89%, and 92 and 88%, respectively. At multivariate analysis, the National Comprehensive Cancer Network score ($p < 0.0001$) and V_{100} ($p = 0.09$) were correlated with BFFS, with V_{100} effect significantly different between patients at low risk and those at intermediate/high risk ($p = 0.04$). Short follow-up and lack of toxicity data represent the main limitations for a global evaluation of LDR-BT.
Conclusion: This first multicentre Italian report confirms LDR-BT as an excellent curative modality for low-/intermediate-risk prostate cancer.
Advances in knowledge: Multidisciplinary teams may help to select adequately patients to be treated with brachytherapy, with a direct impact on the implant quality and, possibly, on outcome.

INTRODUCTION

Males with localized prostate cancer and indication for curative treatment are candidates for radical prostatectomy (RP), external beam radiotherapy (EBRT) or brachytherapy (BT) depending on the disease features, patient age, health conditions and preferences. Few radiation oncology centres in Italy started low-dose-rate brachytherapy (LDR-BT) at the end of the 1990s and >4200 patients have been treated with this modality until 2014 in 13 institutes.

Long-term results have demonstrated the efficacy of this treatment modality and this approach is considered as an established option for low- and intermediate-risk disease.[1–4]

The aim of the present study was to realize the first Italian multicentre low-dose-rate prostate BT data collection, reporting the selection criteria, implant parameters and biochemical outcome of patients treated in Italy using this modality and comparing them with other multi-institutional reports.[5–10]

For this purpose, 11 Italian community and academic hospitals (Figure 1) pooled their data to generate a large patient cohort involving 2237 patients treated with LDR-BT over a period of 14 years, now with a minimum follow-up of 2 years.

METHODS AND MATERIALS

Study design and organization

All the 13 Italian centres performing LDR-BT for prostate cancer were contacted and invited to this study. It is a retrospective multicentre cohort study and consists in a centralized collection and analysis of the clinical and physical parameters of patients who underwent LDR-BT for prostate cancer. The inclusion criteria were as follows: (1) LDR-BT for early prostate cancer; (2) implant performed between May 1998 and December 2011; (3) LDR-BT given as monotherapy; (4) written informed consent and (5) follow-up of minimum of 2 years.

All participating centres were instructed to use the same database previously designed by expert personnel of one centre. Completely anonymized data collection was centrally coordinated by the epidemiology and biostatistics division of another centre.

Database structure, data collection instruments, manuals and processes, especially for the handling of missing data, were standardized and shared by all investigators. Data entry was performed locally by each local data management unit and sent to the coordinating centre for data cleaning and validation.

For the purpose of this study, the following parameters have been collected: age, pre-treatment prostate-specific antigen (PSA) level, Gleason score, *T*-stage, National Comprehensive Cancer Network (NCCN) risk group classification,[11] pre-implant prostate volume, pre-implant androgen deprivation (AD) therapy, implant date, radioactive isotope, prescription dose, post-implant dose received by 90% of target volume (D_{90}), post-implant target volume that received 100% of the prescribed dose (V_{100}), last follow-up date, last post-implant PSA dosage, biochemical failure (BF) and vital status data.

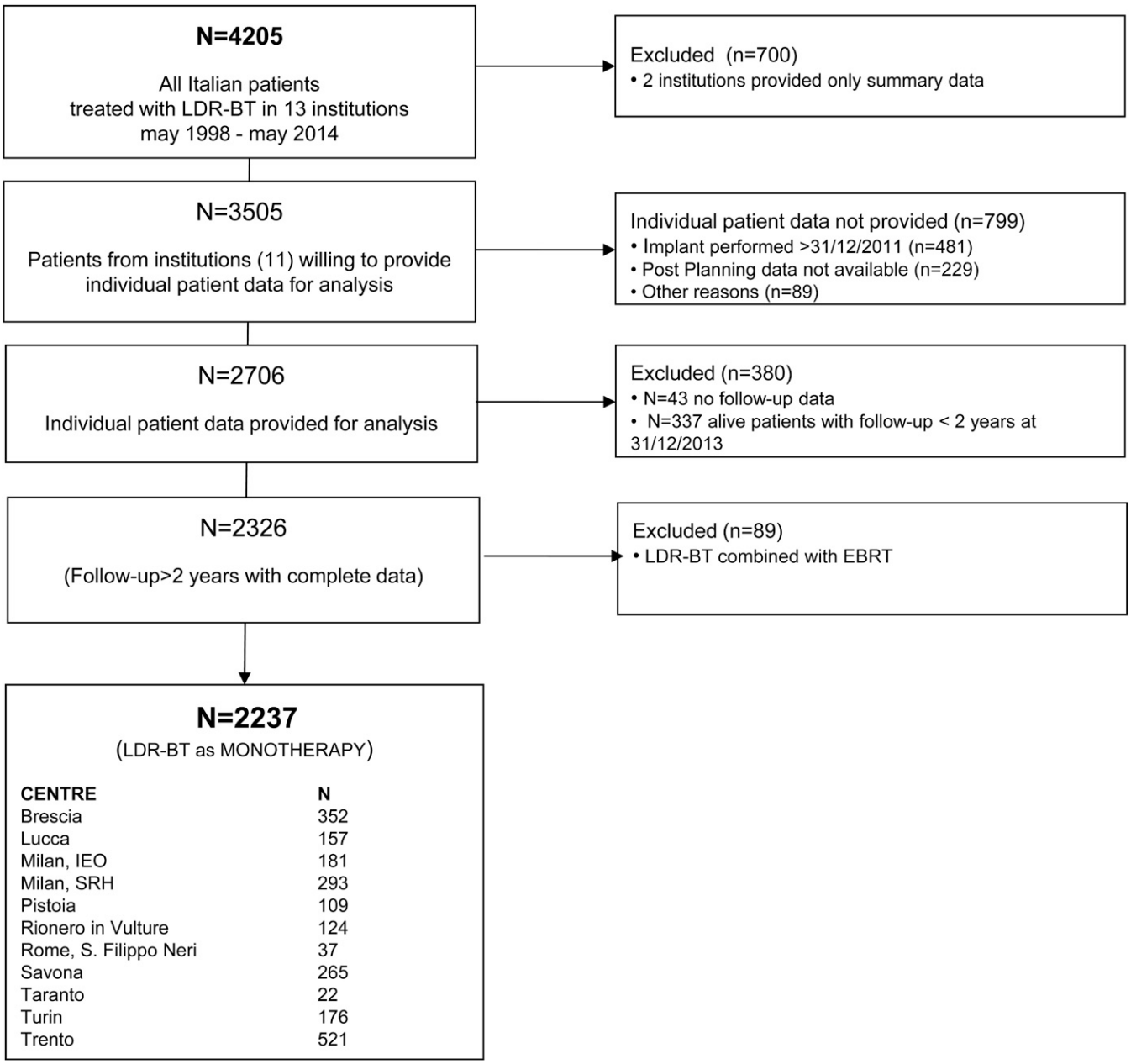
No formal ethics review committee was involved for this retrospective anonymized data collection; all patients gave their written informed consent for LDR-BT, and each step of patient care followed the basic principles outlined in the Declaration of Helsinki.

Statistical analysis

The analyses were performed with SAS statistical software for Windows 9.2 (SAS Institute Inc., Cary, NC).[12] Continuous data were expressed as mean ± standard deviation if normally distributed and as median and range or interquartile range (IQR) otherwise; categorical variables were expressed as percentages.

Patients were stratified according to the NCCN risk group classification into low-, intermediate- and high-risk groups: "low risk" was defined as PSA level ≤10 ng ml^{-1}, Gleason score ≤6 and Stage T1–T2a; "intermediate risk" was defined as one or more risk factors: PSA level 10–20 ng ml^{-1}, Gleason score 7 and

Figure 1. CONSORT flow diagram of the study. EBRT, external beam radiotherapy; LDR-BT, low-dose-rate brachytherapy.



Stage T2b–T2c; and "high risk" was defined as one or more risk factors: PSA >20 ng ml^{-1}, Gleason score >7 and Stage ≥T3a.[11]

BF was considered according to the Phoenix definition (PSA nadir plus 2 ng ml^{-1}).[13] Biochemical failure-free survival (BFFS) was calculated from the date of implantation to the date of event or latest follow-up.

Disease-specific survival and overall survival (OS) were calculated from date of implantation to date of death or latest follow-up. Survival experience was represented by the Kaplan–Meier approach, with differences between groups evaluated by the log-rank test. Multivariable Cox regression model including NCCN risk group classification, D_{90}, post-implant V_{100}, neoadjuvant AD therapy, patient age and prostatic volume at implant was used to evaluate the relationship of covariates with BFFS. All tests were two-sided.

RESULTS

11 Italian institutions provided clinical data of consecutive patients treated with LDR-BT for clinically localized prostate cancer. Between May 1998 and 31 December 2013, 2706 consecutive patients were treated. However, 380 patients did not reach a minimum follow-up of 2 years and an additional 89 patients were treated with a combination of LDR-BT and EBRT. All these patients were excluded. The last patient with at least 2 years of follow-up was treated on 27 December 2011 and the final number of included patients was 2237 (Figure 1).

Patient characteristics

The mean age of patients was 67 ± 7 years with a median pre-treatment PSA value of 6.5 ng ml^{-1} (PSA range: 0.64–96) and the mean pre-implant prostate volume (including the effect of an eventual neoadjuvant AD) of 35.7 ± 9.7 cm^3.

According to the NCCN risk group classification, 66.4% (1485/2237) of the patients were classified as belonging to low-risk group, 26.0% (582/2237) patients as belonging to intermediate-risk group and 1.8% (41/2237) patients as belonging to high-risk group, while 5.8% (129/2237) patients could not be unequivocally categorized (Table 1).

Table 2 reports the proportion of patients who had received AD before BT within each NCCN risk group. The higher the NCCN risk classification, the greater the proportion of patients with a history of AD before LDR-BT implantation.

Treatment procedures

A similar BT protocol was carried out by all 11 institutions. In all the institutions, a multidisciplinary uro-oncologic team, caring also for patients with prostate cancer, was active.

Seed implantation was performed using a transperineal approach with transrectal ultrasound guidance. The radioactive isotope implanted was iodine-125 (^{125}I) in most of the cases and palladium-103 (^{103}Pd) in some of the most dated cases. The intended prescribed dose was changed depending on the isotope used (145 Gy and 135 Gy using ^{125}I and ^{103}Pd, respectively). Dose was prescribed to the prostate volume as defined at ultrasound images and a choice of a margin around prostate was operator dependent, usually ranging between 3 and 5 mm to account for possible extraprostatic extension and for seed release uncertainties.

Neoadjuvant AD therapy with an antiandrogen and/or a luteinizing hormone-releasing hormone analogue was prescribed mainly for volume reduction in patients with large prostate for a short period (3–6 months; median 4 months).[14]

Post-implant CT dosimetry was performed within 1 month (mainly on Day 30) of implantation.[15]

Patients were followed up every 3–6 months with PSA assays for the first 2 years and every 6–12 months thereafter.

Treatment data

^{125}I and ^{103}Pd seeds were implanted in 2185 (97.7%) patients and 52 (2.3%) patients, respectively. The mean D_{90} was 146 Gy (±28 Gy) for patients with ^{125}I seeds and 130 Gy (±24 Gy) for patients with ^{103}Pd seeds; the V_{100} was 91.2% (±7.4%) for patients with ^{125}I seeds and 87.9% (±8.1%) for patients with ^{103}Pd implants (Table 3).

Outcome data

The overall median follow-up time was 65 months (IQR: 42–93 months). 204 deaths were recorded. 172 patients died without any BF, while 32 males died after a BF. For 26 of them, the fatal event was related to metastatic disease progression (Table 4). The 3-, 5- and 7-year OS rates were 96.7, 94.0 and

Table 1. Baseline characteristics

Age, categorical (number of patients) (%)	
<50 years	11 (0.5)
50–59 years	320 (14.3)
60–69 years	966 (43.2)
70–79 years	915 (40.9)
≥80 years	25 (1.1)
Age, continuous (years)	
Mean (SD)	67 (7)
Median (range)	68 (39–86)
NCCN risk group classification (number of patients) (%)	
Low risk	1485 (66.4)
Intermediate risk	582 (26.0)
High risk	41 (1.8)
N/A	129 (5.8)
Gleason score (number of patients) (%)	
≤6	1861 (83.2)
7	271 (12.1)
>7	28 (1.3)
N/A	77 (3.4)
T stage[a] (number of patients) (%)	
T1 (a, b, c)	1597 (71.4)
T2–T2a	354 (15.8)
T2b–T2c	141 (6.3)
T3 (a, b, c)	1 (0.1)
N/A	144 (6.4)
PSA category at entry (number of patients) (%)	
≤10 ng ml^{-1}	1937 (86.6)
10–20 ng ml^{-1}	260 (11.6)
>20 ng ml^{-1}	14 (0.6)
N/A	26 (1.2)
PSA at entry (ng ml^{-1})	
Median (range)	6.5 (0.64–96)
Neoadjuvant AD therapy (number of patients) (%)	
No	1099 (49.1)
Yes	882 (39.4)
N/A	256 (11.5)
Pre-implant prostate volume (cm^3)	
N	2115
Mean (SD)	35.7 (9.7)
Median (range)	35.0 (11.5–83.5)

AD, androgen deprivation; N/A, not available; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen; SD, standard deviation.
[a]American Joint Committee on Cancer staging, 7th edn, 2009.

Table 2. Neoadjuvant androgen deprivation (AD) therapy and risk group classification

Neoadjuvant AD therapy	NCCN risk group classification				
	Low	Intermediate	High	N/A	Total
	Number of patients (%)	Number of patients (%)	Number of patients (%)	Number of patients (%)	Total number of patients (%)
No	795 (58.0)	248 (48.1)	8 (36.4)	48 (66.7)	1099 (55.5)
Yes	576 (42.0)	268 (51.9)	14 (63.6)	24 (33.3)	882 (44.5)
Total with AD therapy information	1371	516	22	72	1981
N/A	114	66	19	57	256
Total	1485	582	41	129	2237

N/A, not available; NCCN, National Comprehensive Cancer Network.

89.2%, respectively, and the 3-, 5- and 7-year disease-specific survival rates were 99.7, 99.5 and 98.4%, respectively (Figure 2).

207 patients experienced a BF and 175 of them were alive at the last follow-up. The median time elapsed between LDR-BT implantation and occurrence of BF was approximately 42 months (IQR: 24–64 months) (Table 4). The 3-, 5- and 7-year BFFS was 95.7, 91.9 and 88.5%, respectively (Figure 3 and Table 5).

Multivariate analysis showed that BFFS was significantly higher among patients in the low-risk group ($p < 0.0001$) and close to be significantly higher among those with $V_{100} \geq 90\%$ ($p = 0.09$). In particular, after inclusion of the interaction term of the two factors in the model, we found that $V_{100} \geq 90\%$ increased BFFS only in the subset of patients in the low-risk group [relative risk = 0.53 (95% confidence interval: 0.33–0.84], while no effect was found among the patients in the intermediate-/high-risk group [relative risk = 1.09 (95% confidence interval: 0.69–1.74); $p = 0.04$] for the interaction term. No other factor exhibited significant influence on BFFS (Table 5).

To check for potential prognostic factors on OS, we performed univariate and multivariate analyses. The intermediate-/high-risk group showed the worst OS compared with the low-risk group ($p = 0.04$ and $p = 0.07$, respectively); OS was also worst in elderly patients ($p < 0.0001$) (Table 6).

DISCUSSION

This early report is a retrospective multicentre cohort study and gives an efficient picture of the practice of BT in Italy, including

Table 3. Treatment modality and dosimetry

Dosimetry	Radioactive isotope		Total
	^{125}I	^{103}Pd	
	$N = 2185$	$N = 52$	$N = 2237$
D_{90} (Gy)			
N	2173	50	2223
Mean (SD)	146 (28)	130 (24)	145 (28)
Median (IQR)	149 (124–167)	134 (123–146)	149 (124–166)
D_{90} (% of the prescribed dose)			
N	2173	50	2223
Mean (SD)	1.01 (0.2)	0.97 (0.17)	1.01 (0.2)
Median (IQR)	1.03 (0.86–1.15)	0.99 (0.91–1.08)	1.03 (0.86–1.15)
V_{100} (%)			
N	2172	52	2224
Mean (SD)	91.2 (7.4)	87.9 (8.1)	91.1 (7.4)
Median (IQR)	93 (89–96)	90 (87–93)	93 (89–96)

^{125}I, iodine-125; ^{103}Pd, palladium-103; D_{90}, dose received by 90% of target volume; IQR, interquartile range; SD, standard deviation; V_{100}, target volume receiving 100% of the prescribed dose.

Table 4. Events

Outcomes	*N* (%)
Follow-up duration (months)[a] (%)	
Mean (SD)	69 (34)
Median (IQR)	65 (42–93)
Vital status (number of patients) (%)	
Alive	2033 (90.9)
Dead	204 (9.4)
Death without BF	172
≤24 months	33
>24 months	139
Death after BF	32
≤24 months	1
>24 months	31
Of whom owing to prostatic cancer	26
BF (number of patients) (%)	
No	2030 (90.7)
Yes	207 (9.3)
Alive at the last follow-up	175
Death after BF	32
Time to BF (months)[a]	
N	207
Mean (SD)	48 (29)
Median (IQR)	42 (24–64)

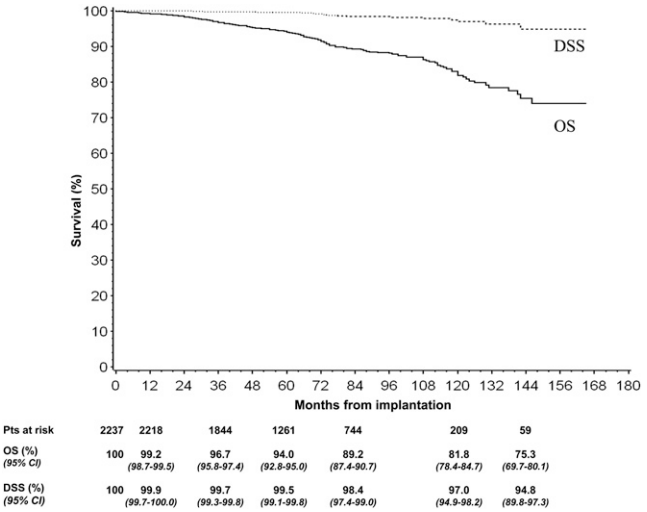
BF, biochemical failure; IQR, interquartile range; SD, standard deviation.
[a]From date of low-dose-rate brachytherapy implantation.

11/13 centres practising it and most of the patients treated in Italy. To the best of our knowledge, this is the largest LDR-BT European series ever reported.

Our results indicate that an implant of good quality, both for case selection and post-implant dosimetric parameters, has been obtained in most patients. The selection criteria show adherence to accepted guidelines based on the European Society for Radiotherapy and Oncology–European Association of Urology–European Organization for Research and Treatment of Cancer recommendations,[16,17] with implant being used for 66.4% of cases in the low-risk group and 26.0% of cases in the intermediate-risk group, with a prescribed dose of 145 Gy for I^{125}; a short AD therapy, was given to 39.4% of patients (mainly for downsizing). Post-implant data show a mean D_{90} of 146 Gy and a mean V_{100} value of 91.2% for patients with I^{125} implants.

The BFFS rates at 5 and 7 years were estimated to be 91.9% and 88.5% for the whole group, respectively, with an event rate of 6.3% (93/1485) in the low-risk group, 15.6% (91/582) in the intermediate-risk group and 24.4% (10/41) in the high-risk group, respectively ($p < 0.0001$). Our results, in agreement with

Figure 2. Kaplan–Meier analysis of overall survival (OS) and disease-specific survival (DSS) with 95% confidence interval (CI). Pts, patients.



other multi-institutional reports[5–8,10] and with two recently published monoinstitutional series,[18,19] indicate that LDR-BT with permanent implant as monotherapy is an adequate modality for the radical treatment of low- and intermediate-risk prostate cancer. Only 89 patients with unfavourable factors were treated combining BT and EBRT and were excluded in the present analysis. Durable cancer control was reported with the BT and EBRT combination in these patients,[20] but there may be an increased toxicity,[21] and LDR-BT alone can produce excellent biochemical control for low- as well as intermediate-risk disease.[4]

Approximately 40% of patients in the present series had previously undergone neoadjuvant AD therapy for 3–6 months. This short period of AD did not impact on BFFS. This is in agreement with other reports.[10,22]

Figure 3. Kaplan–Meier analysis of biochemical failure-free survival (BFFS) with 95% confidence interval (CI). Pts, patients.

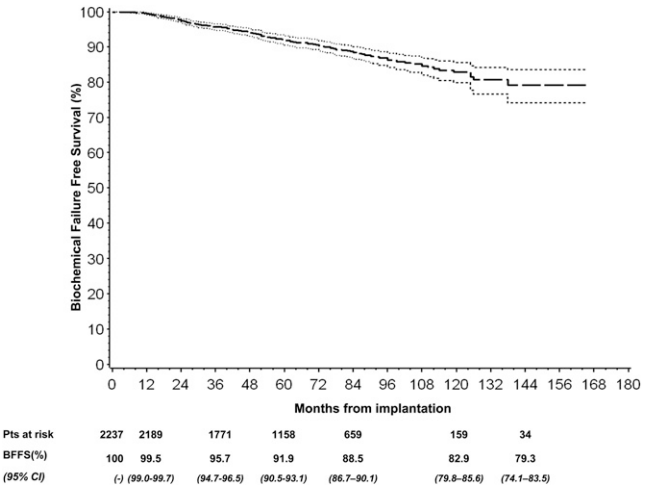


Table 5. Biochemical failure-free survival (BFFS) in subgroups

Subgroups	Total	Events	Univariate analysis				Multivariate analysis[c]	
			3-year BFFS (%)	5-year BFFS (%)	7-year BFFS (%)	*p*-value[a]	RR (95% CI)	*p*-value[b]
All patients[b]	2237	207	95.7	91.9	88.5			
NCCN risk group classification								
Low risk	1485	93	97.0	94.8	92.8	<0.001	1	
Intermediate risk	582	91	93.8	86.0	78.4		2.60 (1.93–3.51)	<0.0001
High risk	41	10	78.9	73.0	73.0		3.02 (1.38–6.60)	0.006
V_{100} (%)								
<90%	642	77	95.3	90.1	86.4	0.03	1	
≥90%	1582	128	96.0	92.8	89.5		0.76 (0.55–1.04)	0.09
D_{90} (% of the prescribed dose)								
<90%	668	62	95.8	91.1	89.1	0.49	1	
≥90%	1555	143	95.8	92.3	88.5		1.01 (0.72–1.42)	0.93
Neoadjuvant AD therapy								
No	1099	96	96.3	92.6	89.2	0.59	1	
Yes	882	80	95.8	92.0	89.1		0.79 (0.58–1.07)	0.13
Radioactive isotope								
^{125}I	2185	202	95.7	91.9	85.5	0.45	1	
^{103}Pd	52	5	96.1	91.7	89.1		0.92 (0.37–2.25)	0.85
Age (years)								
<55	102	7	96.9	95.7	90.9	0.42	1	
55–64	637	56	94.6	93.4	90.8		1.31 (0.59–2.88)	0.51
65–74	1187	112	96.3	91.5	88.0		1.38 (0.64–2.97)	0.42
≥75	311	32	95.2	88.7	84.7		1.50 (0.65–3.46)	0.34
Interactions[d]								
NCCN risk group–V_{100}								
≥90% *vs* <90% (low-risk group)							0.53 (0.33–0.84)	0.04
≥90% *vs* <90% (intermediate-/high-risk group)							1.09 (0.69–1.74)	
NCCN risk group–neoadjuvant AD therapy								
AD therapy *vs* no AD therapy (low-risk group)							0.56 (0.35–0.89)	0.07
AD therapy *vs* no AD therapy (intermediate-/high-risk group)							1.09 (0.69–1.71)	

(Continued)

Table 5. (Continued)

Subgroups	Total	Events	Univariate analysis				Multivariate analysis[c]	
			3-year BFFS (%)	5-year BFFS (%)	7-year BFFS (%)	*p*-value[a]	RR (95% CI)	*p*-value[b]
NCCN risk group–radioactive isotope								
^{103}Pd *vs* ^{125}I (low-risk group)							0.43 (0.10–1.76)	0.10
^{103}Pd *vs* ^{125}I (intermediate-/high-risk group)							2.34 (0.72–7.61)	

^{125}I, iodine-125; ^{103}Pd, palladium-103; AD, androgen deprivation; CI, confidence interval; D_{90}, dose received by 90% of target volume; NCCN, National Comprehensive Cancer Network; RR, relative risk; V_{100}; target volume receiving 100% of prescribed dose.
The sum of the number of patients among levels of a variable could be not equal to the total number of patients ($N = 2237$).
The "not available (N/A)" subgroups, although included both in univariate and multivariate models, have not been shown in this table.
[a]Log-rank test for univariate analysis.
[b]Wald test from Cox regression multivariate model.
[c]Includes NCCN risk group, V_{100}, D_{90}, neoadjuvant AD therapy, radioactive isotope, age and prostatic volume at implantation.
[d]Includes the same variables of [c] plus the interaction term.

The impact of post-implant dosimetric parameters on BFFS in multi-institutional studies is not univocal. Zelefsky et al[5] noted a significant impact of D_{90} on BFFS after a median follow-up of 63 months. These data are reinforced by Stone et al.[9] Contrarily, no post-implant dosimetric factors predicted for biochemical control in a UK multi-institutional series with a median follow-up of 21 months.[7] Morris et al[8] reported results of the British Columbia Cancer Agency BT database after a median follow-up of 7.5 years: D_{90} values of <130 Gy were predictive of an increased risk of recurrence but only for the subset of males who did not receive AD therapy.[10] In our cohort, post-implant V_{100}, but not D_{90}, impacted significantly on biochemical control, in spite of a strict correlation between them. The 5- and 7-year BFFS was 90.1 *vs* 92.8% and 86.4 *vs* 89.5% for V_{100} <90% *vs* ≥90% ($p = 0.03$), whereas the difference was not statistically significant for D_{90} <130 Gy or ≥130 Gy ($p = 0.49$). These results were confirmed after multivariate analysis ($p = 0.09$ and $p = 0.93$, respectively). We think that this may be a consequence of the preponderance of good-quality implants in the present series: only 30% (668/2237) of patients had a D_{90} <90% of the prescribed dose and median D_{90} was 149 Gy for patients with I^{125} seeds. Furthermore, the evaluation of post-implant dosimetric parameters and their impact on BFFS may be less robust owing to differences in post-planning CT timing and interpretation among different institutions;[23] the average D_{90} in our cohort had a standard deviation of 28 Gy. A more standard approach to volume delineation should be an important aspect of quality assurance in prostate BT.[17] As stated by Morris et al[10] in their study, "dose metrics are not equivalent to oncologic end points and must be calibrated against disease-free survival using biochemical and clinical end points for each institution".

Prostate BT seems comparable with both EBRT and RP.[4,24] No randomized trials are available and many comparative outcome studies are largely single-centre studies with limited generalizability, and a population-based study provides the best outcome data. This report details PSA and OS outcomes after LDR-BT in a large and consecutive population-based cohort of patients and together with other multi-institutional studies,[5–8,10] it might give more generalizable data.

There are several limitations of our study. Firstly, data were collected retrospectively. Not all the institutions provided sufficient data and not all the information we had planned to get were actually available in the local databases. The lack of important covariates (comorbidity, smoking history, centre-specific policy regarding frequency of PSA testing during all over the follow-up and site of clinical failure) results in a substantial loss of strength of our multivariate and subgroup analyses. Secondly, the median follow-up was only of 65 months; this time is too short for a substantial evaluation of the real biochemical outcome after a radical treatment. This relatively short follow-up duration and the high rate of patients lost to long-term follow-up produce a loss of power for the 10-year survival estimates. For this reason, in our analysis, we showed estimates at earlier time points.

Thirdly, although these LDR-BT results are encouraging, our series may include the selection bias, especially in the intermediate-risk group (selection of more favourable cases). Therefore, direct comparison of our findings in the intermediate-risk patients with those obtained with other treatment modalities such as EBRT and RP should be performed with caution.

Finally, our study does not provide any data on BT side effects. Evaluation of treatment sequelae in a retrospective multi-institutional study is difficult and uncertain. Still, BT complications and their impact on quality of life in the series of a participating centre have been reported.[25]

Table 6. Overall survival (OS) in subgroups

Subgroups	Total	Events	Univariate analysis				Multivariate analysis[c]	
			3-year OS[c] (%)	5-year OS (%)	7-year OS (%)	*p*-value[a]	RR (95% CI)	*p*-value[b]
All patients[b]	2237	204	96.7	94.0	89.0			
NCCN risk group classification								
Low risk	1485	117	97.2	94.7	91.1	0.001	1	
Intermediate risk	582	69	95.3	91.9	85.7		1.37 (1.01–1.87)	0.04
High risk	41	8	92.9	89.6	77.1		2.12 (0.94–4.76)	0.07
V_{100} (%)								
<90%	642	54	97.6	94.7	90.1	0.16	1	
≥90%	1582	146	96.4	93.8	89.1		1.30 (0.92–1.85)	0.14
D_{90} (% of the prescribed dose)								
<90%	668	50	96.6	93.9	89.9	0.43	1	
≥90%	1555	150	96.9	94.2	89.2		1.22 (0.85–1.76)	0.28
Neoadjuvant AD therapy								
No	1099	89	97.2	94.0	89.7	0.30	1	
Yes	882	99	95.9	93.3	88.6		0.98 (0.73–1.32)	0.90
Radioactive isotope								
^{125}I	2185	197	96.6	94.1	89.3	0.96	1	
^{103}Pd	52	7	98.0	91.6	86.6		1.29 (0.60–2.78)	0.51
Age (years)								
<55	102	1	99.0	99.0	99.0	<0.0001	0.05 (0.01–0.39)	0.001
55–64	637	38	97.9	96.5	92.7		0.33 (0.21–0.52)	<0.0001
65–74	1187	117	96.0	92.9	88.4		0.55 (0.39–0.77)	<0.001
≥75	311	48	95.9	91.2	81.5		1	–

^{125}I, iodine-125; ^{103}Pd, palladium-103; AD, androgen deprivation; CI, confidence interval; D_{90}, dose received by 90% of target volume; NCCN, National Comprehensive Cancer Network; RR, relative risk; V_{100}, target volume receiving 100% of prescribed dose.
The sum of the number of patients among levels of a variable could be not equal to the total number of patients ($N = 2237$).
The "not available (N/A)" subgroups, although included both in univariate and multivariate models, have not been shown in this table.
[a]Log-rank test for univariate analysis.
[b]Wald test from Cox regression multivariate model.
[c]Includes NCCN risk group, V_{100}, D_{90}, neoadjuvant AD therapy, radioactive isotope, age and prostatic volume at implantation.

The retrospective character of our report carries the well-known risks of missing data and selection bias. However, our report provides information on BT results in nearly all patients who underwent LDR-BT in Italy. Reporting these data is now particularly crucial for a realistic comparison with other modalities of radical treatment, such as new surgery and radiotherapy techniques or radiotherapy fractionation schemes, which are rapidly spreading in the community,[26,27] despite a less mature evidence of efficacy and perhaps a higher cost.

CONCLUSION

In conclusion, the findings in this largest European series are in agreement with those previously reported in literature and confirm that LDR-BT is an excellent curative modality for low- and intermediate-risk prostate cancer. The work of the multidisciplinary team involved in the treatment of patients with prostate cancer may help to select adequately patients to be treated with BT and this may impact on the implant quality and possibly on outcome.

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