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ORIGINAL ARTICLE

Comparison of Dosimetric Parameters Among Preplan, Intraoperative Plan and Post-implant Plans in Low Dose Rate Prostate Brachytherapy Applications

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OBJECTIVE

The aim of our study is to analyze the changes in dosimetric parameters obtained in pre-planning (PP), intraoperative planning (IOP), and post-implant dosimetry (PID).

METHODS

The study focused on the prostate as the target volume, with the rectum and urethra designated as organs at risk (OARs). Dosimetric differences between PP and IOP, PP and PID, and IOP and PID were assessed, including parameters such as prostate dose and volumes D90, pV100, pV150; urethral doses uD10, uD30, uD50; urethral volumes uV100, uV150; and rectal volumes rV100, rV150.

RESULTS

Comparing pD90 values between PP and IOP, PP and PID, and IOP and PID applications yielded p-values of 0.393, <0.001, and <0.001, respectively. For pV90 values, comparisons between PP and IOP, PP and PID, and IOP and PID showed p-values of 0.084, <0.001, and 0.001, respectively. No significant differences were observed in pD90, pV100, uD50, uV100, or rV50 when comparing PP with IOP. Similarly, no significant differences were found in uD50 or rV50 when comparing PP with PID. Comparing IOP with PID revealed no significant differences in pV150, uD30, rV50, or pV150. However, significant differences were found in all other parameters among the three applications.

CONCLUSION

The dose distribution in PP undergoes significant alterations due to edema formation and changes in the placement of OARs. Although it was determined that there were changes in PID according to the PP and IOP dose distribution, it was found to be compatible with the criteria reported in AAPM TG 137.

Keywords: Brachytherapy; intraoperative plan; LDR; post-implant dosimetry prostate; pre-plan.

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INTRODUCTION

Prostate cancer is the second most commonly diagnosed cancer and the fifth leading cause of cancer death among men worldwide.[1] Prostate brachytherapy has proven to be an effective treatment for T1-T2 prostate tumors. In low-dose-rate (LDR) prostate brachytherapy, small radioactive iodine sources, specifically Iodine-125 (I-125), are permanently implanted into the prostate. The primary advantage of brachytherapy over external beam radiotherapy (EBRT) is the rapid dose reduction around the radioactive sources, thereby preserving the surrounding normal tissues. I-125 seed implantation requires only a one-day hospital stay.

Prior retrospective investigations have not shown notable outcome disparities among radical prostatectomy, external beam radiotherapy (EBRT), and brachytherapy in the context of low-risk prostate cancer.[2–5] Research has consistently indicated outstanding tumor control and survival rates in localized prostate cancer through I-125 LDR brachytherapy,[6,7] with results comparable to those attained with radical prostatectomy or external beam radiotherapy.[4]

Prostate brachytherapy pre-planning is undertaken to ascertain the prostate volume before treatment, determine the required number of needles/seeds, and assess anatomical barriers in the patient's anatomy, such as the pubic arch. Furthermore, the ultrasound (US) images obtained during pre-planning are utilized to formulate an optimal treatment plan without time constraints. The objective is to replicate the treatment plan developed during pre-planning using online US images obtained intraoperatively.

Real-time planning during the procedure instantly adjusts the dose distribution with each seed placement, compensating for any deviations from the planned coordinates when loading needles based on pre-planning. This allows for the correction of cold and hot spots that may arise during the procedure. Through the assessment of real-time planning, additional seed placements or omissions can be adjusted to achieve the desired dose distribution. In post-implant dosimetry, there is no intervention in the dose distribution; it serves solely as a verification of the application.[8]

The D90, V100, and V90 planning parameters recommended by the American Brachytherapy Society for evaluating plan quality and ensuring that the target volume receives an adequate dose have been assessed in numerous studies.[9–16] Previous studies have shown that rectal and urethral complication rates are dose-dependent.[17,18] It is recommended to report these doses and evaluate them in post-implant dosimetry in clinical practice. During pre-planning and intraoperative treatment planning, US is employed, while post-implant planning is conducted using computed tomography (CT) after the implant. Due to the use of different modalities, variations in timing, and differences in body positions, dosimetric discrepancies between the US plan and post-implant CT analyses are inherent. This study aims to investigate the dosimetric differences between the plans created during pre-planning and the extent to which they can be achieved during intraoperative planning (IOP). Additionally, it explores the dosimetric variations between the dose distribution obtained during the procedure and the post-implant dosimetry (PID) conducted approximately four weeks after the application.

MATERIALS AND METHODS

The study involved 143 patients who underwent low-dose-rate (LDR) prostate brachytherapy between 2000 and 2019. These patients exclusively received brachytherapy monotherapy for low- or intermediate-risk prostate cancer, with the following T stages: T1c in 12 patients, T2a in 68 patients, T2b in 57 patients, and T3 in 6 patients. The median number of needles used was 28 (range: 18–35), and the median number of seeds used was 85 (range: 65–110), with an average seed activity of 0.49 U per seed (range: 0.43–0.50).

Pre-planning and Intraoperative Planning

For all patients, pre-planning was executed using the Permanent Seed Implant Brachytherapy Treatment Planning Software VariSeed™ version 7.1 (Varian Medical Systems, Inc., Palo Alto, Calif.). Transrectal ultrasound (TRUS) images with 5-mm intervals were obtained using B&K Ultrasonography and Probe for treatment planning. Patients were positioned in a high lithotomy position under general anesthesia during both pre-planning and intraoperative planning. A stepping unit provided real-time feedback to the operator and planning system based on TRUS images. A Foley catheter and gel enhanced urethral visibility during imaging. Contours were drawn on the pre-planning images, and optimal treatment plans were formulated. Seed activities, determined based on the treatment plan's needle and seed counts, were approximately 0.49 U per seed on the application day. Most seeds were in strand form, with loose seeds used in regions requiring individual additions. During intraoperative application, seeds were placed according to the pre-plan. Needle placement was

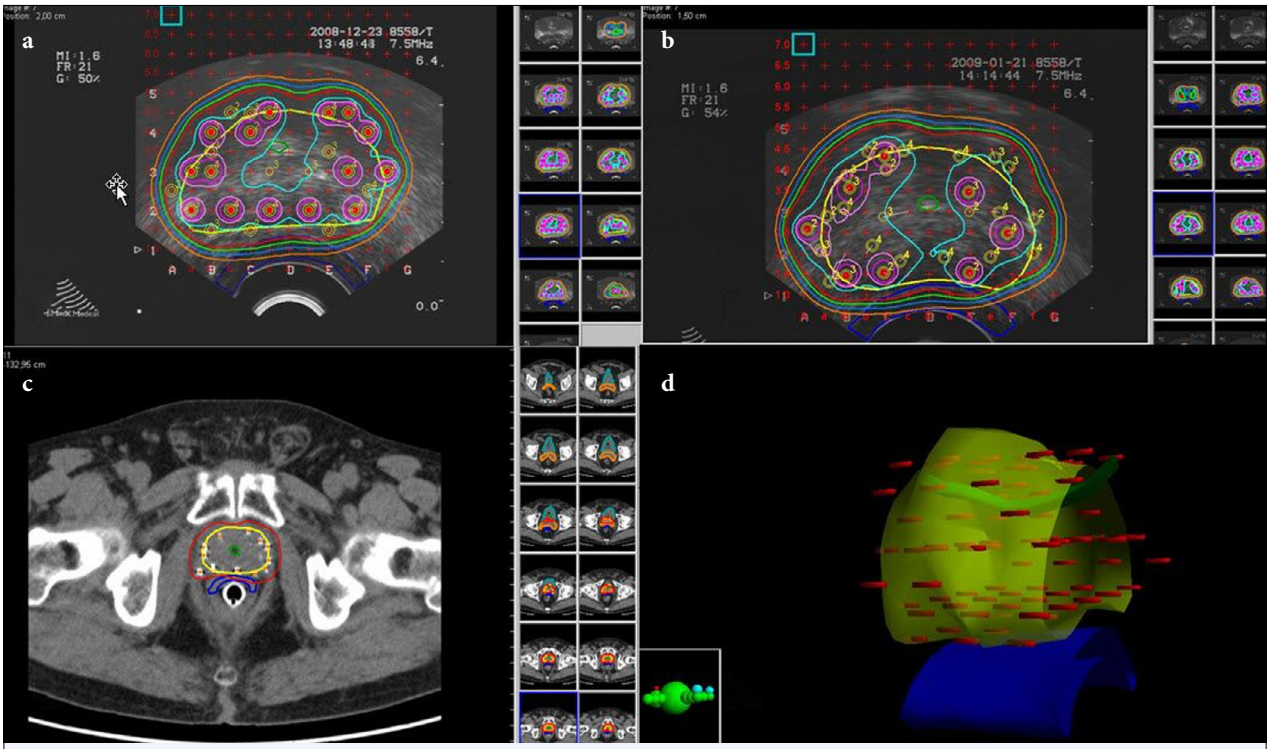

Fig. 1. Patient's (a) Pre-planning (PP), (b) intraoperative planning (IOP), (c) post-implant dosimetry (PID) plans, (d) 3D image of the application.

manually performed based on planned coordinates, with needle position verification using a C-arm fluoroscopy device. In cases where seed implantation to the planned coordinates was hindered by edema and tissue hardness resulting from needle application, seed implantation was adjusted to unplanned points to achieve the same dosimetric parameters as in pre-planning.

The target volume for treatment planning was defined as the prostate, with the rectum and urethra designated as organs at risk. Minimum peripheral doses (mPD) were set at 145 Gy for brachytherapy. In both pre-planning and intraoperative planning, prostate volumes receiving 90%, 100%, and 150% of the prescribed dose (pV90, pV100, pV150), the dose received by 90% of the prostate volume (pD90), and the doses received by 10%, 30%, and 50% of the urethra volume (uD10, uD30, uD50) were determined. Additionally, volumes receiving the entire prescribed dose and 150% of the dose (uV100, uV150), and the rectal volumes receiving the entire prescribed dose and 150% of the dose (rV100, rV150) were assessed. These parameters were evaluated according to the primary treatment criteria based on AAPM TG 137 recommendations. [19] For the prostate: pD90 ≥100% of the prescription dose, pV100 >95%, and pV150 ≤50%. For the rectum: rV100 <2 mL, rV150 <0.1 mL. And for the urethra: D10 <150% of the prescription dose, uD30 <130% of the prescription dose, and uV150 <15%.

Post-implant Dosimetry

Post-implant dosimetry was conducted using CT/MR imaging taken in the supine position approximately four weeks after the application. Verification of the intraoperative plan was carried out by identifying the implanted seeds using the VariSeed software and generating a dose distribution. The prostate, rectum, and urethra were contoured on the sections to obtain dose-volume histogram (DVH) parameters. Performing imaging in the supine position for post-implant dosimetry, without the intraoperative probe and considering edema, led to dosimetric differences. Nevertheless, we believe that a simple comparison, incorporating these effects from CT-based to US-based planning, remains beneficial in the clinical setting. Figure 1 displays a patient's pre-planning (PP), intraoperative planning (IOP), and post-implant dosimetry (PID) plans, along with a 3D image of the application.

Statistical Analysis

Within the study, a comparison was conducted to assess the differences in dose distributions among pre-

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Table 1 Presents the mean±SD results for all prostate volume examined parameters, along with the p-values for the comparisons

Dozimetric parameters	PP mean±SD	IOP mean±SD	PID mean±SD	PP-IOP p	PP-PID p	IOP-PID p	Objective criteria
b Prostate volume (mL)	33.90±10.5	33.5±10.65	30.89±8.57	0.049	<0.001	<0.001	
a pD90 (Gy)	164.42±14.57	164.99±19.3	157.2±19.5	0.393	<0.001	<0.001	≥ 145
pD90 (%)	116.75±6.58	117.12±10.60	111.22±12.80	0.371	<0.001	<0.001	≥ 100
pV90 (%)	99.00±2.22	97.91±5.75	96.32±3.32	0.084	<0.001	<0.001	≥95
b pV90 (mL)	33.54±10.46	32.93±10.71	29.54±8.37	0.051	<0.001	<0.001	
a pV100 (%)	96.92±3.42	96.24±5.53	93.10±5.51	0.388	<0.001	<0.001	>%95
b pV100 (mL)	33.52±11.58	32.22±10.2	29.38±8.72	0.007	<0.001	<0.001	
pV150 (%)	56.22±8.26	60.88±9.8	64.84±10.63	<0.001	<0.001	0.004	≤50
pV150 (mL)	19.00±6.21	20.35±7.15	21.18±10.01	<0.001	0.002	0.319	

a: Paired sample T test; b: Two related samples test -wilcoxon. SD: Standard deviation; PP: PrePlan; IOP: Intra Operative Plan; PID: Post Implant Dosimetry; pD90: Dose covering 90% of prostate volume; pV90: Prostate volume covered by 90% of the prescription dose; pV100: Prostate volume covered by 100% of the prescription dose; pV150: Prostate volume covered by 150% of the prescription dose

planning (PP), intraoperative planning (IOP), preplanning and post-implant dosimetry (PID), as well as intraoperative planning and post-implant dosimetry. To analyze these distinctions, statistical analyses were performed using paired sample T-tests and Two Related Samples Test-Wilcoxon tests.

RESULTS

Dosimetric data and the volumetric comparisons for the prostate are summarized in Table 1. The mean prostate volume was measured as 33.9 mL in preplanning, 33.5 mL in intra-op, and 30.89 mL in postplanning. The study revealed a significant difference between pre-planning (PP) and intraoperative planning (IOP) prostate volumes (p=0.049). However, the differences were more pronounced between IOP and post-implant dosimetry (PID) (p<0.001) and between PP and PID (p<0.001). In the PID performed four weeks after implantation, prostate volumes were found to be significantly smaller.

The pD90 values (Gy) for PP, IOP, and PID were 164.42±14.6 Gy, 164.99±19.3 Gy, and 157.2±19.5 Gy, respectively. When comparing pD90 between PP and IOP, PP and PID, and IOP and PID applications, the p-values were found to be p=0.393, p<0.001, and p<0.001, respectively. Regarding the prostate volume receiving 90% of the prescribed dose (pD90), it was observed that in PP, IOP, and PID treatment plans, it was 116.75%, 117.12%, and 111.22%, respectively. All parameters met the recommended values (>100%) for prostate D90.

For pV90 (%), the mean ± standard deviation for PP, IOP, and PID were found to be 99±2.22, 97.91±5.75, and 96.32±3.32, respectively. When comparing pV90 between IOP and PP, PP and PID, and IOP and PID applications, the p-values were found to be p = 0.084, p<0.001, and p<0.001, respectively. The target for this value was to achieve ≥95%. The mean pV100 (%) was found to be 96.92% in PP and 96.24% in IOP, meeting the desired level of 95%. However, in PID, it was lower at 93.1%. Significant differences were observed when comparing pV100 (mL) between PP and IOP, PP and PID, and IOP and PID applications.

Although it is preferred for the prostate volume receiving 150% of the prescribed dose (pV150) to remain at 50%, in both PP and IOP treatment plans, it was found to be higher than expected at 56% and 60%, respectively. Also, in the PID planning, it surpassed the anticipated value, reaching 64%. Table 1 displays the mean±SD results and comparison p-values for all prostate parameters in PP, IOP, and PID.

As shown in Table 1, the reference value of pD90 ≥100% Rx is achieved in all three plans. pV100 >95% is attained in PP and IOP, with a 2% lower value in PID. The volume is found to be 6.22% higher in PP, 10.88% higher in IOP, and 14.84% higher in PID than the recommended pV150 ≤50%.

Table 2 presents the dosimetric parameters and their comparisons for the urethra. The difference between urethra volumes in PP and IOP was not found to be significant (p=0.226). However, significant differences were observed between IOP and PID (p<0.001) and between PP and PID (p<0.001) for urethra volumes. The recommended value for uD10 <150% Rx is achieved in PP and IOP, but in PID, it is found to be 156%, which is 6% higher than the suggested value. Similarly, for uD30 <130% Rx, it is achieved in PP and IOP, but in PID, it is found to be 136%, which is 6% higher than the recom-

Table 2 Presents the mean±SD results uretra volume examined parameters, along with the p-values for the comparisons

Dozimetric parameters	PP mean±SD	IOP mean±SD	PID mean±SD	PP-IOP p	PP-PID p	IOP-PID p	Objective criteria
b Urethra volume (mL)	0.629±0.78	0.56±0.57	1.10±0.89	0.226	<0.001	<0.001	
a uD10 (%)	129.98±7.88	138.11±14.93	156.5±26.99	<0.001	<0.001	<0.001	<%150
uD10 (Gy)	181.87±19.35	192.94±26.12	218.89±42.01	<0.001	<0.001	<0.001	
a uD30 (%)	124.39±8.61	130.84±13.7	136.35±27.75	<0.001	0.007	0.349	<%130
uD30 (Gy)	174.02±19.15	182.63±24.13	194.26±33.52	<0.001	<0.001	<0.001	
a uD50 (%)	117.06±9.79	121.5±13.54	119.16±20.15	0.003	0.542	0.066	
uD50 (Gy)	163.61±18.99	167.66±31.21	163.96±39.14	0.216	0.925	0.074	
b uV100 (%)	77.70±13.5	78.04±15.2	68.72±37.48	0.146	<0.001	<0.001	
uV100 (mL)	0.54±1.47	0.95±6.16	0.71±0456	0.773	<0.001	<0.001	
b uV150 (%)	1.25±5.16	11.02±29.6	23.9±19.06	<0.001	<0.001	<0.001	<%15
uV150 (mL)	0.12±1.38	0.034±0.086	0.24±0.21	<0.001	<0.001	<0.001	

a: Paired sample T test; b: Two related samples test -wilcoxon. SD: Standard deviation; PP: PrePlan; IOP: Intra Operative Plan; PID:Post Implant Dosimetry; uD10: Dose covering 10% of the urethra; uD30: Dose covering 30% of the urethra; uD50: Dose covering 50% of the urethra; uV100: Urethra volume covered by 100% of the prescription dose; uV1150: Urethra volume covered by 150% of the prescription dose

Table 3 Presents the mean±SD results for rectum volume examined parameters, along with the p-values for the comparisons

Dozimetric parameters	PP mean±SD	IOP mean±SD	PID mean±SD	PP-IOP p	PP-PID p	IOP-PID p	Objective criteria
b Rectum volume (mL)	7.07±2.39	7.33±2.94	7.81±3.25	0.244	<0.001	<0.001	
rV50 (%)	44.02±18.77	47.00±22.34	50.66±19.61	0.48	0.35	0.582	
rV50 (mL)	3.73±1.51	3.98±1.72	3.51±1.67	0.028	0.206	0.017	
rV100 (%)	1.07±2.63	1.93±3.30	10.2±9.64	0.019	<0.001	<0.001	
rV100 (mL)	0.23±0.70	0.24±0.371	0.59±0.65	<0.001	<0.001	<0.001	<1cc
rV150 (%)	0.031±0.116	0.021±0.67	1.68±3.35	0.654	0.103	0.051	
rV150 (mL)	0.001±0.007	0.005±0.002	0.088±0.025	0.102	0.003	0.001	<0.1cc

b: Two related samples test – Wilcoxon. SD: Standard deviation; PP: PrePlan; IOP: Intrao Operative Plan; PID: Post Implant Dosimetry; rV50: Rectal volume covered by 50% of the prescription dose; rV100: Rectal volume covered by 100% of the prescription dose; rV150: Rectal volume covered by 150% of the prescription dose

mended value. In terms of uV150 <15%, it is achieved in PP and IOP, whereas in PID, it is 23.9%, which is 8.9% higher. The intended parameter values for the urethra were met in the PP and IOP plans. In PID, D10 and D30 doses, as well as V150 volume, were found to be slightly higher than intended.

Table 3 displays the dosimetric parameters and comparisons for the rectum. No significant difference was found between the volumes in pre-planning (PP) and intraoperative planning (IOP) (p=0.244). However, significant differences were observed between IOP and post-implant dosimetry (PID) (p<0.001) as well as between PP and PID (p<0.001) for rectum volumes.

The recommended value for rV100 <2 mL was achieved in pre-planning (PP), intraoperative planning (IOP), and post-implant dosimetry (PID), with values of 0.23 mL, 0.24 mL, and 0.59 mL, respectively, which are significantly lower than the suggested values. For rV150 <0.1 mL, representing the rectal volume receiving 150% of the Rx dose, it is close to zero in all three plans. All intended parameters were successfully obtained in the rectum for all three plans.

Although there was a significant difference between IOP and PID DVH parameters, the dose constraints for the urethra were found to be well below the intended values. The intended values for the urethra were set at uD10 <150% Rx (217.5 Gy—150% of the prescribed dose of 145 Gy, equivalent to 217.5 Gy). In PID, the mean±SD was found to be 218.89±42.01, and uD30 was aimed to be < 130% Rx (188.5 Gy), with a mean±SD in PID of 194.26±33.52. For uV150, the goal was set at <15%, but the mean±SD was found to be 23%. As for rectal dose constraints, rV100 was intended to be <2 cc, and in PID, the mean±SD was 0.59±0.65. Similarly, for rV150 <0.1 cc, the intended value was achieved with a mean±SD of 0.088±0.025.

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DISCUSSION

In this study, the primary objective was to investigate the consistency of dose distributions obtained from pre-planning (PP), intraoperative planning (IOP), and post-implant dosimetry (PID) in low-dose-rate prostate brachytherapy.

However, it was observed that the dose distribution designed in pre-planning could not be replicated in the intraoperative plan due to changes in patient position and shifts in seed placement during the application. Furthermore, the dose distribution obtained during intraoperative application differed from the intraoperative plan. Statistically significant differences in dose distribution and dose-volume histograms of the seeds on the post-plan dosimetry day were observed due to factors such as seed displacement and prostate volume enlargement due to edema.

In a study conducted by Ishiyama et al.,[20] differences were identified between intraoperative ultrasound (US)-based dosimetry and postoperative computed tomography (CT)-based dosimetry. They noted that certain dosimetric disparities were expected between the analyses of US-based plans and post-implant CT plans, particularly due to the presence of the probe during US planning. It was emphasized that despite variations in rectal shape deformation and rectal contouring, the high-dose area near the prostate remained consistent. The study indicated that these rectum-related contouring differences did not significantly impact the data.

In this study, even though the definition of rectal wall volume differed between US and CT images, it was found that rV100 (rectal volume receiving the entire prescription dose) was lower than 1 mL, similar to rV50 doses in the post-op CT plan compared to the intra-op plan. In Ishiyama et al.[20]'s study, they observed that prostate parameters tended to be higher in US-based intraoperative dosimetry than in CT-based postoperative dosimetry. This difference was attributed to seed locations being more centrally defined in the prostate, resulting in higher US parameters compared to CT parameters. In my study, I preferred peripheral seed placement, and I observed that prostate parameters, except for pV150 volumes, tended to decrease in the post-operative plan compared to the intra-operative plan. However, urethra doses tended to increase in post-plan dosimetry, despite the preference for peripheral placement.

In their study, Gregory et al.[21] examined the impact of contouring and image alignment uncertainty on dosimetric outcomes when employing different prostate implantation (PID) methods. They reported that the dosimetry method utilizing CT images in PID disregards the effect of edema, and D90 values may fluctuate due to swelling and edema of the prostate caused by needle insertion during application. They further highlighted that the most significant impact might be on the D90 dose due to contour differences induced by edema and variations in the inferior-superior direction during contouring. In our study, we observed that the pD90 value was similar in the pre- and intra-operative plans but tended to decrease in post-implant dosimetry. Although the pD90 dose in PID was lower than in the pre-plan and intra-operative plans, it was considered to still exceed the prescribed dose (157.2±19.5 Gy) to account for uncertainties.

In our study, the post-implant dosimetry results were evaluated based on AAPM TG 137.[19] Treatment criteria for prostate pD90 ≥100% of the prescription dose, pV100 >95%, and pV150 ≤50%, it was found that D90 was better than the recommended values, while V100 and V150 values were very close to the recommended values. For the rectum: rV100 <2 mL, rV150 <0.1 mL. According to the criteria, V100 and V150 volumes were within the recommended criteria. For the urethra: D10 <150% of the prescription dose, uD30 < 130% of the prescription dose, and uV150 <15%, D10 and D30 doses and V150 volume were found to be slightly higher than the recommended values.

While there were changes in dose-volume histogram (DVH) parameters between pre-planning (PP), intraoperative planning (IOP), and PID plans, our previous study found that the 5-, 10-, and 12-year disease-free survival rates were 99.9%, 93%, and 93% in the low-risk group and 100%, 92%, and 74% in the medium-risk group.[22,23]

Despite efforts to replicate the dose distribution obtained in pre-planning in the IOP plan for all patients, significant differences were observed in the PID results. Target volume conformality and high-dose target volume results met the desired values in all three plans.

CONCLUSION

Studies have consistently reported that transperineal I-125 brachytherapy for localized prostate cancer yields favorable clinical control, overall survival, and acceptable late-term toxicity. In our study, we successfully maintained the target volume and rectal anterior wall (RAO) doses within tolerance limits, with dose control confirmed through post-implant dosimetry. Although significant differences were observed between the applications, it can be confidently asserted that low-dose-rate (LDR) prostate brachytherapy represents a viable treatment option for both early and late-stage toxicity when evaluated in terms of treatment efficacy and side effects.

Ethics Committee Approval: The study was approved by the Acıbadem Mehmet Ali Aydınlar University Medical Research Ethics Committee (no: 2024-4/136, date: 14/03/2024).

Authorship contributions: Concept – Ö.Ş., E.T.; Design – Ö.Ş., E.T., I.A.; Supervision – I.A., G.K.; Materials – I.A., A.A., G.K., S.K.; Data collection and/or processing – H.K., G.K.; Data analysis and/or interpretation – Ö.Ş., E.T., I.A.; Literature search – Ö.Ş., E.O.G., E.T.; Writing – Ö.Ş., E.T., I.A.; Critical review – H.K., S.K.

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