ISSN: 2577 - 8005

Review Literaure

Medical & Clinical Research

Low-dose-rate brachytherapy in low-risk prostate cancer- treatment results, radiation toxicity and quality of life-dissertation project with literature review

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Submitted: 01 Jun 2023; **Accepted**: 03 July 2023; **Published**: 15 July 2023

Citation: *Kahchiev N, Marinova L, Vasileva V, Gabrovski L, Valchev G (2023). Low-dose-rate brachytherapy in low-risk prostate cancer- treatment results, radiation toxicity and quality of life-dissertation project with literature review. Medical & Clinical Research, 8(7), 01-08.*

Abstract

Low-dose-rate brachytherapy (LDR-BT) is a an internal radiation therapy method for the treatment of localized prostate cancer The treatment modality has been known for several decades. The choice of the treatment modality for prostate cancer patients depends mainly on the stage of the disease and the prognostic factors. Brachytherapy monotherapy is a well-tolerated procedure compared to alternative treatments. Based on a literature review, we have considered a prospective study on the treatment efficiency after LDR-BT with a permanent iodine-125 (I-125) implant, compared to that of hypo-fractionated external beam radiotherapy (EBRT) alone. The working thesis is to present the advantages and disadvantages of LDR-BT for low-risk prostate carcinoma, compared to a similar group of patients treated with definitive intensity-modulated hypo-fractionated radiotherapy (IMHRT).

Keywords: Prostate Cancer, Low-Dose-Rate Brachytherapy, Permanent Iodine-125 Implant, Intensity-Modulated Radiotherapy, Hypo-Fractionated Radiotherapy

Introduction

Prostate cancer remains the most common non-cutaneous cancer among US men, with an estimated 268,490 new cases and 34,500 deaths in 2022 [1]. Low-dose-rate brachytherapy (LDR-BT) is a radiation method that has been used for several decades in the treatment of localized prostate cancer (PC) [2]. The choice of the treatment modality for prostate cancer patients depends mainly on the stage of the disease and the prognostic factors [3]. Some physicians suggest that radical treatment methods should be offered to patients with an estimated survival time longer than 5-10 years [4]. Our goal in the forthcoming dissertation project is to present the advantages and disadvantages of LDR-BT in low and intermediate-risk PC after comparing it to definitive intensity-modulated hypo-fractionated radiotherapy (IMHRT) in a similar group of patients. A prospective study is needed for the treatment results (local tumor control (LTC) and biochemical relapse-free survival (BRFS), acute and chronic radiation toxicity, and quality of life) in two individual patient groups after radiotherapy (RT) with the two radiation methods.

Literature Review

Independent predictive factors in prostate cancer

Initial PSA, clinical T category, and biopsy-based Gleason score have been shown to be independently predictive of various combinations of PC-related endpoints in a variety of treatment scenarios in the non-metastatic setting [5]. Gleason grading can be reported in a variety of ways, including primary, secondary, and tertiary; total Gleason score (sum of primary and secondary grades); modified Gleason score (e.g., 3+4 with tertiary pattern 5 equals overall Gleason 8 cancer); and sub-classifications of Gleason scores (e.g., Gleason 7; 4+3 vs. 3+4) [6]. Gleason grading remains the main pathological reporting system for prostate cancer due to a consistently strong association with prostate cancer outcome [7,8]. Increasing levels of PSA prior to treatment have been shown to be associated with increasing tumor volume/stage and Gleason score, the risk of extracapsular/seminal vesicle or lymph node involvement or positive margins, and ultimately with prostate cancer outcomes [9,10]. Several risk stratification systems have been described and variously utilized, including risk groups, risk scores, and nomograms [11, 12]. Depending on the above predictive factors, prostate carcinoma is divided into three risk groups: low-risk, intermediate-risk, and high-risk stratification. The European Society for Medical Oncology uses a three-tiered system for risk stratification of localized prostate cancer [13].

- Low-risk–T1-T2a and Gleason score ≤6 and PSA ≤10 ng/mL
- Intermediate-risk–T2b and/or Gleason score 7 and/or PSA 10 to 20 ng/mL

● High-risk –≥T2c or Gleason score 8 to 10 or PSA >20 ng/mL (Table 1)

For asymptomatic patients with low- or intermediate-risk prostate cancer, the probability of nodal or distant metastasis is low [14-16]. Therefore, abdominopelvic computed tomography (CT) scan (Figure 1) and bone scan are unlikely to be helpful and should not be routinely obtained [17-19].

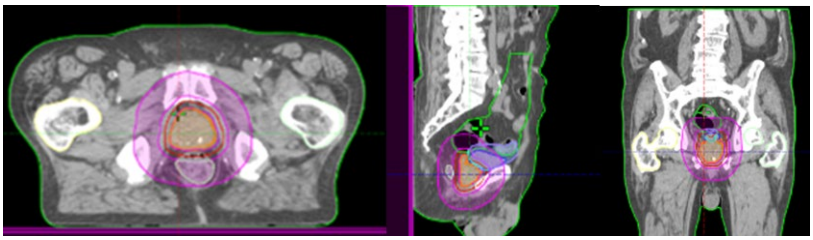

Figure 1: Computed tomography that outlines targeted volumes and normal organs and structures in the preparation of external beam radiotherapy.

	Low risk	Intermediate risk	High risk
NCCN	T1-T2a and GS 2-6 and PSA≤10 not very low-risk AND very-low risk category: T1c and GS≤6 and PSA<10 and Fewer than 3 biopsy cores positive and ≤50% cancer in each core	T2b or T2c and/or GS =7 and/or PSA>10-20 not low-risk	T3a or PSA >20 or GS 8-10 not very high risk AND very high-risk category: T3b-4
ESMO	T1-T2a and GS ≤6 and PSA<10	Not high risk and not low risk (the remainder)	T3-4 or PSA >20 or GS 8-10

Table 1: Risk groups stratification of patients in prostate carcinoma.

In patients with low- or favorable intermediate-risk prostate cancer stratification electing RT, clinicians can offer dose-escalated hypo-fractionated EBRT (moderate or ultra), permanent low-dose rate (LDR) seed implant, or temporary high-dose rate (HDR) prostate implant as equivalent forms of treatment. (Strong Recommendation; Evidence Level: Grade B) [17-19].

Radiobiology of prostate cancer

Technological developments, such as intensity-modulated radiation therapy (IMRT) and improved target localization, including the use of nanoparticles as targeted therapy, have been combined with radiation biology to generate enthusiasm for hypo-fractionated regimens [20,21]. The modern radiobiology began with the creation of the linear-quadratic model (LQ) formalism for mammalian cell killing caused by radiation. This model predicts that the survival rate of the cell depends on factors such as the overall radiation dose, dose per fraction, and the overall treatment time [22].

The alpha/beta ratios of prostate tumors appear to be as low as 1.5 Gy (95% confidence interval 1.3-1.8 Gy), in contrast with the value of about 10 Gy for most other types of tumors [20]. Brenner and Hall [23] were the first to point out (in 1999) that there is clinical evidence supporting the idea that prostate tumors have exceptionally low values of alpha/beta. They used the documented result that similar biochemical long-term control is achieved using external beam doses of about 70 Gy in 1.8/2.0 Gy fractions and a dose of 145 Gy from permanent Iodine 125 low-dose-rate irradiation. α/β values for prostate cancer ranging from 1 to 4 have been addressed, but they are based on clinical datasets for patients with early and intermediate-risk prostate cancer [24-26].

Emerging evidence accumulating from multiple recent studies indicates that more convenient and efficient shortened courses of radiotherapy for prostate cancer yield outcomes that are equivalent and possibly superior to the lengthier standard regimens. The scientific rationale for such “hypofractionated” treatment lies in the unique radiobiologic properties of prostate cancer [27]. The brachytherapy method has the capability to eliminate the errors of the internal organ movement and set-up variability, which are concerns in external beam radiotherapy. These parameters enable accurate high-dose delivery to the clinical target volume (CTV) while protecting the organs at risk [22].

Hypofractionated EBRT

Conventional fractionation of 1.8-2.0 Gy/day is based on the premise that the therapeutic ratio, defined as the chance of eradicating tumor cells divided by the risk of normal tissue injury in late-responding normal tissues, is optimized by using small doses per fraction [27]. The α/β ratio for prostate cancer is believed to be in the range 1-4 Gy [26,28]. Based on the α/β model for prostate cancer radiobiology, hypofractionation would theoretically offer increased therapeutic benefit with improved tumor control, without increasing late toxicity [23]. There are several advantages to a hypofractionated radiation treatment regimen, including convenience for patients, increased treatment capacity, and decreased cost [29].A Canadian hypofractionated randomized trial compared a conventional dose of 66 Gy in 33 fractions, to a hypofractionated regimen of 52.5 Gy in 20 fractions (dose per fraction 2.625 Gy) in men with low- and intermediate-risk prostate cancer, showing slightly better results

for the conventional fractionation, but in that study both doses were suboptimal according to the current understanding of dose response in prostate cancer[30].

Low-dose-rate brachytherapy (LDR-BT)

Brachytherapy is used as the sole treatment method mainly in the low-risk group of patients. A large number of individual LDR-BT procedures are performed in this group of patients worldwide. This is supported by the very good treatment results reported in various publications, the relatively small number of side effects, and the short time of treatment [31-36]. Progress in LDR brachytherapy as it relates to prostate cancer biology, local control, toxicity reduction with function preservation, external beam integration, medical event prevention, patient selection, and comparative brachytherapy is reviewed [37].

The principle of brachytherapy is the rapid decrease of the radiation dose (inversely proportional to the square of the distance) with increasing distance from the radioactive isotope. The application of permanent seed implants is a curative treatment alternative in patients with organ-confined cancer, without extracapsular extension of the tumor [38-42]. Compared with radical prostatectomy, permanent seed implantation is a short, one-day therapy with a lower complication rate during and after the procedure (bleeding, urinary incontinence, impotence) [36]. A D90 value of >140 Gy showed improved biochemical control [33]. Low-dose-rate (LDR) prostate brachytherapy involves the insertion of radionuclides (e.g., iodine-125 [I-125], palladium-103 [Pd-103], or cesium-131 [Cs-131]) into the prostate gland under trans-rectal ultrasound (TRUS) guidance (Table 2).

	Half-life (day)	Avarage energy (keV)	Year introduced	Typical monotherapy seed strength	Suggested monotherapy dose (Gy)
Iodine-125	59,4	28,4	1965	0,4-0,8	144-145
Palladium-103	17,0	20,7	1986	1,5-3,0	125
Cesium-131	9,7	30,4	2004	1,6-2,5	115

Table 2: Radionuclides for permanent prostate brachytherapy.

Specific selection of radioactive isotopes and their correct localization allows a high dose to be deposited into the prostate with a rapid fall-off of the dose outside the area of treatment and, at the same time, better preservation of organs at risk (OARs) [43,44]. Patients who are appropriate candidates for LDR monotherapy usually belong to the low or sometimes intermediate-risk group according to ABS (American Brachytherapy Society) [45]. Although brachytherapy monotherapy is associated with increased urinary obstructive and irritative symptoms that peak within the first 3 months after treatment, the median time toward symptom resolution is approximately 1 year for iodine-125 and 6 months for palladium-103 [46]. Biochemical recurrence was defined as any PSA increase to >2 ng/mL above the nadir value (ASTRO Phoenix definition) [47]. Patients should have a prostate anatomy suitable for implantation, as assessed using transrectal ultrasound (TRUS), computed tomography (CT), or MRI.

Contraindications for brachytherapy

The most frequently cited contraindications for brachytherapy are a life expectancy of less than 5 years, distant metastases, a history of transurethral resection of the prostate (TURP) with chronic significant damage to the gland within 3 months before brachytherapy, and recurrent hematuria [2]. Relative contraindications include severe urinary irritative/obstructive symptomatology, extensive TURP defect, substantial median lobe hyperplasia, prostate dimensions larger than the grid (>60 mm in width and >50 mm in height), severe pubic arch interference, gross seminal vesicle involvement, prior pelvic radiotherapy, inflammatory bowel disease, and pathologic involvement of pelvic lymph nodes. Absolute contraindications for TRUS-guided prostate brachytherapy include an inability to tolerate general, spinal, or local anesthesia in the dorsal lithotomy position, absence of a rectum, active inflammatory bowel disease, or unacceptable operative risks, distant metastases, and life expectancy<5 years [3,45,48].

Required measures to prevent radiation side effects to adjacent normal organs (bladder and rectum) after LDR brachytherapy: Brachytherapy monotherapy is associated with transient urinary irritative symptoms that peak within the first 3 months of treatment and tend to resolve toward baseline at 1 year for I-125 and 6 months for Pd-103. Special consideration should be made for patients with large prostate glands, large median lobes, or a prior history of transurethral resection of the prostate (TURP) [49]. Patients with large prostate volumes (>60 cc) may benefit from a TRUS [50], CT [51], or MRI-guided [52] volume study to ensure minimal pubic arch interference. Such patients may also be at greater risk of urinary retention [53] and late urinary toxicity [54].

Radiobiological advantages and disadvantages of LDR brachytherapy: As monotherapy, LDR-BT seems to be a reliable choice for early-stage prostate cancer, considering the low morbidity rate, good results, and short hospitalization. It is a curative alternative to radical prostatectomy and external beam radiation (e.g., 3D CRT, IMRT) with comparable long-term survival, biochemical control, and favorable toxicity [55]. With brachytherapy, a high radiation dose can be locally delivered with a steep dose gradient in the surrounding healthy tissues [56]. Lee et al. found the number of needles and prostate volume to be significant factors predicting urinary retention after brachytherapy [57]. Early et al. found that excessive radiationto the apical and peri-apical urethra was associated with a higher incidence of an urethral stricture [58]. Daphna et al showed a grade 1 and 2 rectal toxicity in 9.5% of the patients

after brachytherapy with a peak at 8 months, all resolved in 3.5 years [59,60]. Using the International Index of Erectile Function (IIEF), brachytherapy induced erectile dysfunction and occurred in 50% of the patients at 3 years; Others mentioned a global reduction in all areas of the questionnaire after 12 months of completion of brachytherapy [61,62]. Brachytherapy monotherapy is a well-tolerated treatment compared with the alternative modalities. Although brachytherapy is associated with increased urinary irritative symptoms that peak within the first 3 months after treatment, the median time toward symptom resolution is 1 year for I-125, and 6 months for Pd-103 [63].

Technique for LDR Prostate Brachytherapy with Iodine-125 [I-125]

The team of specialists required for the placement of sources in LDR-BT is interdisciplinary and includes a radiation oncologist, medical physicist, radiotherapy dosimetrist, urologist, nurse, and support staff. Effective communication, a well-defined workflow, and understanding the roles of team members are crucial for maximizing treatment outcomes. Seed implantation can be performed using pre-loaded needles with sources arranged at appropriate distances or through the use of a Mick® applicator with a cartridge containing a specific number of seeds (Figure 2A,B).

Currently, a combination of transrectal ultrasound (TRUS) and guidance from a coordinate grid (Figure 2C) is commonly used. However, some experienced brachytherapists choose not to use ultrasound to avoid interference from the pubic arch, which can lead to errors in source positioning. Biplanar transrectal ultrasound guidance allows visualization of needles in both axial and sagittal planes, significantly improving the accuracy of source placement. To ensure precise dosing within the prostate, the use of nomograms (accounting for adequate activity per volume) combined with real-time TRUS and treatment planning system is essential [64]. Both loose and stranded seeds can be used for prostate seed implantation. Loose seeds are loaded in sterile cartridges, while stranded seeds can be delivered using pre-loaded needles or constructed intraoperatively [49].

During digital examination, physicians and physicists should obtain isodoses that overlap the gland at various percentages (50%, 80%, 90%, 100%, 150%, and 200%) of the prescribed dose and compare them to dose-volume histograms (DVH) from previous CT scans [3]. Intraoperative planning with careful seed placement is necessary to achieve a high D90 while avoiding proximity to the penis, apical urethra, and rectum [65]. The prescribed dose in the planning target volume should not exceed 150%, and adjusting the number of seeds can help mitigate potential "hot-spots" [40].

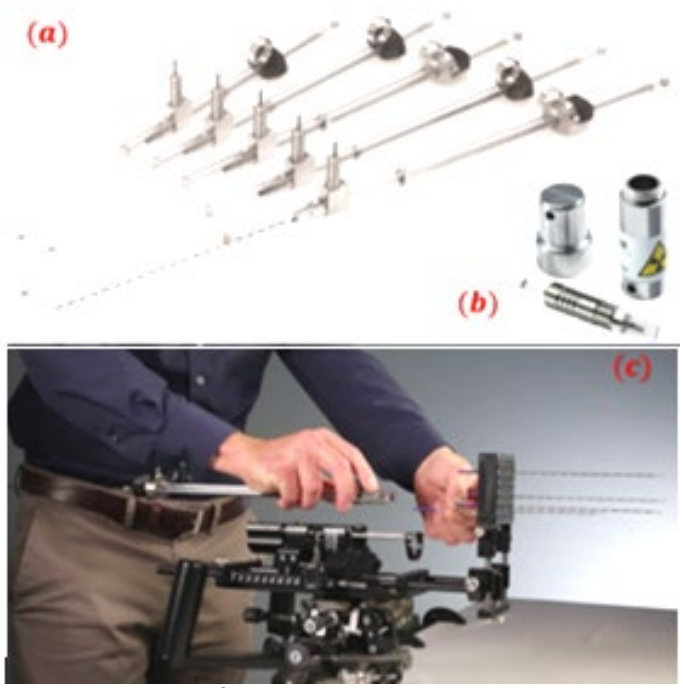

Figure 2: A) Mick® TP/TPV LDR-BT applicator; B) Mick® seed cassette with I-125; C/ Steper-stable module for the coordinate grille to which application needles are attached to (Eckert & Ziegler BEBIG Company).

Patients with permanently placed radiation sources require isolation in specially protected premises due to the potential radiation danger they pose to others. To address this issue, two approaches are commonly employed: 1) the use of sources with very low-energy photon radiation that is fully absorbed within the patient's body, and 2) the utilization of radionuclides with short half-lives to reduce the duration of stay in isolated hospital rooms. Permanent implantation sources emitting low-energy photon radiation are widely utilized.

Discussion

Phase II prospective RTOG 9805 study enrolled 101 low-risk disease patients treated with I-125 monotherapy (145 Gy). Among 94 eligible patients with a median follow-up of 8.1 years, the

8-year cumulative incidences of biochemical failure and metastasis were 8% and 1.1%, respectively [66]. Two single institutional randomized trials conducted by Giberti et al. reported no difference in biochemical progression-free survival (bPFS) between LDR brachytherapy and radical prostatectomy at 5 years [67] and 2 years [68] for low-risk disease. Other studies have demonstrated similar outcomes between LDR brachytherapy and conventional external beam radiation therapy (EBRT) alone [69]. However, there is a lack of prospective studies comparing treatment outcomes and radiation side effects between LDR-BT and definitive hypo-fractionated EBRT alone for prostate carcinoma (Figure 3). Therefore, a prospective study comparing treatment efficacy after LDR-BT with permanent I-125 implantation and hypo-fractionated EBRT alone is needed to evaluate the advantages and disadvantages of LDR-BT for low-risk prostate carcinoma compared to a similar group of patients receiving definitive intensity-modulated hypo-fractionated radiotherapy (IMHRT).

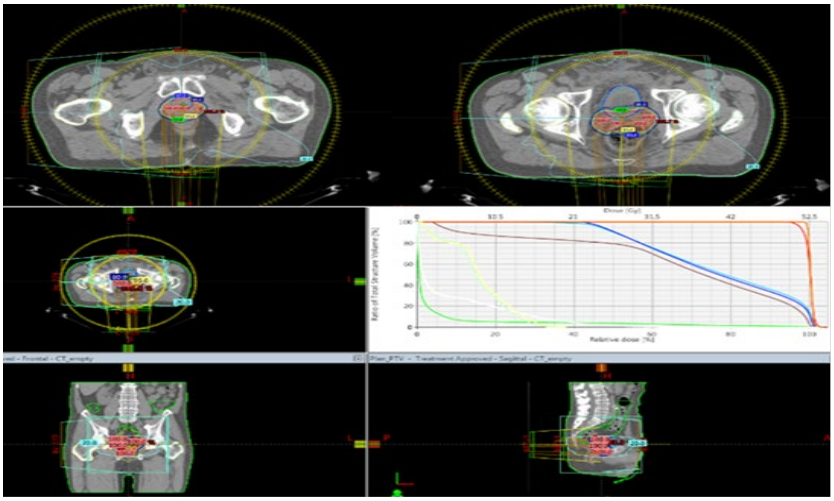

Figure 3: Definitive intensity-modulated hypo-fractionated radiotherapy by VMAT method with daily dose of 3 Gy up to a total dose of 60 Gy/ 20 fractions BED=120Gy; EQD2=72Gy.

The patient population of interest comprises individuals undergoing primary treatment for NCCN-defined low and intermediate-risk prostate cancer. The study will consist of two groups, each consisting of 35 patients. The prospective study will evaluate various treatment outcomes, including local tumor control (LTC), disease-free survival (DFS), disease-specific survival (DSS), overall survival (OS), biochemical recurrence-free survival (BRFS), or biochemical freedom from failure rate (BFFF). It will also assess acute and chronic physician-assigned toxicity and patient-reported quality of life during the first, second, and third years following radiotherapy. Patient follow-up will occur at 1 month, 3 months, and annually for the first, second, and third years post-procedure.

Conclusion

Brachytherapy monotherapy is a well-tolerated treatment option compared to alternative modalities. To further explore its treatment efficacy, a prospective study will be conducted to compare LDR-BT with a permanent I-125 implant to hypo-fractionated EBRT alone. The study aims to present the advantages and disadvantages of LDR-BT for low-risk prostate carcinoma in comparison to a group of patients who underwent definitive intensity-modulated hypo-fractionated radiotherapy.

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A (2022) Cancer statistics, 2022. Ca Cancer J Clin 72:7.
2. Januesz S (2013) Brachytherapy in the therapy of prostate cancer-an interesting choice Contemp Oncol (Pozn) . 17(5): 407-412.
3. Skowronek J (2013) Low-dose-rate or high-dose-rate brachytherapy in treatment of prostate cancer-between options. J Contemp Brachytherapy 5:33-41.
4. Mohler J, Bahnson RR, Boston B, Busby JE, D'Amico A, et al. (2010) NCCN clinical practice guidelines in oncology: prostate cancer. J Natl Compr Canc Netw 8:162-200.
5. Sutcliffe P, Hummel S, Simpson E, Young T, Rees A, et al. (2009) Use of classical and novel biomarkers as prognostic risk factors for localised prostate cancer: a systematic review. Health Technol Assess 13:1-219.
6. Chan TY, Partin AW, Walsh PC, Epstein JI (2000) Prognostic significance of Gleason score 3+4 versus Gleason score 4+3 tumor at radical prostatectomy. Urology 56:823-827.
7. Partin AW, Kattan MW, Subong EN, Walsh PC, Wojno KJ, et al. (1997) Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update. JAMA 277:1445-1451.
8. D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, et al. (1998) Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA 280:969-974.
9. Aleman M, Karakiewicz PI, Kupelian P, Kattan MW, Graefen

M, et al. (2003) Age and PSA predict likelihood of organ-confined disease in men presenting with PSA less than 10 ng/mL: implications for screening. Urology 62:70-74.
10. Shekarriz B, Upadhyay J, Bianco FJ Jr, Tefilli MV, Tiguert R, et al. (2001) Impact of preoperative serum PSA level from 0 to 10 ng/ml on pathological findings and disease-free survival after radical prostatectomy. Prostate 48:136-143.
11. Sanda MG, Cadeddu JA, Kirkby E, Chen RC, Crispino T, et al. (2018) Clinically localized prostate cancer: AUA/ASTRO/SUO guideline. part I: risk stratification, shared decision making, and care options. J Urol 199:683.
12. National Comprehensive Cancer Network (2021) Prostate Cancer Version 2.2022. November 30, 2021.
13. Parker C, Castro E, Fizazi K, Heidenreich A, Ost P et al. (2020) Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up .Ann Oncol 31(9):1119-1134.
14. Merdan S, Womble PR, Miller DC, Barnett C, Ye Z , et al. (2014) Toward better use of bone scans among men with early-stage prostate cancer. Urology 84:793.
15. Risko R, Merdan S, Womble PR, Barnett C, Ye Z, et al. (2014) Clinical predictors and recommendations for staging computed tomography scan among men with prostate cancer. Urology 84:1329.
16. Makarov DV, Trock BJ, Humphreys EB, Mangold LA, Walsh PC, et al. (2007) Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partins tables) based on cases from 2000-2005. Urology 69:1095.
17. Eastham JA, Auffenberg GB, Barocas DA, Chou R, Crispino T, et al. (2022) Clinically localized prostate cancer: AUA/ASTRO guideline, part I: introduction, risk assessment, staging, and risk-based management. J Urol 208(1):10-18.
18. Eastham JA, Auffenberg GB, Barocas DA, Chou R, Crispino T, et al. (2022) Clinically localized prostate cancer: AUA/ASTRO guideline, part II: principles of active surveillance, principles of surgery, and follow-up. J Urol 208(1):19-25.
19. Eastham JA, Auffenberg GB, Barocas DA, Chou R, Crispino T, et al. (2022) Clinically localized prostate cancer: AUA/ASTRO guideline. Part III: principles of radiation and future directions. J Urol 208(1):26-33.
20. Fowler JF (2005) The radiobiology of prostate cancer including new aspects of fractionated radiotherapy. Acta Oncol 44(3):265-276.
21. Shahbazi-Gahrouei D, Abdolahi M, Zarkesh-Esfahani SH, Laurent S, Sermeus C, et al. (2013) Laurent S, Sermeus C, Gruettner C. Functionalized magnetic nanoparticles for the detection and quantitative analysis of cell surface antigen. Biomed Res Int 2013:349-408.
22. Arabpour A, Shahbazi-Gahrouei D (2017) Effect of Hypofractionation on Prostate Cancer Radiotherapy. Int J Cancer Manag 10(10): e12204.
23. Brenner DJ, Hall EJ (1999) Fractionation and protraction for radiotherapy of prostate carcinoma. Int J Radiat Oncol Biol Phys 43:1095-1101.
24. Khoo VS, Dearnaley DP (2008) Question of dose, fractionation and technique: ingredients for testing hypofractionation in prostate cancer--the CHHiP trial. Clin Oncol (R Coll Radiol) 20(1):12-14.
25. Fowler J, Chappell R, Ritter M (2001) Is alpha/beta for prostate tumors really low?. Int J Radiat Oncol Biol Phys 50(4):1021-1031.
26. Brenner DJ, Martinez AA, Edmundson GK, Mitchell C, Thames HD, et al. (2002) Direct evidence that prostate tumors show high sensitivity to fractionation (low alpha/beta ratio), similar to late-responding normal tissue. Int J Radiat Oncol Biol Phys 52(1):6-13.
27. Cho LC, Timmerman R, Kavanagh B (2013) Hypofractionated External-Beam Radiotherapy for Prostate Cancer .Prostate Cancer 2013:103547.
28. Leborgne F, Fowler J, Leborgne JH, Mezzera J (2012) Later outcomes and alpha/beta estimate from hypofractionated conformal three-dimensional radiotherapy versus standard fractionation for localized prostate cancer. International Journal of Radiation Oncology, Biology, Physics 82(3):1200-1207.
29. Kupelian PA, Reddy CA, Klein EA, Willoughby TR (2007) Short course intensity-modulated radiotherapy (70 Gy at 2.5 Gy per fraction) for localized prostate cancer: Cleveland Clinic experience. Int J Radiat Oncol Biol Phys 68 (5):1424-1430.
30. Lukka H, Hayter C, Julian JA, Warde P, Morris WJ, et al. (2005) Randomized trial comparing two fractionation schedules for patients with localized prostate cancer. J Clin Oncol 23(25):6132-6138.
31. Chicheł A, Kanikowski M, Skowronek J, Dymnicka M, Piotrowski T (2009) Correlation between treatment plan parameters and particular prognostic factors in prostate cancer treated with high-dose-rate brachytherapy (HDR-BT) as a boost. J Contemp Brachyther 1:11-17.
32. Peeters ST, Heemsbergen WD, van Putten WL, Slot A, Tabak H, et al. (2005) Acute and late complications after radiotherapy for prostate cancer: results of a multicenter randomized trial comparing 68 Gy to 78 Gy. Int J Radiat Oncol Biol Phys 61:1019-1034.
33. Machtens S, Baumann R, Hagemann J, Warszawski A, Meyer A, et al. (2006) Long-term results of interstitial brachytherapy (LDR-Brachytherapy) in the treatment of patients with prostate cancer. World J Urol 24:289-295.
34. Makarewicz R, Lebioda A, Terlikiewicz J, Biedka M, Wiśniewski T (2009) PSA bouncing after brachytherapy HDR and external beam radiation therapy: a study of 121 patients with minimum 5-years follow-up. J Contemp Brachyther 1:92-96.
35. Martinez AA, Demanes J, Vargas C, Schour L, Ghilezan M, et al. (2010) High-dose-rate prostate brachytherapy: an excellent accelerated-hypofractionated treatment for favorable prostate cancer. Am J Clin Oncol 33:481-488.
36. 36. Jacobs BL, Smith RP, Beriwal S, Benoit RM (2011) Changes in lower urinary tract symptoms after prostate

brachytherapy. J Contemp Brachyther 3:115-120.
37. Patrick W McLaughlin, Vrinda N (2020) Progress in Low Dose Rate Brachytherapy for Prostate Cancer. Semin Radiat Oncol 30(1):39-48.
38. Horwich A, Parker C, Bangma C, Kataja V (2010) ESMO Guidelines Working Group. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 129-133.
39. Thompson I, Thrasher JB, Aus G, Burnett AL, Canby-Hagino ED, et al. (2007) Guidelines for the management of clinically localized prostate cancer: 2007 update. J Urol 177:2106-2131.
40. Garbaulet A, Potter R, Mazeron JJ, Meertens H, Van Limbergen E (2002) Brussels: The GEC ESTRO Handbook of Brachyther 473-480.
41. Ash D, Flynn A, Battermann J, de Reijke T, Lavagnini P, et al. (2000) ESTRO/EAU/EORTC recommendations on permanent seed implantation for localized prostate cancer. Radiother Oncol 57:315-321.
42. Skowronek J, Kanikowski M, Zwierzchowski G, Chicheł A (2009) Brachyterapia LDR w leczeniu raka gruczołu krokowego. Contemp Oncol (Pozn) 13:316-322.
43. Pujades MC, Camacho C, Perez-Calatayud J, Richart J, Gimeno J, et al. (2011) The use of nomograms in LDR-HDR prostate brachytherapy. J Contemp Brachyther 3:121-124.
44. Knaup C, Mavroidis P, Stathakis S, Smith M, Swanson G, et al. (2011) Evaluation of the effect of prostate volume change on tumor control probability in LDR brachytherapy. J Contemp Brachyther 3:125-130.
45. Hsu I-Ch, Yamada Y, Vigneault E, Pouliot J (2010) American Brachytherapy Society Prostate High-Dose Rate prostate brachytherapy. Brachytherapy 11(1):20-32.
46. King MT, Keyes M, Frank SJ, Crook JM, Butler WM, et al. (2021) Low dose rate brachytherapy for primary treatment of localized prostate cancer: A systemic review and executive summary of an evidence-based consensus statement. Brachytherapy 20(6):1114-1129.
47. Roach M, Hanks G, Thames H, Jr, Schellhammer P, Shipley WU, et al. (2006) Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix Consensus Conference. Int J Radiat Oncol Biol Phys 65:965-974.
48. Kovács G, Pötter R, Loch T, Hammer J, Kolkman-Deurloo IK, et al. (2005) GEC/ESTRO-EAU recommendations on temporary brachytherapy using stepping sources for localised prostate cancer. Radiother Oncol 74:137-148.
49. Clerk JA, Talcott JA (2001) Symptom indexes to assess outcomes of treatment for early prostate cancer. Med Care 39(10):1118-1130.
50. Wallner K, Ellis W, Russell K, Cavanagh W, Blasko J (1999) Use of TRUS to predict pubic arch interference of prostate brachytherapy. Int J Radiat Oncol 43: 583-585.
51. Bellon J, Wallner K, Ellis W, Russell K, Cavanagh W, et al. (1999) Use of pelvic CT scanning to evaluate pubic arch interference of transperineal prostate brachytherapy. Int J Radiat Oncol 43:579-581
52. Martin GV, Pugh TJ, Mahmood U, Kudchadker RJ, Wang J, et al. (2017) Permanent prostate brachytherapy pubic arch evaluation with diagnostic magnetic resonance imaging. Brachytherapy 16:728-733.
53. Crook J, McLean M, Catton C, Yeung I, Tsihlias J, et al. (2002) Factors influencing risk of acute urinary retention after TRUS-guided permanent prostate seed implantation. Int J Radiat Oncol 52:453-460.
54. Keyes M, Miller S, Moravan V, Pickles T, McKenzie M, et al. (2009) Predictive factors for acute and late urinary toxicity after permanent prostate brachytherapy: long-term outcome in 712 consecutive patients. Int J Radiat Oncol Biol Phys 73:1023-1032.
55. Marek Kanikowski, Janusz Skowronek, Magda Kubaszewska et al. (2008) Permanent implant in treatment of prostate cancer. Reports of Practical Oncology & Radiotherapy 13(3):150-167.
56. Nag S, Beyer D, Friedland J, Grimm P, Nath R (1999) American Brachytherapy Society (ABS) recommendations for transperineal permanent brachytherapy of prostate cancer. Int J Radiat Oncol Biol Phys 44:789-799.
57. Lee N, Wuu CS, Brody R, Laguna JL, Katz AE, et al. (2000) Factors predicting for postimplantation urinary retention after permanent prostate brachytherapy. Int J Radiat Oncol Biol Phys 48:1457-1460.
58. Earley JJ, Abdelbaky AM, Cunningham MJ, et al. (2012). Correlation between prostate brachytherapy-related urethral stricture and peri-apical urethral dosimetry: a matched case-control study. Radiother Oncol 104:187-191.
59. Buckstein M, Carpenter TJ, Stone NN, Stock RG (2013) Long-term outcomes and toxicity in patients treated with brachytherapy for prostate adenocarcinoma younger than 60 years of age at treatment with minimum 10 years of follow-up. Urology 81:364-368.
60. Gelblum DY, Potters L (2000) Rectal complications associated with transperineal interstitial brachytherapy for prostate cancer. Int J Radiat Oncol Biol Phys 48:119-124.
61. Matsushima M, Kikuchi E, Maeda T, Nakashima J, Sugawara A, et al. (2013) A prospective longitudinal survey of erectile dysfunction in patients with localized prostate cancer treated with permanent prostate brachytherapy. J Urol 189:1014-1018.
62. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Anderson RL, et al. (2005) Erectile function after prostate brachytherapy. Int J Radiat Oncol Biol Phys 62:437-447.
63. King MT, Keyes M, Frank SJ, Crook JM, Butler WM, et al. (2021) Low dose rate brachytherapy for primary treatment of localized prostate cancer: A systemic review and executive summary of an evidence-based consensus statement. Brachytherapy 20(6):1114-1129.
64. Pujades MC, Camacho C, Perez-Calatayud J, Richart J, Gimeno J, et al. (2011) The use of nomograms in LDR-HDR prostate brachytherapy. J Contemp Brachytherapy 3:121-124.
65. Logghe P, Verlinde R, Bouttens F, Van den Broecke C, Deman N,, et al. (2016) Long term outcome and side effects in patients receiving low-dose I125 brachytherapy: a retrospective

analysis. Int Braz J Urol 42(5): 906-917.
66. Lawton CA, Hunt D, Lee WR, Gomella L, Grignon D, et al. (2011) Long-term results of a phase II trial of ultrasound-guided radioactive implantation of the prostate for definitive management of localized adenocarcinoma of the prostate (RTOG 98-05). Int J Radiat Oncol 81:1-7.
67. Giberti C, Chiono L, Gallo F, Schenone M, Gastaldi E (2009) Radical retropubic prostatectomy versus brachytherapy for low-risk prostatic cancer: a prospective study. World J Urol 27:607-612.
68. Giberti C, Gallo F, Schenone M, Gastaldi E, Cortese P, et al. (2017) Robotic prostatectomy versus brachytherapy for the treatment of low risk prostate cancer. Can J Urol 24(2): 8728-8733.
69. Smith GD, Pickles T, Crook J, Martin AG, Vigneault E, et al. (2015) Brachytherapy improves biochemical failure–free survival in low- and intermediate-risk prostate cancer compared with conventionally fractionated external beam radiation therapy: a propensity score matched analysis. Int J Radiat Oncol 91:505-516.