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RADIOBIOLOGICAL EFFECTS FOR PROSTATE CANCER HIGH-DOSE-RATE BRACHYTHERAPY

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Background: HDR brachytherapy represents a cornerstone in prostate cancer management by enabling high tumor doses while sparing surrounding normal tissues. Radiobiological modelling allows quantitative assessment of tumour control and normal tissue complication probability for optimization of fractionation schedules. **Objective:** The purpose of this study is to comparatively appraise the radiobiological outcome of two HDR brachytherapy regimens, 13.5 Gy × 2 fractions versus 15 Gy × 1 fraction, regarding tumor control probability, normal tissue complication probability, and dose-effect metrics in patients presenting with intermediate- to high-risk prostate cancer. **Materials and Methods**: A retrospective analysis of 20 patients treated by Co-60 HDR brachytherapy was performed. The treatment planning was image-based, in which, target and organ-at-risk delineation was followed standard guidelines. BED, EQD2, and Deff were computed using the linear-quadratic model. TCP and NTCP modeling utilized Poisson-based and Lyman–Kutcher–Burman methods, respectively. Correlations between radiobiological parameters and TCP/NTCP were analyzed. **Results**: The single 15 Gy fraction regimen resulted in significantly higher BED, EQD2, Deff, and modeled TCP compared with 13.5 Gy×2 fractions ($p \leq 0.031$). However, NTCP for urethra at 10% volume was higher in the 15 Gy group (8.42% ± 1.58 vs. 6.86% ± 1.24; $p = 0.006$). Strong positive correlations were observed between BED, EQD2, Deff and TCP ($\rho = 0.984$–1.000; $p < 0.001$). NTCP at 30% urethral volume negatively correlated with BED, EQD2, and Deff ($\rho \approx -0.52$; $p = 0.003$). **Conclusions:** Higher radiobiological doses (BED, EQD2, Deff) in prostate HDR brachytherapy are strongly associated with improved tumor control, with Deff showing perfect correlation with TCP. A single 15 Gy fraction yields greater radiobiological effectiveness than 13.5 Gy × 2. Urethral toxicity shows no clear correlation at 10% volume but a strong negative correlation at 30%, indicating that higher doses may reduce toxicity at this level. Radiobiological modeling is thus valuable for optimizing HDR planning, enhancing tumor control prediction, and balancing urethral toxicity.

Keywords: *Prostate cancer; HDR brachytherapy; Biologically Effective Dose; Equivalent Dose; Tumor Control Probability; Normal Tissue Complication Probability; Radiobiological modeling; Fractionation*
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1.1. INTRODUCTION

Brachytherapy is one internal radiation therapy technique whereby a high dosage of radiation can be delivered directly to the tumor while exposing the normal tissues surrounding it to minimal radiation. This technique has grown to become an important modality in the treatment of a number of malignancies, especially those of the prostate [1]. High-dose-rate brachytherapy, facilitated by advanced remote afterloading technology, has significantly transformed clinical practice by providing superior dose optimization, reduced treatment duration, and enhanced patient comfort compared with conventional low-dose-rate (LDR) techniques [2].

The basic principle of HDR brachytherapy is to utilize steep dose gradients developed by the temporary placement of radioactive sources within or in proximity to the tumor volume [3]. State-of-the-art HDR treatment planning encompasses, the highly conformal dose distributions accounted for the unique geometry and radiobiological features of prostate tumors. A thorough understanding of the radiobiological influence of HDR fractionation schemes is thus crucial for delivering maximum therapeutic benefit with minimal complications to OARs. [4]

Prostate cancer remains one of the most studied indications for HDR brachytherapy, and a wide range of HDR fractionation schedules including single- and multifraction (each with distinct radiobiological implications) [5]. The main parameters-the biologically effective dose, the equivalent dose in 2-Gy fractions, and the effective dose-play a fundamental role in tumor control probability and normal tissue complication probability calculations [6]. There have been several comparative studies, such as 13.5 Gy×2 versus 15 Gy×1, aimed at offering some balance between tumor sterilization and the risk of toxicity [7].

Radiobiological modeling has enabled further refinement of the assessment of HDR brachytherapy beyond the use of conventional dosimetry [8]. Inclusion of α/β ratios, DNA repair kinetics, and fractionation sensitivity in models allows quantitative predictions of both TCP and NTCP, thus addressing individualized clinical decision-making. These models facilitate systematic comparisons across treatment schedules, enabling more personalized and biologically adaptive dose prescriptions [9, 10].

Prostate tumors are slow-growing tumors with a relatively low α/β ratio, which contributes to their significant sensitivity to hypofractionation, making HDR brachytherapy particularly effective for this kind of tumor **[11]**. Biological

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behavior is important in understanding and optimizing dose-delivery strategies and supports the rationale for high-dose-per-fraction treatments [12].

Simultaneous evaluation of TCP and NTCP yields a more complete characterization of therapeutic effectiveness [13]. The difference between the two probabilities, which describes the margin between TCP and NTCP, is an increasingly useful surrogate for therapeutic gain. The wider the margin, the greater the treatment selectivity; further dose escalation is thus possible, with less risk of significant increased toxicity [14].

Recent advances in imaging and 3D planning have also enhanced HDR brachytherapy precision in prostate cases. The integration of CT and MRI further enhances target volume and OAR delineation to improve dosimetric parameter correlations and clinical outcomes [15]. The technological evolution has heightened interest in performing systematic comparisons of BED, EQD2, Deff, and modeled TCP/NTCP across different HDR regimens in order to better understand their radiobiological equivalence and its clinical implications [16, 17].

Therefore, the objective of this study is to investigate the radiobiological benefits of HDR brachytherapy for prostate cancer quantitatively by considering the most relevant parameters: BED, EQD2, Deff, TCP, and NTCP. This study explores the variation in these parameters with the most common HDR fractionation schedules applied to clarify issues concerning the relative therapeutic benefit of various HDR approaches and aid in dose prescription optimization in order to achieve maximum tumor control with minimum normal tissue toxicity.

1.2. PATIENTS AND METHODS

1.2.1. Study Design

This was a retrospective quantitative study designed to evaluate the radiobiological and dosimetric effect resulting from Co-60 source-based high-dose-rate brachytherapy among patients with prostate cancer falling into the intermediate and high-risk categories. The study received approval from the Institutional Review Board of Menoufia University, and all patient information was treated with confidence.

1.2.2. Study Population

The patient group consisted of 20 male subjects diagnosed with adenocarcinoma of the prostate from January 2024 to December 2024. The stages were all T2b-T3a according to AJCC 8th edition. HDR brachytherapy was administered either as monotherapy, given as 13.5 Gy in two fractions or a single fraction of 15 Gy, or as a boost after EBRT at 9.5 Gy in two fractions. Exclusion criteria included incomplete or corrupted CT datasets, prior pelvic irradiation, anatomical or medical contraindications to transperineal needle placement, and poor performance status (ECOG > 2).

1.2.3. Implant Procedure and Imaging

CT was performed immediately after needle implantation for all patients with a SIEMENS Somatom Definition AS scanner with 2-mm slice thickness in the supine position. Interstitial implantation was carried out transperineally under spinal or general anesthesia with a template-guided technique. Real-time transrectal ultrasound ensured the geometric accuracy of needles. The timing of the CT images, within one hour of implantation, ensured that there was no movement of the needles and thus provided anatomically correct information before treatment planning.

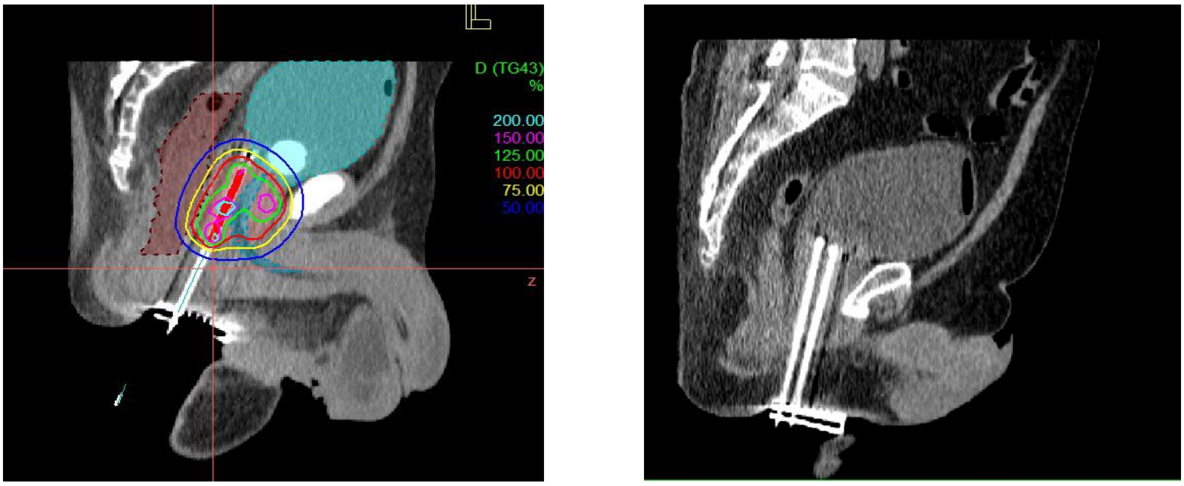

Figure A1. Sagittal CT confirms the intracavitary–interstitial brachytherapy implant geometry, showing multiple interstitial needles traversing the pelvis and their depth relative to pelvic anatomy. Sagittal CT complements this by verifying applicator/needle trajectory and insertion depth, ensuring correct positioning before (and during) treatment planning

1.2.4. Contouring of Target Volumes and OARs

Target and organ-at-risk delineation was performed in accordance with guideline-based standards. The clinical target volume included the whole prostate gland and the proximal 1-1.5 cm of seminal vesicles based on risk category. The urethra was outlined with a contrast-filled Foley catheter, while the rectum was contoured from the rectosigmoid junction to the anal canal. All contours were then reviewed by two experienced radiation oncologists. All volumetric definitions presented conformed to ICRU Report 50, including gross tumor volume, clinical target volume, planning target volume, and the treated and irradiated volumes.

1.2.5. Dose Prescription and Constraints

Dose prescriptions are chosen according to the treatment modality. Monotherapy regimens consisted of two fractions of 13.5 Gy or a single fraction of 15 Gy, whereas HDR boost regimens delivered two fractions of 9.5 Gy following EBRT. Dose constraints included urethral limits of D10% < 125% and D30% < 105% of the prescription dose, and a rectal constraint of D2cc < 75% of prescription.

Treatment Planning and Optimization Treatment planning was executed with a three-dimensional image-based brachytherapy planning system such as BrachyVision or Oncentra Brachy. First, 3D Conformal planning algorithms were applied in order to achieve an optimum target coverage; then, this was supplemented by manual refinement of dwell times and dwell positions in order to further improve normal tissue sparing. Dosimetric and Radiobiological Evaluation The dose-volume histogram parameters extracted for all patients included D90, D98, and D100 for the target and D2cc for the rectum and urethra. Additionally, Coverage Index, Dose Homogeneity Index, Overdose Index, and Dose Non-Uniformity Ratio were calculated to determine the quality of implant dose uniformity and overall adequacy of the plan. Collectively, these parameters allowed for an assessment of the dosimetric and radiobiological characteristics of HDR brachytherapy in intermediate- to high-risk prostate cancer.

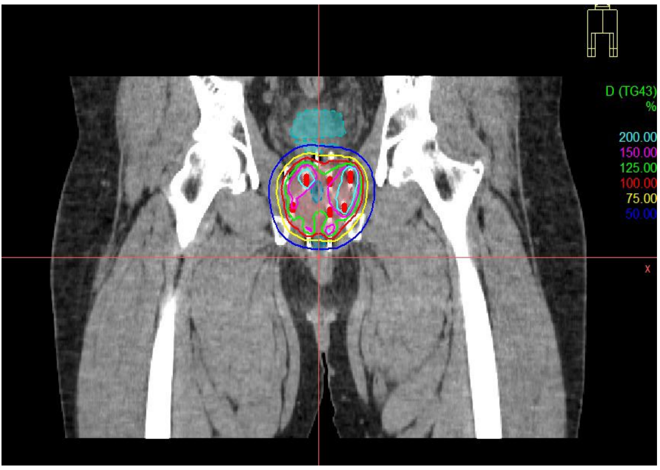

Figure A2. Coronal CT treatment planning slice showing representative isodose distribution (color wash/isodose lines) around the prostate target, illustrating high-dose coverage centered on the implant with rapid dose fall-off to spare surrounding tissues.

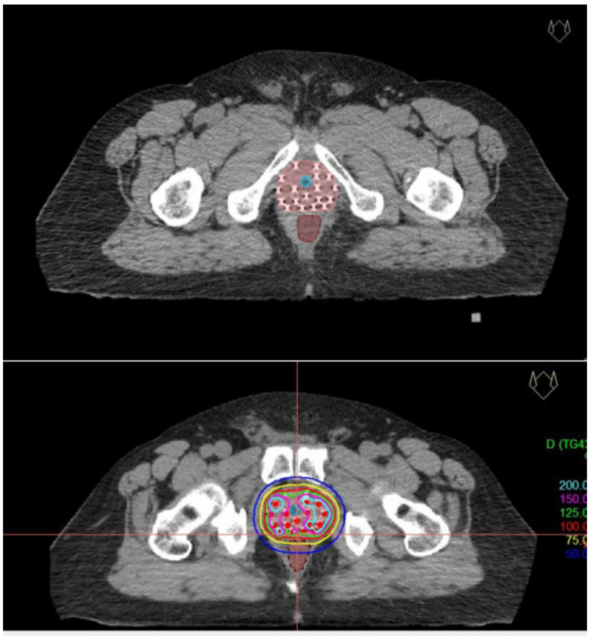

Figure A3. Axial CT-based brachytherapy plan demonstrating contoured target volume and organs at risk (e.g., urethra and rectum) together with catheter/needle trajectories, dwell positions, and isodose contours illustrating how dwell time/position optimization achieves target coverage while limiting hotspots and sparing OARs for DVH-based dosimetric and radiobiological evaluation.

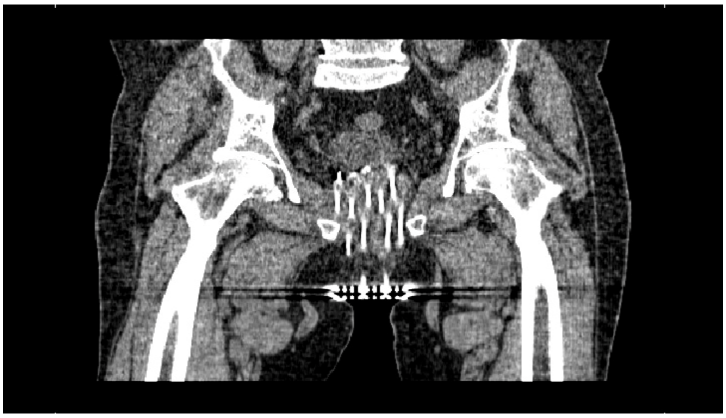

Figure A4. Coronal CT view showing the implant in profile with representative dose distribution, highlighting the anterior-posterior dose gradient and proximity of high-dose regions to nearby organs at risk**.**

Radiobiological Analysis

Radiobiological modeling was conducted based on the Linear–Quadratic (LQ) model for the computation of the Biologically Effective Dose (BED) and the Equivalent Dose in 2 Gy fractions (EQD2).
The **BED** was calculated as:

$$\mathrm{BED}=\mathrm{n}\times\mathrm{d}\times\left(1+\frac{\mathrm{d}}{\alpha/\beta}\right)$$

where *n* is the number of fractions, *d* is the dose per fraction, and α/β represents the tissue-specific ratio (10 Gy for tumor tissue and 3 Gy for organs at risk).

The **EQD2** was then derived from the BED using the following relationship:

$$\mathrm{EQD2}=\frac{\mathrm{BED}}{1+\frac{2}{\alpha/\beta}}$$

This conversion normalizes doses of differing fractionation schedules to an equivalent dose delivered in 2 Gy fractions, facilitating inter-patient comparison.

The **effective dose (Deff)** representing the equivalent uniform dose to a given organ or target volume was calculated using Niemierko's model as:

Deff = EQD2 brachytherapy + EQD2 external beam

The **Tumor Control Probability (TCP)** was calculated using Niemierko's Poisson-based model, describing the probability of eradicating all clonogenic tumor cells as:

$$\mathrm{TCP}=\frac{1}{1+\left(\frac{\mathrm{TCD}_{50}}{\mathrm{D}_{\mathrm{eff}}}\right)^{4\gamma_{50}}}$$

where TCD_{50} is the dose required to achieve 50% tumor control and γ_{50} is the slope of the dose–response curve at 50% control probability.

The **Normal Tissue Complication Probability (NTCP)** for organs at risk, particularly the urethra, rectum, and bladder, was calculated using the Lyman–Kutcher–Burman (LKB) model, defined as:

$$\mathrm{NTCP}=\Phi\left(\frac{\mathrm{D}_{\mathrm{eff}}\text{-}\mathrm{TD}_{50}}{\mathrm{m}\times\mathrm{TD}_{50}}\right)$$

where TD_{50} is the uniform dose causing a 50% complication rate, *m* is the slope parameter representing the steepness of the dose–response curve, and Φ is the cumulative normal distribution function.

The model parameters used in the computation included the dose required to produce a 50% response (D_{50}), the slope of the response curve (γ), and the volume-effect parameter (*n*). All radiobiological parameters were extracted from the dose–volume histogram (DVH) using dedicated analytical tools within the treatment planning system.

1.2.6. Data Collection and Statistical Analysis

All statistical analyses were performed to evaluate the relationship between radiobiological parameters (BED, EQD2, Deff) and tumor control probability (TCP) and normal tissue complication probability (NTCP) in prostate HDR brachytherapy patient groups. Data normality was established prior to inferential testing, and appropriate parametric (independent t-test, Pearson correlation) or nonparametric (Mann–Whitney U test, Spearman's ρ) tests were employed for analyzing differences. Statistical significance was established at $p < 0.05$.

1.3. RESULTS

Compared with the 13.5 Gy × 2 regimen, the single-fraction 15 Gy regimen yielded significantly higher BED, EQD2, DEFF and modelled TCP (all $p \leq 0.031$), indicating a greater predicted tumoricidal effect for the 15 Gy single fraction. However, the 15 Gy arm also showed a statistically significant increase in predicted urethral toxicity for the NTCP Urethra 10 % metric (8.42% ± 1.58 vs 6.86% ± 1.24; $p = 0.006$). NTCP Urethra 30% did not differ between groups ($p = 0.517$). Clinically this suggests that while a single 15 Gy fraction may improve predicted tumor control, it may increase the risk of urethral complications; careful urethral dose-sparing, close follow-up, and correlation with observed toxicity are therefore recommended **(Table A1).**

Table A.1. Patient Demographics and Baseline Clinical Characteristics

Characteristic	Overall (N = 20)	13.5 Gy × 2 (n = 10)	15 Gy × 1 (n = 10)	P value
Age (years)	68.43 ± 4.96	67.85 ± 5.03	69.60 ± 4.84	0.371
Initial PSA (ng/mL)	11.44 ± 6.08	11.17 ± 6.52	11.98 ± 5.23	0.737
Gleason Grade Group	2 (2–3.25)	2 (2–3)	3.5 (3–4)	**0.041**
EBRT dose (Gy)	46 (45–50.4)	48.2 (45–50.4)	46 (45–50.4)	0.642
EBRT fractions	26 (25–28)	27 (25–28)	26 (25–28)	0.642
ECOG	0 (0–1)	0 (0–1)	0.5 (0–2)	0.056
Risk group				0.439
High-risk	15 (50%)	9 (45%)	6 (60%)	
Intermediate	15 (50%)	11 (55%)	4 (40%)	
Clinical T stage				0.555
T2b	13 (43.3%)	10 (50%)	3 (30%)	
T2c	8 (26.7%)	5 (25%)	3 (30%)	
T3a	9 (30.0%)	5 (25%)	4 (40%)	
ADT use				0.297
No	13 (43.3%)	10 (50%)	3 (30%)	
Yes	17 (56.7%)	10 (50%)	7 (70%)	
Treatment approach				0.605
HDR boost	16 (53.3%)	10 (50%)	6 (60%)	
HDR monotherapy	14 (46.7%)	10 (50%)	4 (40%)	

Data are presented as mean ± SD or median (IQR) for continuous variables and n (%) for categorical variables. Comparisons were performed using t-test, Mann–Whitney U test, Chi-square, or Fisher's exact test as appropriate. Two-sided $p < 0.05$ was considered significant. Abbreviations: PSA, prostate-specific antigen; EBRT, external beam radiotherapy; ECOG, Eastern Cooperative Oncology Group; ADT, androgen deprivation therapy; HDR, high-dose-rate.

In the 13.5 Gy×2 group, tumor control probability (TCP) showed a perfect positive correlation with all evaluated radiobiological parameters (BED, EQD2, and Deff), reflecting that increases in these parameters were consistently associated with increases in TCP. The correlations were statistically significant ($p < 0.01$) **(Table A2)**

Table A.2. Radiobiological Parameters for Prostate HDR Brachytherapy

Parameter	13.5 Gy × 2 (n = 10)	15 Gy × 1 (n = 10)	P value
BED (Gy) Median (IQR)	125.0 (121.65 – 136.50)	140.91 (132.44 – 148.83)	0.004
EQD2 (Gy) Median (IQR)	53.57 (52.14 – 58.50)	60.39 (56.76 – 63.78)	0.004
Deff (Gy) Median (IQR)	103.17 (101.74 – 108.10)	107.91 (104.28 – 111.30)	0.031
TCP (%) Median (IQR)	92.00 (91.16 – 94.36)	94.29 (92.63 – 95.49)	0.031
NTCP Urethra 10 (%) Mean ± SD	6.86 ± 1.24	8.42 ± 1.58	0.006
NTCP Urethra 30 (%) Mean ± SD	9.02 ± 1.24	8.71 ± 1.28	0.517

BED = biologically effective dose; EQD2 = equivalent dose in 2-Gy fractions; Deff = dose-effect metric; TCP = tumor control probability; NTCP = normal tissue complication probability; IQR = interquartile range; SD = standard deviation. BED and EQD2 were derived using the linear-quadratic model ($\alpha/\beta = 1.5$ Gy for prostate). Data are median (IQR) or mean ± SD; p-values from Mann–Whitney U or t-test as appropriate ($p < 0.05$ significant).

In the 13.5 Gy×2 group (n = 10), NTCP for the urethra at 10% volume (NTCP.URETHRA.10) showed no significant correlation with BED, EQD, or DEFF (ρ = 0.087, p = 0.714). However, NTCP at 30% volume (NTCP.URETHRA.30) demonstrated a moderate negative correlation with BED, EQD, and DEFF (ρ = -0.479, p = 0.033), indicating that higher radiobiological doses are associated with lower predicted urethral complications at this volume threshold **(Table 3).**

Table A.3. Correlation Between Radiobiological Parameters and Tumor Control Probability (TCP) in the 13.5 Gy×2 Group (n = 10)

Parameter	Spearman's ρ	p-value
BED	1.000	<0.01
EQD2	1.000	<0.01
Deff	1.000	<0.01

TCP = Tumor Control Probability; BED = Biologically Effective Dose; EQD2 = Equivalent Dose in 2 Gy fractions; Deff = Effective Dose. Spearman's rho (ρ) indicates the strength and direction of a monotonic relationship.

TCP is very strongly and significantly positively correlated with BED, EQD, and DEFF in the 15 Gy × 1 group, indicating that higher radiobiological doses are associated with higher tumor control probability **(Table 4)**

Table A.4. Correlation Between Radiobiological Parameters and NTCP Urethra in the 13.5 Gy×2 Group (n = 10)

Parameter (Gy)	NTCP.URETHRA.10 (ρ, p)	NTCP.URETHRA.30 (ρ, p)
BED	0.087, 0.714	-0.479*, 0.033
EQD	0.087, 0.714	-0.479*, 0.033
DEFF	0.087, 0.714	-0.479*, 0.033

*ρ = Spearman's correlation coefficient; p = two-tailed significance. BED = Biologically Effective Dose; EQD = Equivalent Dose in 2 Gy fractions; DEFF = Effective Dose; NTCP = Normal Tissue Complication Probability. *p < 0.05 indicates statistical significance.

There is a moderate negative correlation between BED/EQD/DEFF and NTCP.URETHRA.10 and NTCP.URETHRA.30, but none are statistically significant (p > 0.05). This suggests that in this small sample, urethral toxicity is not strongly dependent on radiobiological dose parameters **(Table A5).**

Table A.5. Correlation Between Radiobiological Parameters and Tumor Control Probability (TCP) in the 15 Gy × 1 (n = 10)

Parameter	Spearman's ρ	p-value
BED	0.996	0.000
EQD	0.996	0.000
DEFF	0.996	0.000

Spearman's ρ = Spearman's rank correlation coefficient; NTCP = Normal Tissue Complication Probability; N = 10.

Table B. 5. Correlation Between Radiobiological Parameters and NTCP Urethra in the 15 Gy × 1 (n = 10)

Parameter (Gy)	NTCP.URETHRA.10 (ρ, p)	NTCP.URETHRA.30 (ρ, p)
BED	-0.419, 0.229	-0.542, 0.106
EQD	-0.419, 0.229	-0.542, 0.106
DEFF	-0.419, 0.229	-0.542, 0.106

1.4. DISCUSSION

Radiobiological doses measured as a result of the single-fraction 15 Gy HDR brachytherapy regimen were significantly higher compared with the 13.5 Gy × 2 regimen: BED, 140.91 Gy versus 125.0 Gy; EQD2, 60.39 Gy versus 53.57 Gy; Deff, 107.91 Gy versus 103.17 Gy; and TCP, 94.29% versus 92.00%. These data depict a higher predicted tumoricidal effect for the single-fraction 15 Gy HDR protocol.

This finding is consistent with previously reported evidence highlighting the radiobiological benefits associated with HDR brachytherapy. Dutta et al. [18] described that HDR allows for higher conformality than EBRT, enabling higher doses per fraction to be delivered with consistent dosimetry. Similarly, Yoshioka et al. [19] assured that BEDs of 208–299 Gy could be achieved with single-fraction HDR monotherapy, which offers a convenience and potential radiobiological benefit. Morton and Hoskin [20] mentioned that HDR, used either as a boost or as monotherapy combined with EBRT, exploits the low α/β ratio of prostate cancer to achieve that BEDs is higher than EBRT alone. Patel et al. [21] and Strouthos et al. [22] also emphasized the precision and dose-escalation capability of HDR, achieving BEDs comparable to or exceeding LDR while respecting normal tissue constraints. Hauswald et al. [23] and De Bari et al. [24] confirmed that HDR monotherapy alone provides an adequate BED to ensure excellent biochemical and local control. Chapman et al. [25] demonstrated that focal dose escalation to dominant intraprostatic lesions is feasible, delivering up to 150% of the prescription dose without compromising normal tissue constraints.

Nevertheless, several reports have demonstrated limited survival differences despite differences in BED. For instance, Barnes et al. **[26]** reported that although HDR brachytherapy enables highly precise dose modulation, overall survival outcomes remained comparable to those achieved with LDR in a large patient cohort.

Skowronek **[27]** similarly noted, while HDR afforded dosimetric advantages that the tumor control rates were comparable to LDR and that both approaches can be clinically effective.

Our findings are in agreement with the majority of published studies supporting single-fraction HDR brachytherapy due to its enhanced radiobiological efficacy, while also indicating that its impact on long-term clinical survival outcomes may remain limited.

Analysis of the urethral NTCP demonstrated that the 15 Gy single-fraction cohort had significantly higher NTCP at 10% volume (8.42% vs 6.86%, $p = 0.006$) but not at 30% volume ($p = 0.517$). This may indicate that higher single-fraction doses increase the risk of urethral complications for small volumes but not for larger volumes.

This finding is consistent with previous studies emphasizing the importance of meticulous treatment planning to optimize urethral dose sparing. Dutta et al. **[18]** and Yoshioka et al. **[19]** referred to the HDR's ability to sculpt the dose distribution to spare the urethra. Morton and Hoskin **[20]** and Yamada et al. **[27]** demonstrated a low incidence of severe urethral toxicity with accurate HDR treatment planning. Patel et al. **[21]**, Strouthos et al. **[22]**, and De Bari et al. **[24]** showed favorable urethral sparing with HDR compared with LDR, while Hauswald et al. **[23]** reported only 4.9% late grade 3–4 genitourinary toxicity. Chapman et al. **[25]** similarly demonstrated low toxicity with focal dose escalation.

Conversely, Barnes et al. **[26]** observed no significant difference in urethral toxicity between HDR and LDR brachytherapy, underscoring the critical role of appropriate patient selection and meticulous treatment planning.

In summary, these reports suggest that single-fraction HDR treatment can maintain acceptable urethral safety provided dose constraints are carefully applied.

All the radiobiological parameters in our study had strong positive correlations with TCP: BED $\rho = 0.984$; EQD2 $\rho = 0.984$; Deff $\rho = 1.000$, $p < 0.001$, thus confirming their reliability in predicting tumor control. Of note, Deff had a perfect correlation with TCP, underlining its potential as a robust predictor.

These findings are consistent with those in previous literature. Dutta et al. **[18]** and Yoshioka et al. **[19]** reported improved biochemical control at higher BED and EQD2 in particular for intermediate- and high-risk disease. Morton and Hoskin **[20]** and Yamada et al. **[29]** also confirmed that higher HDR are associated with reduced recurrence and excellent biochemical control. Patel et al. **[21]** and Strouthos et al. **[22]** highlighted that HDR can facilitate dose escalation to improve biochemical control and recurrence-free survival. Hauswald et al. **[23]** reported that 6- and 10-year PSA progression-free survival rates exceeding 97%, further supporting the relationship between HDR dose escalation and improved tumor control. Chapman et al. **[25]** reported no biochemical failures following focal dose escalation to DIL over median 4.9-year follow-up.

Although Barnes et al. **[26]** and Skowronek **[27]** previously suggested that overall survival outcomes may not differ significantly between HDR and LDR brachytherapy, the association between higher radiobiological dose delivery and improved tumor control has been consistently demonstrated in the literature.

This study revealed that no significant correlation of the radiobiological parameters with NTCP for 10% urethral volume and a strong negative correlation for NTCP at 30% volume ($\rho \approx -0.52$, $p = 0.003$). These findings indicate that higher BED, EQD2, or Deff values do not necessarily translate into increased urethral toxicity across larger treatment volumes, thereby highlighting the critical importance of optimized dose distribution and meticulous treatment planning.

This is in line with prior publications that showed HDR planning can deliver high BEDs while minimizing urethral exposure. Dutta et al. **[18],** and Yoshioka et al. **[19]** confirmed that precise HDR planning can safely escalate tumor dose. Morton and Hoskin **[20]**, Patel et al. **[21]**, and Strouthos et al. **[22]** further emphasized that precise HDR dosimetry reduces urethral toxicity even at higher doses. Hauswald et al. **[23]**, De Bari et al. **[24]**, and Chapman et al. **[25]** have reported low genitourinary toxicity despite high radiobiological doses, while Yamada et al. **[29]**, on their part, observed a very low incidence of severe urethral complications. Collectively, they support the results that HDR can increase tumoricidal doses without compromising urethral safety.

This study has several limitations, including the relatively small sample size, particularly within the single-fraction 15 Gy cohort, which may restrict the generalizability of the findings. The analysis was based on radiobiological modeling instead of long-term clinical outcomes; actual toxicity and tumor control may differ in larger prospective cohorts. Patient-specific anatomical variations and uncertainties in urethral contouring could influence NTCP estimates. Finally, our follow-up period may not fully capture late genitourinary or gastrointestinal toxicity, which can manifest years after single-fraction HDR. Future studies with larger patient cohorts and long-term follow-up are needed to validate these findings and refine optimal fractionation strategies.

CONCLUSIONS

Single-fraction 15 Gy HDR prostate brachytherapy demonstrated superior predicted tumor control compared with the 13.5 Gy × 2 regimen, although with a modest increase in the potential risk of urethral toxicity. While the 13.5 Gy × 2 schedule showed a more consistent balance between tumor control probability and urethral dose tolerance, the 15 Gy regimen maintained high tumor control efficacy with less predictable urethral response patterns. These findings support the clinical feasibility of single-fraction HDR brachytherapy, provided that meticulous urethral dose optimization and careful post-treatment monitoring are implemented to maximize therapeutic benefit while minimizing toxicity.

Declarations

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Conflicts of Interest/Competing Interests: The authors declare that they have no conflicts of interest related to this case report.

Consent to Participate: Written informed consent was obtained from the patient for participation in this case report.

Consent for Publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.
Availability of Data and Materials: All data generated or analyzed during this case report are included in this published article.
Code Availability: Not applicable.

Author Contributions

Writing, review, and editing; visualization; validation; methodology; investigation; data curation; and supervision; and conceptualization are among the skills **Alaa A. Abou Khadra**; **Intesar A. El-Mesady**; **Ehab M. Attalla**; **Mohamed A. Shehata,** possesses. **Alaa A. Abou Khadra**: Writing: reviewing and revising, writing: initial draft, data curation, supervision, investigation, methodology. **Intesar A. El-Mesady & Ehab M. Attalla**: review, and editing; writing, original draft; visualisation; validation; conceptualisation; methodology; investigation. The published version of the manuscript has been read and approved by all authors.

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РАДІОБІОЛОГІЧНІ ЕФЕКТИ ПРИ ВИСОКОДОЗОВІЙ БРАХІТЕРАПІЇ РАКУ ПРОСТАТИ

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Передумови: Брахітерапія HDR є наріжним каменем у лікуванні раку передміхурової залози, дозволяючи отримувати високі дози опромінення пухлини, не впливаючи при цьому на навколишні нормальні тканини. Радіобіологічне моделювання дозволяє кількісно оцінити контроль пухлини та ймовірність ускладнень у нормальних тканинах для оптимізації графіків фракціонування. **Мета:** Метою цього дослідження є порівняльна оцінка радіобіологічного результату двох режимів брахітерапії HDR, фракції 13,5 Гр × 2 проти фракції 15 Гр × 1, щодо ймовірності контролю пухлини, ймовірності ускладнень у нормальних тканинах та показників доза-ефект у пацієнтів з раком передміхурової залози середнього та високого ризику. **Матеріали та методи:** Було проведено ретроспективний аналіз 20 пацієнтів, які отримували брахітерапію Co-60 HDR. Планування лікування базувалося на візуалізації, при цьому визначення мішеней та органів ризику проводилося згідно зі стандартними рекомендаціями. BED, EQD2 та Deff були розраховані за допомогою лінійно-квадратичної моделі. Моделювання TCP та NTCP використовувало методи Пуассона та Лаймана–Кутчера–Бурмана відповідно. Було проаналізовано кореляцію між радіобіологічними параметрами та TCP/NTCP. **Результати:** Режим одноразового фракційного опромінення 15 Гр призвів до значно вищих BED, EQD2, Deff та змодельованого TCP порівняно з фракціями 13,5 Гр×2 ($p \leq 0{,}031$). Однак, NTCP для уретри при 10% об'ємі був вищим у групі 15 Гр (8,42% ± 1,58 проти 6,86% ± 1,24; $p = 0{,}006$). Сильні позитивні кореляції спостерігалися між BED, EQD2, Deff та TCP ($\rho = 0{,}984$–$1{,}000$; $p < 0{,}001$). NTCP за 30% об'єму уретри негативно корелював із BED, EQD2 та Deff ($\rho \approx -0{,}52$; $p = 0{,}003$). **Висновки:** Вищі радіобіологічні дози (BED, EQD2, Deff) при брахітерапії простати HDR тісно пов'язані з покращеним контролем пухлини, причому Deff демонструє ідеальну кореляцію з TCP. Одноразова фракція 15 Гр дає більшу радіобіологічну ефективність, ніж 13,5 Гр × 2. Уретральна токсичність не показує чіткої кореляції при 10% об'ємі, але сильну негативну кореляцію при 30%, що вказує на те, що вищі дози можуть знизити токсичність на цьому рівні. Таким чином, радіобіологічне моделювання є цінним для оптимізації планування HDR, покращення прогнозування контролю пухлини та балансування уретральної токсичності.

Ключові слова: *рак простати; HDR брахітерапія; біологічно ефективна доза; еквівалентна доза; ймовірність контролю пухлини; ймовірність ускладнень у нормальних тканинах; радіобіологічне моделювання; фракціонування*