ONLINE FIRST

This is a provisional PDF only. Copyedited and fully formatted version will be made available soon.

REPORTS OF PRACTICAL
ONCOLOGY AND
RADIOTHERAPY

ISSN: 1507-1367

e-ISSN: 2083-4640

Ultra-low dose rate brachytherapy (uLDR-BT) in treatment of patients with unfavorable intermediate-risk group prostate cancer — retrospective analysis

Authors: Adam Kluska, Artur Chyrek, Wojciech Maria Burchardt, Marcin Włodarczyk, Grzegorz Bielęda, Adam Chicheł

DOI: 10.5603/rpor.103135

Article type: Research paper

Published online: 2024-10-31

Ultra-low dose rate brachytherapy (uLDR-BT) in treatment of patients with unfavorable intermediate-risk group prostate cancer — retrospective analysis

DOI: 10.5603/rpor.103135

Adam Kluska[1], Artur Chyrek[1, 2], Wojciech Maria Burchardt[1, 2], Marcin Włodarczyk[3], Grzegorz Bielęda[1, 2], Adam Chicheł[1]

[1]Brachytherapy Department, Greater Poland Cancer Centre, Poznan, Poland

[2]Electroradiology Department, Poznan University of Medical Sciences, Poznan, Poland

[3]Breast Surgical Oncology Department, Greater Poland Cancer Centre, Poznan, Poland, Poznan, Poland

[4]Medical Physics Department, Greater Poland Cancer Centre, Poznan, Poland

Corresponding Author: Adam Kluska, Greater Poland Cancer Centre, Brachytherapy, Garbary 15, 61–866 Poznan, Poland; e-mail: adam.kluska@wco.pl

Abstract

Background: Treatment with sole ultra-low dose rate brachytherapy (uLDR-BT) for unfavorable intermediate risk factor (IUR) group prostate cancer patients is not recommended by guidelines due to the lack of strong evidence of its effectiveness. However, there were numerous patients treated with good results with this method in older trials. Purpose of this work was to retrospectively asses effectiveness of uLDR-BT in IUR group treated in our department.

Materials and methods: We performed retrospective analysis of 39 IUR prostate cancer patients treated in our department with uLDR-BT between 2015–2019. All Patients had confirmed prostate cancer in biopsy and had local staging assessed with digital rectal examination and either transrectal ultrasound (TRUS) or magnetic resonance imaging (MRI) before treatment. Treatment was performed using ^{125}I seeds, and the dose prescribed to the clinical target volume was 145 Gy. After treatment, all patients were followed in our outpatient ambulatory one month after the procedure and every 3–6 months later on. Toxicity was assessed using the International Prostate Symptom Score (IPSS) and Radiation Therapy Oncology Group (RTOG) scales.

Results: The median follow-up was 56,3 months [interquartile range (IQR): 36.9–73.4]. The mean nadir prostate-specific antigen (PSA) was 0.20 ng/mL (range 0.001–1.7). The actuarial 5-year biochemical failure-free survival (BFFS) was 87.02%. There was no statistically significant difference in BFFS between groups with antigen deprivation therapy (ADT) and without ($p = 0.439$). Analysis also showed no impact on BFFS of each intermediate group risk factors: initial PSA (iPSA) ($p = 0.595$). Gleason ($p = 0.671$) and Tumor stage ($p = 0.694$). There were no statistically significant differences in BFFS depending on number of those factors ($p = 0.330$). Conclusion The uLDR-BT may be an effective option for selected IUR prostate cancer patients.

Key words: prostate cancer; brachytherapy; low-dose brachytherapy

Introduction

Prostate cancer remains one of the most common cancers in men worldwide. Brachytherapy (BT), together with external beam radiotherapy (EBRT) and radical prostatectomy, is effective and widely used as monotherapy for low-risk and favorable intermediate-risk prostate cancer [1]. Besides, BT plays a relevant role in combined therapy as a boost in treating unfavorable intermediate-risk (IUR) and high-risk prostate cancer [1]. Depending on the radiation delivery rate, BT is divided into high-dose-rate (HDR), where the dose is delivered by temporal implantation of a radioactive source using applicators, and ultra-low-dose rate (uLDR), with the dose delivered with permanent seeds implantation [iodine-125 (^{125}I)**, ^{103}Pd or ^{131}Cs).** Rate of dose of uLDR is defined as 0.01–0.3 Gy/h and is lower than in traditional LDR (**^{226}Ra, ^{137}Cs**) which is defined by the International Commission on Radiation Units and Measurements (ICRU) 38 report as 0.4–2 Gy/h [2]. Guidelines define IUR as prostate cancer without high-risk factors and with Gleason 4+3, or with at least 2 of intermediate risk factors: Gleason 3 + 4, prostate-specific antigen (PSA) > 10 ng/mL, local stage of T2b/T2c or one intermediate risk factor and 50% or more biopsy cores positive [3]. National Comprehensive Cancer Network (NCCN) recommends two treatment options for UIR: prostatectomy with or without lymphadenectomy or combined treatment of EBRT with antigen deprivation therapy (ADT) and BT boost [3]. Treatment with sole uLDR-BT for IUR group prostate cancer patients is not recommended as a standard treatment by guidelines due to the lack of solid evidence of its effectiveness. It may be only an option for patients unwilling to undergo the treatment recommended above [1, 3]. However, in some trials regarding the efficacy of this method in the intermediate group, numerous patients were treated with promising results [4, 5]. As far as we are concerned, no prospective trials compared uLDR-BT as monotherapy in treating IUR with other treatment methods, including combined treatment of EBRT, BT and ADT. There are few retrospective analyses and validations of new risk stratification groups in previously intermediate group patients treated with BT monotherapy [6, 7]. Some showed worse results of BT monotherapy [8]; others found no differences with combined treatment and reported the benefit of BT monotherapy compared to EBRT alone in this group [6, 9]. The purpose of this work was to retrospectively assess the effectiveness of uLDR-BT in the IUR group treated in our department.

Materials and methods

We reviewed the department's database of patients treated with iodine-125 (^{125}I) uLDR-BT to identify intermediate-risk patients. In a retrospective analysis, 39 IUR prostate cancer patients were identified. They were treated with ^{125}I uLDR-BT monotherapy between 2015–2019. All patients had confirmed prostate cancer in biopsy and had local staging assessed with digital rectal examination and either TRUS or MRI before treatment. Treatment was performed using ^{125}I seeds (Eckert & Ziegler BEBIG® stranded seeds Isocord®) with activity between 0.45 and 0.48 mCi and the rate of dose at the beginning of the therapeutic process about 0.07 Gy/h. Rate of dose decreased during treatment to 0.007 Gy/h on the 200th day after source application and to 0.001 Gy/h after one year. The dose prescribed to the clinical target volume, which was prostate with a 1-3 mm margin, was 145 Gy. Treatment was planned using transrectal ultrasound (TRUS) (BK Medical Pro Focus 2202), integrated with a dedicated treatment planning system (SPOT Pro 3.1, Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden). From 2018 on, the treatment was performed using BK Medical Pro Focus 3000 and OncentraProstate v. 4.1 (Elekta Company, Elekta AB, Stockholm, Sweden) planning system. The application of ^{125}I seeds was conducted under general anesthesia. During treatment planning, dose constraints for clinical target volume (CTV) and organs at risk were fulfilled according to Groupe Européen de Curiethérapie–Advisory Committee for Radiation Oncology Practice–European Society for Radiotherapy and Oncology (GEC-ACROP-ESTRO) guidelines with an additional constraint of D2 ccm of less than 70 Gy for the bladder

[10]. Throughout the insertion of the radioactive sources, after the insertion of each needle, the position of the sources was updated relative to the initial treatment plan. Such an approach ensures that the reported post-treatment plan is consistent with the actual location of the seeds. Computed tomography was done one day after application with a catheter still in the bladder for source position verification.

Further verification with CT was performed one month and six months after the seeds implantation. After treatment, all patients were followed in our outpatient ambulatory one month after the procedure, every three months during the first year, and every 3-6 months later, with laboratory tests, including PSA, on each visit. Biochemical failure was determined using the Phoenix definition. Treatment toxicity was assessed using the International Prostate Symptom Score (IPSS) and Radiation Therapy Oncology Group (RTOG) scales. Statistical tests and figures were made using Statistica v. 13 (Statsoft, Tulsa, USA). An unpaired t-test was used to compare differences between groups and repeated measures ANOVA was used to compare differences between IPSS scores. Kaplan-Meier analysis was done for biochemical failure-free survival. A log-rank test was used to compare survival between two groups, and a chi-square test was used to compare more than two groups. P-values below 0.05 were considered statistically significant.

Results

We enrolled in the analysis 39 patients with IUR prostate cancer. The median age was 69 [interquartile range (IQR) 64–75]. Tumor–Nodules–Metastasis (TNM) staging was determined in all patients before treatment: T1c — 6 patients, T2a — 9 patients, T2b — 10 patients, and T2c — 14 patients. Histopathology reports confirmed prostate adenocarcinoma in all patients, with Gleason 3 + 3 in 11 cases, 3 + 4 in 15, and 4 + 3 in 13 patients. The mean initial PSA was 10.61 (range 4.9–17.02). The mean prostate volume was 36.05 ml (range 11-70). Twenty-nine patients were given neoadjuvant or adjuvant ADT. The mean time of ADT was 7.5 months (range 1-24). All patients' characteristics are presented in Table 1.

The median follow-up was 56.3 months [IQR 36,9-73,4]. The mean nadir PSA was 0.20 ng/mL (range 0.001–1.7). Nadir PSA in the group with ADT was 0.10 (range 0.001–1.34) and 0.485 (range 0.058–1.7) in the group with no ADT ($p = 0.011$). 31 from 39 patients reached nadir PSA below 0.2 ng/ml. Biochemical failure occurred in 6 cases. The actuarial 5-year biochemical failure-free survival (BFFS) was 87.02% (Fig. 1). Median time to BF was 32.75 months (IQR 21.52–60.55). There was no statistically significant difference in BFFS between groups with ADT and without (p = 0.439) (Supplementary File — Fig. S1). Analysis also showed no impact on BFFS of each intermediate group risk factors: initial PSA (iPSA) (p = 0.595) (Suppementary File — Fig. S2), Gleason (p = 0.671) (Supplementary File — Fig. S3) and tumor stage (p = 0.694) (Supplementary File — Fig. S4). There were no statistically significant differences in BFFS depending on number of those factors (p = 0.330) (Fig. 2). The actuarial 5-year BFFS in the group with nadir < 0.2 ng/mL was 88.11% and 80% in the group that did not reach < 0.2 ng/mL nadir level (p = 0.180).

There was only one case of RTOG grade 3 acute toxicity. No other acute or late toxicity higher than grade 2 was reported. Pre-treatment IPSS was scored only in 9 patients, with a mean score of 4.22 (range 0–10); 28 IPSS were collected at the first follow-up visit with a mean score of 12.29 (range 1–31). The mean score of the last recorded IPSS during follow-up (n = 32) was 6.09 (range 1–25) (p = 0.264) (Supplementary File — Fig. S5).

Discussion

The uLDR brachytherapy has well-defined efficiency in the treatment of low and favorable intermediate-risk prostate cancer, with 10-year BFFS of around 80% [11, 12]. Therefore, it is one of the recommended treatment options for these patients, concurrently with prostatectomy and EBRT [3]. There are no randomized trials comparing those modalities' effectiveness, but reports claim that BT has the lowest toxicity among those three [13, 14]. However, it is not recommended in IUR patients due to insufficient solid evidence, as no prospective randomized trials has compared this modality with standard treatment yet.

Prostatectomy or EBRT followed by BT boost, combined with ADT, are two options that are standard of care in this group [3]. Reliable evidence that one of those modalities is superior is lacking, and the difference in cancer-specific survival between both options is probably lower than 1% [15]. It was shown that the BFFS rate after prostatectomy in IUR is lower than in the favorable intermediate risk (FIR) group and amounts to 68% at four years, which may be linked to a higher rate of positive margins in this group in comparison to FIR (29.8% vs. 21.8%) [16]. Adding short-time ADT to high-dose radiotherapy improves 5-year BFFS in the intermediate group up to 84% [17]. Those rates are comparable to those achieved by BT monotherapy in some previous reports and with our findings. Frank et al. examined the efficiency of uLDR BT as monotherapy in the intermediate group. Selected patients with unfavorable risk factors were also enrolled in the study, as inclusion criteria were: stage up to

T2bN0, Gleason 6, with PSA level 10–15 ng/mL; or Gleason 7 with PSA < 10. The 5-year biochemical failure-free probability in the trial was 97.3% [5].

In another series, Pickles et al. researched effectiveness of this modality only in the IUR group, finding no difference if ADT was added with 5-year biochemical control of 86% in the ADT group and 85% without ADT [4]. This result corresponds to our findings.

In RTOG 0232 trial, Michalski et al. observed no difference in freedom from progression between uLDR brachytherapy alone and combined uLDR-BT with EBRT in selected IUR patients. Notwithstanding, combined treatment was linked with higher toxicity [18]. Those results correspond to the findings of Willen et al. which reported only a difference in toxicity between HDR-BT alone and combined with EBRT in IUR patients [19]. One of the studies showed an advantage of mono uLDR-BT compared to combined treatment with EBRT [6]. On the other hand, in validation of the NCCN subgroup conducted by Tom et al., authors observed that in the IUR group 5-year biochemical failure rate was significantly higher than in the FIR group (17% vs. 4%), and was higher in group with more risk factors. Once again, no impact of adding ADT was found [7]. Although these findings suggest that treatment escalation in the IUR group is justified, biochemical failure rates are similar to those reported in studies concerning standard treatment [16, 17].

In our analysis, 5-year BFFS was 87%, which is consistent with previously published studies. Also, similarly to other authors, we found no relevance of adding ADT, which has to be taken with caution, as disproportion between the number of patients that were given ADT and treated without it is relevant in our group. We found no statistically significant differences in BFFS, depending neither on risk factors nor number of those factors. However, it may be biased by a small number of subjects, as a trend toward a worse outcome with more risk factors is visible, similarly to findings of other authors [7]. We also did not observe significant variance depending on whether the patient reached the nadir level of less than 0,2 ng/mL, which is proven to be a significant factor associated with uLDR treatment success [20]. However, it may be due to a small number of patients that did not reach that level in our group. Our study has numerous limitations, such as its retrospective nature which leads to the lack of some data in a few subjects; the number of positive biopsy cores was not reported in all cases, which would provide further insight into the role of this risk factor in outcomes of uLDR treatment in this group. Lack of systematic and homogenous staging before treatment as not all patients were staged with one modality, which is a standard in prospectively conducted trials, made it impossible to correlate MRI findings with other clinical factors.

Another limitation is the small number of subjects in analysis and lack of 10-year BFFS endpoint with median follow up of only 56 months. Nevertheless, we believe that this study adds to the discussion whether uLDR BT may be effective in IUR prostate cancer. Prospective assessment of this treatment modality in this group of patients should be carried out, as should be randomized trials comparing it with standard treatment.

Conclusion

The uLDR-BT may be an effective option for selected IUR prostate cancer patients. There is a scope for prospective studies to fully establish this method's effectiveness in treating IUR prostate cancer.

Ethic statement

Ethical approval was not necessary for the preparation of this article.

Funding

This publication was prepared without any external source of funding.

Conflicts of interest

Authors declare no conflict of interests.

References

1. Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol. 2021; 79(2): 243–262, doi: 10.1016/j.eururo.2020.09.042, indexed in Pubmed: 33172724.
2. Yavaş G. Dose Rate Definition in Brachytherapy. Turk J Oncol. 2019, doi: 10.5505/tjo.2019.1924.
3. National Comprehensive Cancer Network. Prostate Cancer (Version 2.2023). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf (July 23, 2023).

4. Pickles T, Morris WJ, Keyes M. High-intermediate prostate cancer treated with low-dose-rate brachytherapy with or without androgen deprivation therapy. Brachytherapy. 2017; 16(6): 1101–1105, doi: 10.1016/j.brachy.2017.08.003, indexed in Pubmed: 29032014.

5. Frank SJ, Pugh TJ, Blanchard P, et al. Prospective Phase 2 Trial of Permanent Seed Implantation Prostate Brachytherapy for Intermediate-Risk Localized Prostate Cancer: Efficacy, Toxicity, and Quality of Life Outcomes. Int J Radiat Oncol Biol Phys. 2018; 100(2): 374–382, doi: 10.1016/j.ijrobp.2017.09.050, indexed in Pubmed: 29229325.

6. Tsumura H, Tanaka N, Oguchi T, et al. Direct comparison of low-dose-rate brachytherapy versus radical prostatectomy using the surgical definition of biochemical recurrence for patients with intermediate-risk prostate cancer. Radiat Oncol. 2022; 17(1): 71, doi: 10.1186/s13014-022-02046-x, indexed in Pubmed: 35410307.

7. Tom MC, Reddy CA, Smile TD, et al. Validation of the NCCN prostate cancer favorable- and unfavorable-intermediate risk groups among men treated with I-125 low dose rate brachytherapy monotherapy. Brachytherapy. 2020; 19(1): 43–50, doi: 10.1016/j.brachy.2019.10.005, indexed in Pubmed: 31813740.

8. Robin S, Chabaud S, Serre AA, et al. Eligibility criteria according to EAU/ESTRO/SIOG guidelines for exclusive iodine-125 brachytherapy for intermediate-risk prostate adenocarcinoma patients: impact on relapse-free survival. J Contemp Brachytherapy. 2021; 13(4): 373–386, doi: 10.5114/jcb.2021.108592, indexed in Pubmed: 34484351.

9. Andruska N, Fischer-Valuck BW, Carmona R, et al. Outcomes of Patients With Unfavorable Intermediate-Risk Prostate Cancer Treated With External-Beam Radiotherapy Versus Brachytherapy Alone. J Natl Compr Canc Netw. 2022; 20(4): 343–350.e4, doi: 10.6004/jnccn.2021.7061, indexed in Pubmed: 35193114.

10. Henry A, Pieters BR, André Siebert F, et al. UROGEC group of GEC ESTRO with endorsement by the European Association of Urology. GEC-ESTRO ACROP prostate brachytherapy guidelines. Radiother Oncol. 2022; 167: 244–251, doi: 10.1016/j.radonc.2021.12.047, indexed in Pubmed: 34999134.

11. Kittel JA, Reddy CA, Smith KL, et al. Long-Term Efficacy and Toxicity of Low-Dose-Rate ^{125}I Prostate Brachytherapy as Monotherapy in Low-, Intermediate-, and High-Risk Prostate Cancer. Int J Radiat Oncol Biol Phys. 2015; 92(4): 884–893, doi: 10.1016/j.ijrobp.2015.02.047, indexed in Pubmed: 25962627.

12. Henry AM, Al-Qaisieh B, Gould K, et al. Outcomes following iodine-125 monotherapy for localized prostate cancer: the results of leeds 10-year single-center brachytherapy experience. Int J Radiat Oncol Biol Phys. 2010; 76(1): 50–56, doi: 10.1016/j.ijrobp.2009.01.050, indexed in Pubmed: 20005453.

13. Ciezki JP, Weller M, Reddy CA, et al. A Comparison Between Low-Dose-Rate Brachytherapy With or Without Androgen Deprivation, External Beam Radiation Therapy With or Without Androgen Deprivation, and Radical Prostatectomy With or Without Adjuvant or Salvage Radiation Therapy for High-Risk Prostate Cancer. Int J Radiat Oncol Biol Phys. 2017; 97(5): 962–975, doi: 10.1016/j.ijrobp.2016.12.014, indexed in Pubmed: 28333019.

14. Lardas M, Liew M, van den Bergh RC, et al. Quality of life outcomes after primary treatment for clinically localized prostate cancer: a systematic review. Eur Urol. 2017; 72(6): 886–887, doi: 10.1016/j.eururo.2017.06.035, indexed in Pubmed: 28757301.

15. Roach M, Ceron Lizarraga TL, Lazar AA. Radical Prostatectomy Versus Radiation and Androgen Deprivation Therapy for Clinically Localized Prostate Cancer: How Good Is the Evidence? Int J Radiat Oncol Biol Phys. 2015; 93(5): 1064–1070, doi: 10.1016/j.ijrobp.2015.08.005, indexed in Pubmed: 26581143.

16. Beauval JB, Ploussard G, Cabarrou B, et al. Committee of Cancerology of the Association of French Urology. Improved decision making in intermediate-risk prostate cancer: a multicenter study on pathologic and oncologic outcomes after radical prostatectomy. World J Urol. 2017; 35(8): 1191–1197, doi: 10.1007/s00345-016-1979-z, indexed in Pubmed: 27987030.

17. Dubray BM, Beckendorf V, Guerif S, et al. Does short-term androgen depletion add to high-dose radiotherapy (80 Gy) in localized intermediate-risk prostate cancer? Intermediary analysis of GETUG 14 randomized trial (EU-20503/NCT00104741). J Clin Oncol. 2011; 29(15_suppl): 4521–4521, doi: 10.1200/jco.2011.29.15_suppl.4521.

18. Michalski JM, Winter KA, Prestidge BR, et al. Effect of Brachytherapy With External Beam Radiation Therapy Versus Brachytherapy Alone for Intermediate-Risk Prostate Cancer: NRG Oncology RTOG 0232 Randomized Clinical Trial. J Clin Oncol. 2023; 41(24): 4035–4044, doi: 10.1200/JCO.22.01856, indexed in Pubmed: 37315297.

19. Willen BD, Salari K, Zureick AH, et al. High-dose-rate brachytherapy as monotherapy versus as boost in unfavorable intermediate-risk localized prostate cancer: A matched-pair analysis. Brachytherapy. 2023; 22(5): 571–579, doi: 10.1016/j.brachy.2023.05.002, indexed in Pubmed: 37328337.

20. Crook JM, Tang C, Thames H, et al. A biochemical definition of cure after brachytherapy for prostate cancer. Radiother Oncol. 2020; 149: 64–69, doi: 10.1016/j.radonc.2020.04.038, indexed in Pubmed: 32442822.

Figure 1. Kaplan-Meier graph presents the cumulative proportion of biochemical failure-free survival (BFFS) in patients after low-dose-rate brachytherapy of unfavorable intermediate risk factor (IUR) prostate cancer

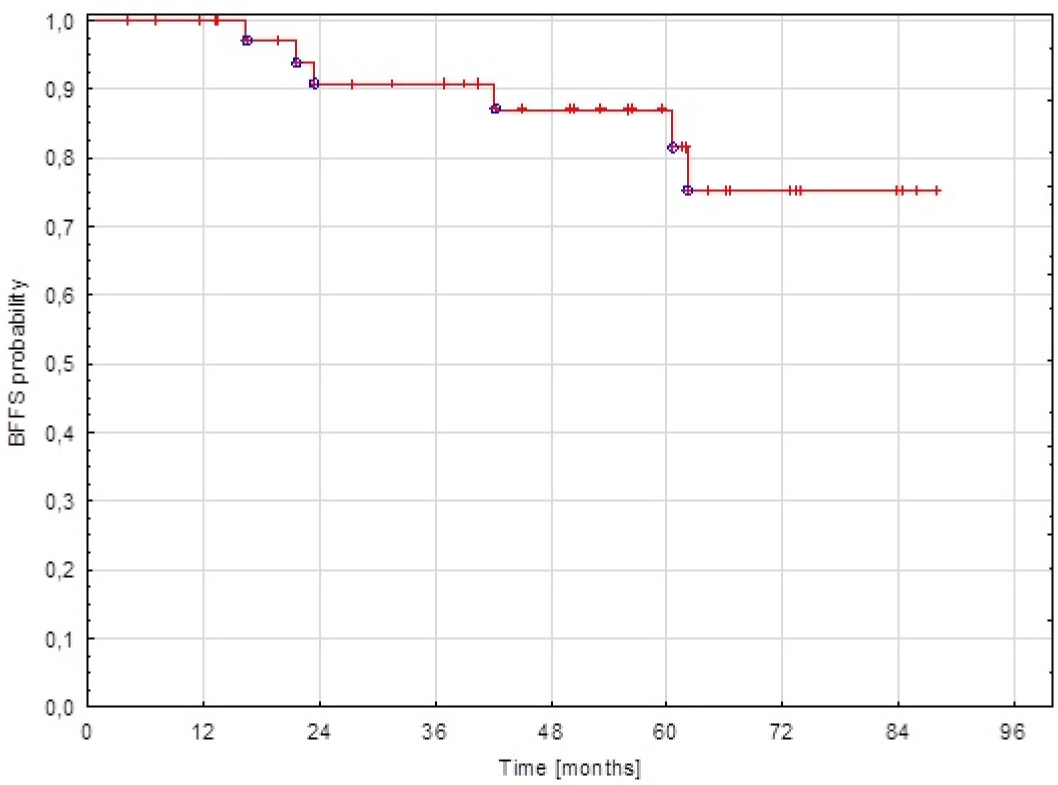

Figure 2. Comparison of the cumulative proportion of biochemical control in patients after low-dose rate brachytherapy of unfavorable intermediate risk factor (IUR) prostate cancer depending on the number of intermediate group risk factors (p = 0.330)

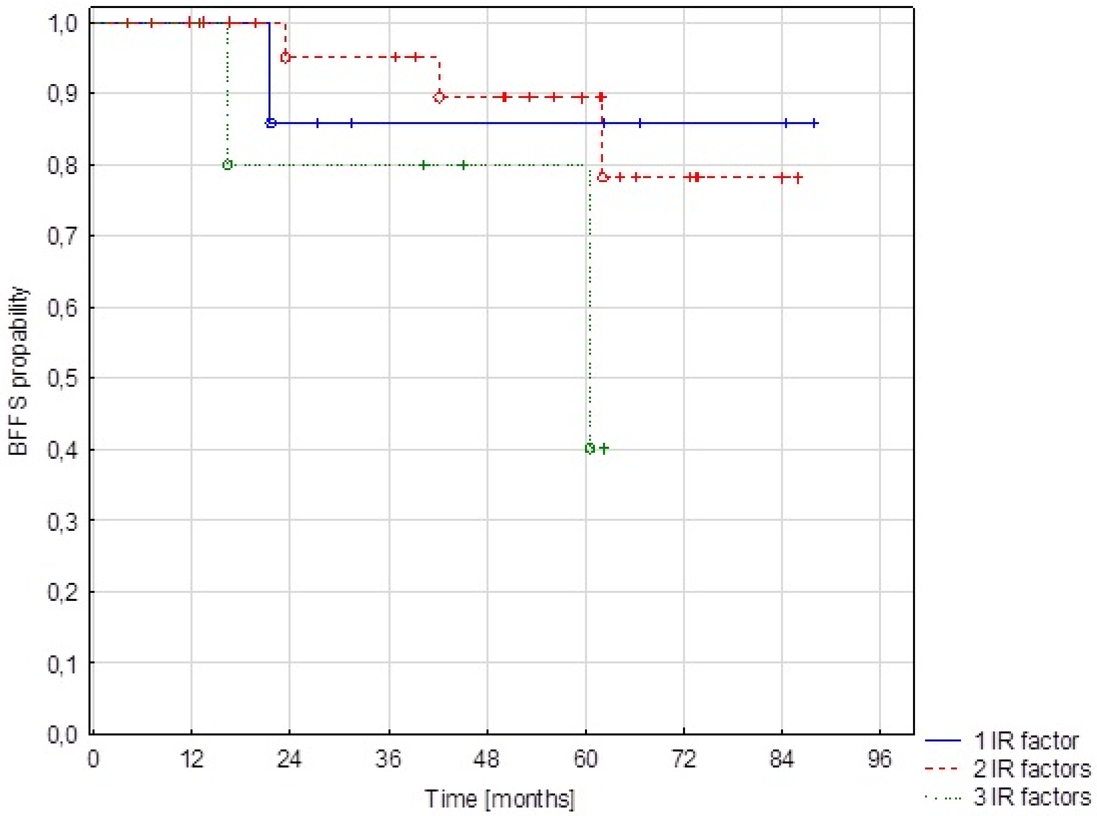

Table 1. Patient's characteristics

Age of patients [years]	
Median [IQR]	69 [64–75]
TNM	
T1cN0M0	6 (15%)
T2aN0M0	9 (23%)
T2bN0M0	10 (26%)
T2cN0M0	14 (36%)
Gleason Score	
Gleason 3 + 3	11 (28%)
Gleason 3 + 4	15 (39%)
Gleason 4 + 3	13 (33%)
ADT	
Yes	29 (74%)
No	10 (26%)
iPSA	
iPSA [ng/mL]	10,61

< 10 ng/mL	15 (39%)
> 10 ng/mL	24 (61%)
Number of IUR	
1	7 (18%)
2	27 (69%)
3	5 (13%)

IQR — interquartile range; TNM — tumor–node–metastasis; ADT — antigen deprivation therapy; iPSA — initial prostate-specific antigen; IUR — unfavorable intermediate risk factor

Supplementary File

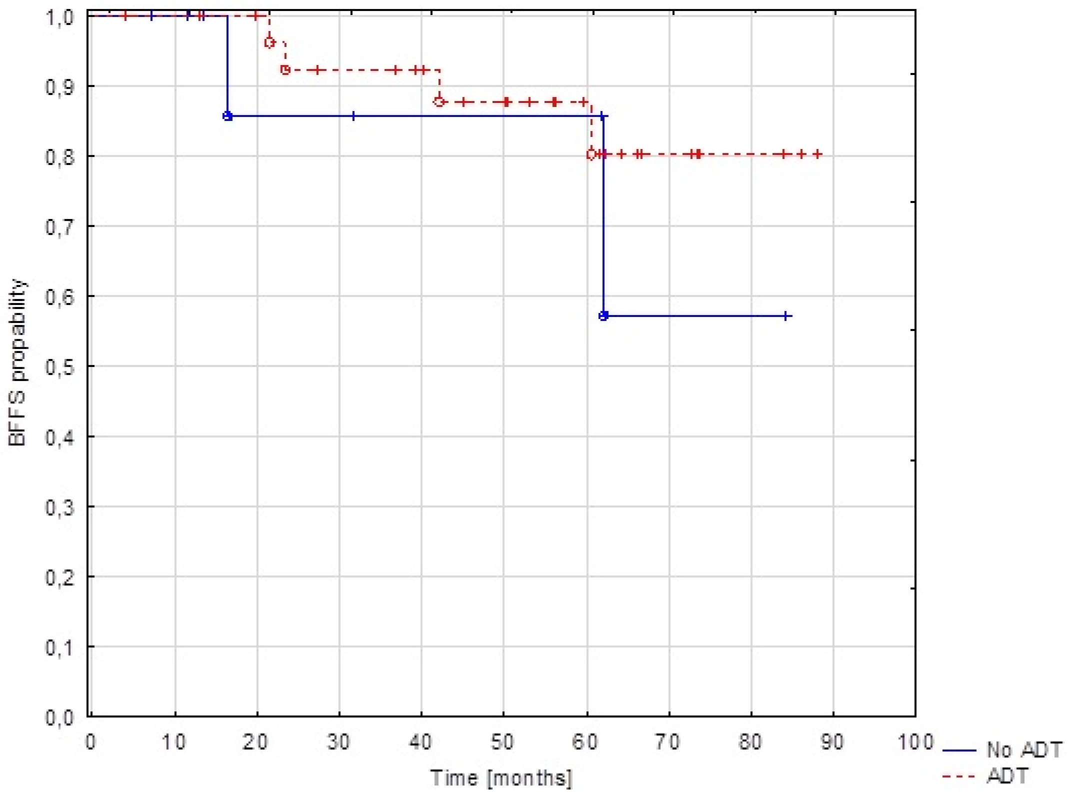

Figure S1. Comparison of the cumulative proportion of biochemical failure-free survival (BFFS) in patients after low-dose-rate brachytherapy of unfavorable intermediate risk group of prostate cancer with antigen-deprivation therapy (ADT) and without ADT (No ADT, p = 0.439).

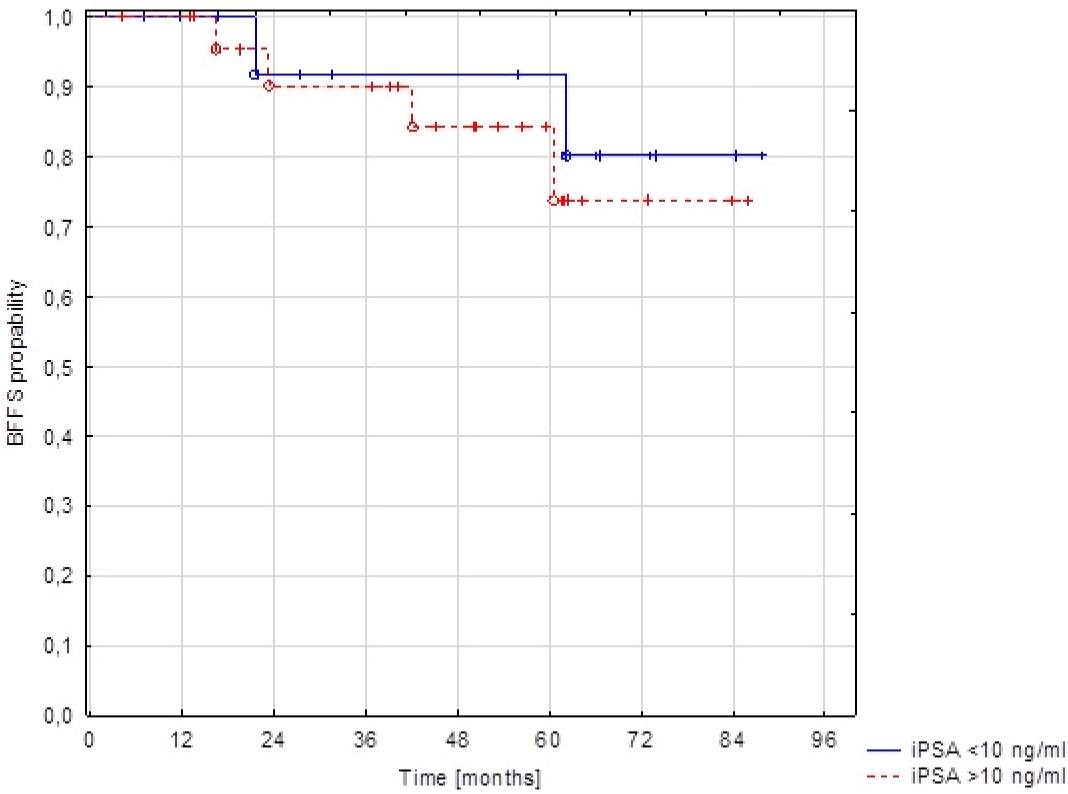

Figure S2. Comparison of the cumulative proportion of biochemical failure-free survival (BFFS) in patients after low-dose-rate brachytherapy of unfavorable intermediate-risk prostate cancer group depending on initial prostate-specific antigen (iPSA) (p=0.595).

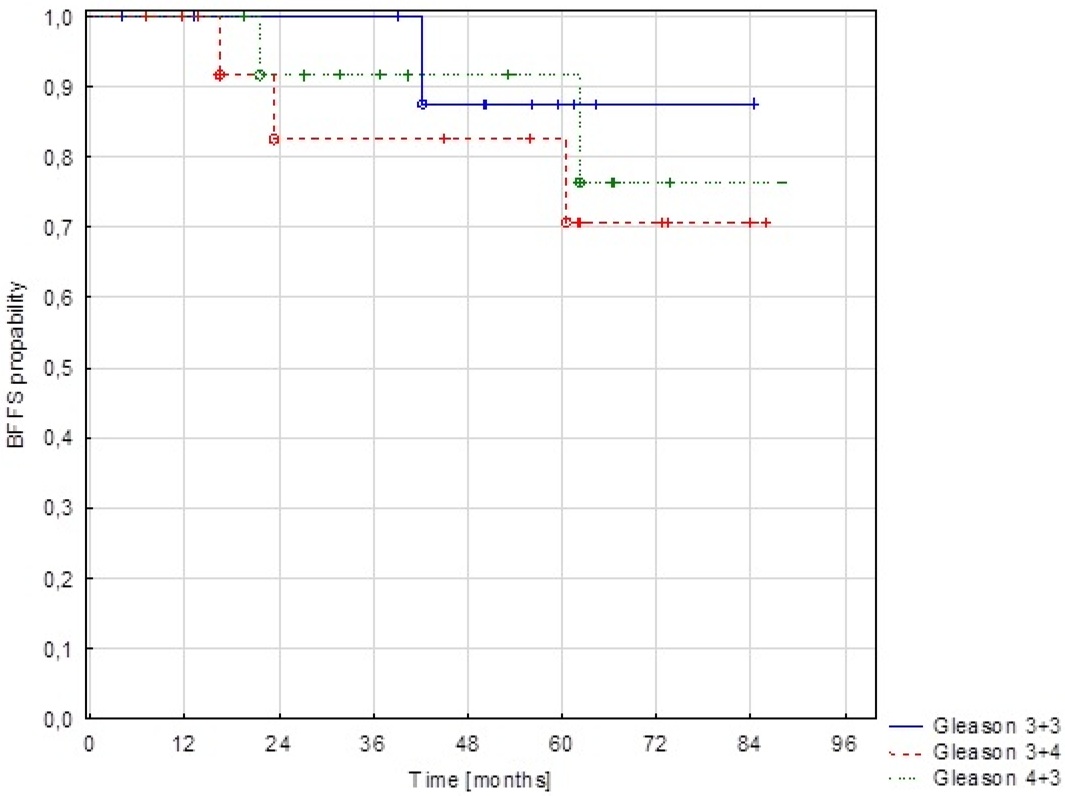

Figure S3. Comparison of the cumulative proportion of biochemical failure-free survival (BFFS) in patients after low-dose-rate brachytherapy of unfavorable intermediate risk factor (IUR) prostate cancer depending on Gleason (p = 0.671)

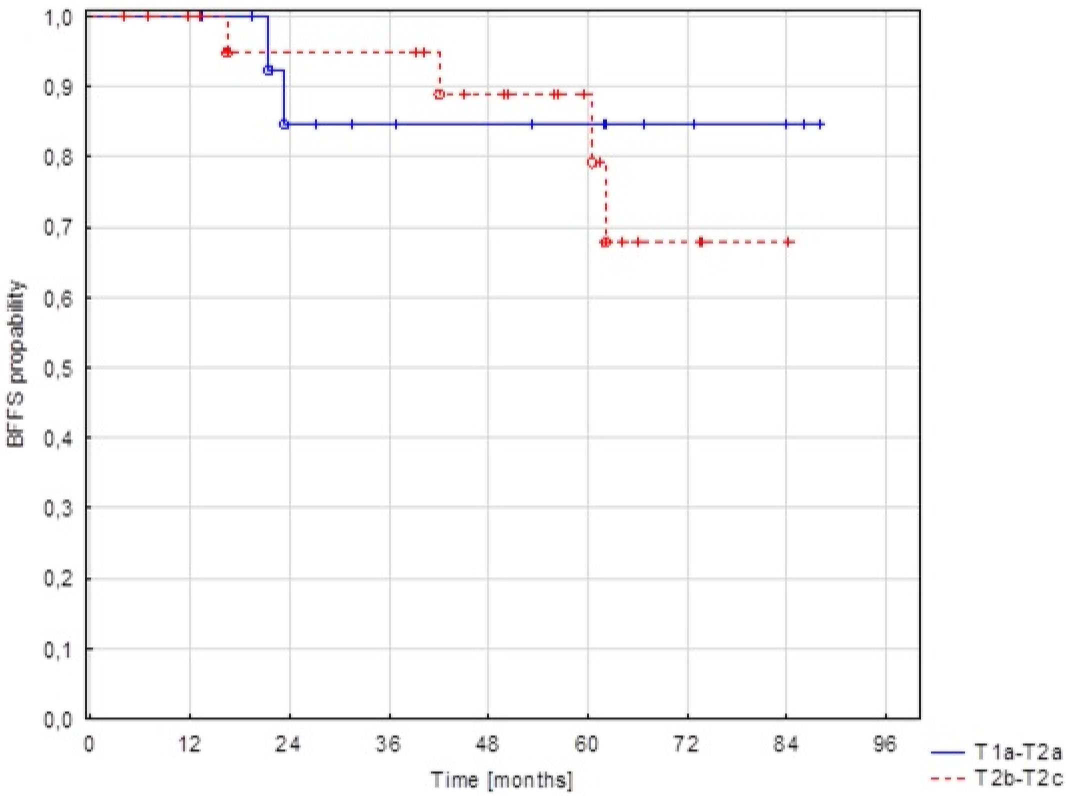

Figure S4. Comparison of the cumulative proportion of biochemical control in patients after low-dose-rate brachytherapy of unfavorable intermediate risk factor (IUR) prostate cancer depending on tumor stage risk factor (p = 0.694)

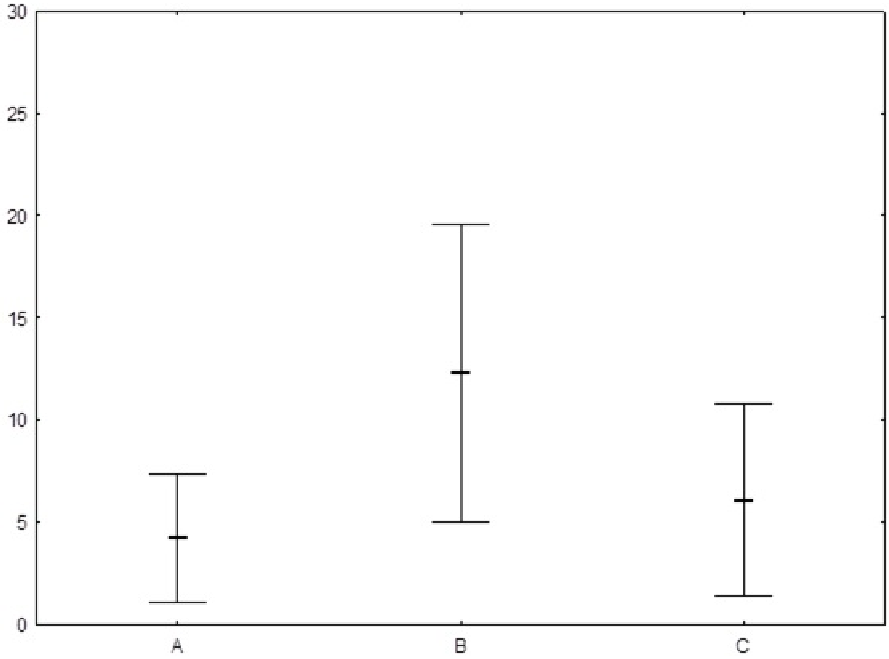

Figure S5. Comparison of the International Prostate Symptom Score (IPSS scale score collected: A — before treatment, B — the first follow-up after one month, C — the last recorded scale score during follow-up) (p = 0.264)