Modern Brachytherapy in the Treatment of Prostate Cancer

Janusz Skowronek*

Brachytherapy Department, Greater Poland Cancer Center & Electroradiology Department, Poznań University of Medical Sciences, 15 Garbary Street, 61-866 Poznań, Poland

Abstract: There are several therapeutic modalities that can be performed in order to treat prostate cancer, such as: external beam radiation therapy (EBRT), prostatectomy, cryotherapy or interstitial brachytherapy (BT). Brachytherapy of prostate cancer is one of the oldest methods and means implantation of radioactive sources directly into the prostate. Brachytherapy is a curative alternative of radical prostatectomy or external beam radiation (i.e. 3D conformal external beam radiation therapy (CRT), Intensity Modulated Radiation Therapy (IMRT)) with comparable long-term survival and biochemical control and most favorable toxicity. Low-dose rate brachytherapy (LDR-BT) is one of the radiation methods that is known for several years in treatment of localized prostate cancer. The main idea of this method is to implant small radioactive seeds as a source of radiation, directly into the prostate gland. Modern high-dose-rate brachytherapy (HDR-BT) of prostate cancer enables the delivery of a very high single or multiple dose of radiation to the target volume (e.g. prostate capsule) and, at the same time, preventing the organs at risk from unnecessary radiation (e.g. urethra and rectal wall). Although initially LDR-BT was favored for low risk prostate cancers, and HDR-BT for intermediate and advanced disease, both types of brachytherapy now have a place across all the risk groups of localized prostate cancer. This article will review indications and patient selection, planning and technical aspects, toxicity and efficacy for both techniques. Possible similarities and differences between both brachytherapy modalities are discussed.

Keywords: Brachytherapy, HDR, LDR, prostate cancer, seeds.

INTRODUCTION

All the observations indicate a steady increase in prostate cancer incidence rate worldwide. In many countries of the world this is the most frequently diagnosed type of cancer, e.g. in the USA in 2010 a total of 217,730 new prostate cancer cases were recorded (28%) and 116,750 cases of lung cancer, respectively. A similar tendency is evident in many countries in Western Europe [1, 2]. More and more patients are diagnosed at the early stage of the disease, which enables effective treatment. This is further enhanced by the increasing popularity of the Prostate-Specific Antigen test (PSA).

The treatment of patients with prostate cancer depends mainly on the progression of the disease. A highly precise diagnosis of the progression of the disease is possible by means of using imaging techniques such as computer tomography (CT), magnetic resonance (MRI), transrectal ultrasonography (TRUS) in parallel with clinical assessment (digital rectal examination - DRE) and PSA test results. Knowing the TNM classification, PSA levels, and the result of pathology grading of the carcinoma it is possible to select the appropriate treatment option. It is recommended to use the guidelines of ABS, GEC-ESTRO/EUA, NCCN and ASTRO [3-6]. Partin tables, Roach's mathematical equations and on-line calculators (http://www.capcalulator.org) are also useful [7].

There are many treatment options for cases of prostate cancer limited to the organ itself, as per the recommendations of most associations dealing with the treatment of such cases [3-10]. There are several modalities that can be performed in order to treat this kind of cancer, such as: external beam radiation therapy (EBRT), prostatectomy, cryotherapy or interstitial brachytherapy (BT). Brachytherapy is one of the oldest methods and means implantation of radioactive sources directly into the prostate. Some physicians suggest that radical treatment methods should be offered to patients with an estimated survival time longer than 5-10 years [5]. This is mainly associated with the nature of the cancer which has a fairly slow cell-division cycle and its duplication time is between 16 and 61 days [11]. Most physicians, however, tend to initiate treatment just because of the lack of possibilities to forecast the progression of cancer. It has also been observed that a younger age of incidence is usually associated with a higher risk of increased tumour malignancy.

Brachytherapy of prostate cancer (this concerns both techniques – High-Dose-Rate (HDR-BT) and Low-Dose-Rate (LDR-BT)) is used more frequently, as it is associated with a smaller risk of potency disorders and urination disorders [12-15]. It is moreover better tolerated by patients burdened with different concomitant diseases, especially cardiological diseases, which disqualify the patient from surgical

*Address correspondence to this author at the Brachytherapy Department, Greater Poland Cancer Center, 15 Garbary Street, 61-866 Poznań, Poland; Tel: +48 61 8850818; Fax: +48 61 8850834;
E-mail: janusz.skowronek1@gmail.com

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treatment; this method is also used in the case of patients who do not consent to surgery. For many men an increasingly more important factor is the possibility to return to daily activities, including their jobs, sooner.

The goal of this paper is to discuss the indications, techniques, present results and possible complications. We also present the potential advantages and disadvantages of brachytherapy compared to other methods.

BRACHYTHERAPY

Brachytherapy (Greek *brachy* – from a small distance) is a method, which employs the energy of photons and/or particles created by the decay of radioactive isotopes. Brachytherapy of prostate cancer is an interstitial brachytherapy, i.e. a source of radiation is put directly into the gland using applicators. The principle of brachytherapy is the rapid decrease of the radiation dose (inversely proportional to the square of the distance) along with the increasing distance from the radioactive isotope. Results, expressed as disease free survival, are significantly related to selection of patients and vary from 85 to 90% for low-risk patients to 70-80 % for intermediate and 60-70 % for high risk patients. Overall survival rates are similar/comparable/ overlapping to the results from EBRT and surgery. Compared to EBRT brachytherapy increases the concentration of the dose within the tumour area, enables the administration of increased fractionated doses and higher biological equivalent doses, while significantly reducing the time of treatment. Hospitals that use brachytherapy may benefit from the significant cost reduction associated with one-time anaesthesia and application of isotopes (shorter in-patient treatment time). Obtaining such good prostate cancer treatment results depends on selecting the right patients for treatment [3-6,16-18].

Depending on the method of application and the power of the source dose in the target volume, (prostatic gland) brachytherapy is divided into high-dose rate brachytherapy (HDR-BT) and low-dose rate brachytherapy (LDR-BT). LDR-BT is an implantation of low-dose rate radioactive sources into the prostatic gland, which stay inside until the end of the patient's life. This is usually done using iodine-125 (^{125}I), palladium-103 (^{103}Pd) and caesium-131 (^{131}Cs) isotopes. HDR-BT is a temporal type of brachytherapy where the high-dose rate radioactive source (usually iridium 192 (^{192}Ir) or cobalt 60 (^{60}Co)) is put in the prostate during the applicator implantation procedure.

Brachytherapy is used as the sole treatment method mainly in the low risk group. A large number of individual LDR-BT procedures are performed in this group of patients worldwide. This is supported by the good treatment results reported in various publications, a relatively small number of side effects and a short time of treatment [19-21]. The procedures in which permanent implants are used is safe and does not require the use of special rooms with radiation shields, as is the case for HDR-BT. Moreover, due to the large competition between radiation source manufacturers in the USA and the number of procedures performed, the cost of the procedure is relatively low and these procedures are commonly available [3,9,20]. The situation in Europe is different, as for at least 30 years HDR-BT has been developing in parallel [4,22-26]. HDR equipment is commonly available and the radioactive source used for treatment is the same as in the case of other neoplasms.

Initially, HDR-BT was introduced as a high-dose rate supplement for EBRT and proved to be an effective and safe method of treatment [17,23,27-29]. Treatment of patients from the low and intermediate risk groups with HDR-BT monotherapy was initiated at the end of the previous decade [3,4,30-35].

BRACHYTHERAPY TECHNIQUES [36]

Low-Dose-Rate Brachytherapy (LDR-BT)

LDR-BT is one of the radiation methods that is known for almost 30 years in treatment of localized prostate cancer. The main idea of this method is to implant small radioactive seeds as a source of radiation, directly into the prostate gland. LDR-BT is applied as a monotherapy and also used along with EBRT as a boost. It is used as a sole radical treatment modality, however not as a palliative treatment. The application of permanent seeds implants is a curative treatment alternative in patients with organ-confined cancer, without extracapsular extension of the tumour [8,9,37-41]. As monotherapy LDR-BT seems to be a reliable choice for early stage prostate cancer, according to low morbidity rate good results and short hospitalization. It is curative alternative of radical prostatectomy or EBRT (i.e. 3D CRT, IMRT) with comparable long-term survival and biochemical control and most favorable toxicity [12,15,20,42-44]. LDR-BT represents the most conformal radiation therapy and the number of patients referred for this radical treatment, has grown rapidly in last 15 years, especially in the United States. There are several reasons why LDR-BT achieved such popularity. Better toxicity profile

with higher dose applying to prostate gland are the main points for brachytherapy in comparison with EBRT. Comparing with radical prostatectomy permanent seed's implantation is a short, one-day therapy with lower complication rate during and after the procedure (bleeding, urinary incontinence, impotence). Specific selection of radioactive isotopes and their correct localization, allows to deposit high dose into the prostate tumour with rapid fall off the dose outside the area of treatment and – at the same time - allows to preserve Organs at Risk (OaRs).

High-Dose-Rate Brachytherapy (HDR-BT)

HDR-BT is a temporary type of brachytherapy where the high-dose rate radioactive source (usually iridium 192 (^{192}Ir) or cobalt 60 (^{60}Co)) is put in the gland during the applicator implantation procedure. In Europe, since at least 30 years ago, HDR-BT has been developed in parallel to LDR-BT [4,23-26,45], and, during the last years, also it is been used in USA with growing interest. HDR equipment is commonly available and the radioactive source used for treatment is the same as in the case of other neoplasms. The dwell-time position of the source in the applicators may be freely programmed during the procedure. The dwell time may be adapted to the requirements of treatment. In the course of treatment and real-time planning the possibility of imprecise indication of the applicators position in relation to the treated gland is minimal, which ensures high precision of the treatment.

Patients Selection

The selection of a method for radiotherapy of the prostatic gland depends mainly on the characteristics of the disease and the treatment capabilities of the centre. Patients are usually divided into risk groups (Table **1**).

In the low risk group the most often used method of treatment is HDR-BT or LDR-BT alone (isotopes ^{125}I, ^{103}Pd, ^{131}Cs) and also EBRT alone or combined with HDR-BT. Some of the patients are operated using different surgery techniques. Patients in this group do not usually require additional hormone therapy.

When analysing the division of patients into risk groups for prostate cancer it is evident that the indications in the low risk group are clearly determined, whereas for the groups with a worse prognosis they differ. Patients who are appropriate candidates for HDR monotherapy are usually people from the low or sometimes intermediate risk group according to ABS [3]. The National Comprehensive Cancer Network (NCCN) [5] recommends brachytherapy alone for the low risk group. These are patients with iPSA $\leq$10, Gleason 2-6, T1-2a. International leading interstitial brachytherapy centres, which treat patients with prostate cancer in the low risk group and sometimes patients in the intermediate risk group (T2b or iPSA<15 ng/ml or Gleason=7) have a 95% cure rate [30,33,51,52].

Patients suffering from prostate cancer in the intermediate risk group are the most heterogeneous group as far as possible methods of treatment are concerned. Patients in this group may be treated in accordance with several different protocols: combination therapy EBRT + HDR-BT boost, EBRT alone, or HDR-BT alone all approaches together with short-term hormone therapy (usually - 6 months). In the

Table 1: The Risk Groups of Prostatic Cancer Patients

Risk Group	Very Low Risk	Low Risk	Intermediate Risk	High Risk	Very High Risk
Seattle/MSKCC [46]	-	iPSA $\leq$10,0 and Gleason 2-6 and T1-2b	iPSA >10 or Gleason $\geq$7 or T$\geq$2c	2 from 3 risk factors from Intermediate Risk	-
Mt. Sinai [47]	-	iPSA $\leq$10 and Gleason 2-6 and T1-2a	iPSA 10-20 or Gleason 7 or T=2b	2 from 3 risk factors from Intermediate Risk or iPSA >20 ng/ml or Gleason 8-10 or T$\geq$2c	-
D'Amico *et al*. [48]	-	iPSA $\leq$10,0 and Gleason 2-6 and T1-2a	iPSA = 10-20 and/or Gleason 7 and/or T=2b	iPSA >20 ng/ml or Gleason 8-10 or T$\geq$2c	-
NCCN [5]	T1a and Gleason $\leq$ 6 PSA<10 ng/ml Fewer than 3 biopsy cores positive, $\leq$ cancer in each one, PSA density <0.15 ng/ml/g	iPSA $\leq$10,0 Gleason 2-6 T1-2a	iPSA 10-20 or Gleason 7 or T2b-2c	2 from 3 risk factors from Intermediate Risk or iPSA >20 ng/ml or Gleason 8-10 or T3a	2 from 3 risk factors from High Risk or T3b-T42

MSKCC – Memorial Sloan-Kettering Cancer Center; NCCN – National Comprehensive Cancer Network; *in NCCN recommendation are two groups which are not mentioned in other classification.

USA patients in this group also undergo EBRT with LDR-BT.

Prostate cancer in the high risk group without distant metastases and especially with a high value of the PSA test and a T≥2c should be treated with EBRT, possibly with irradiation of lymph nodes in the pelvis and boosting the local dose by means of brachytherapy together with long-term hormone therapy (contradicting recommendations include a treatment period of 2-3 years).

Summarized patient selection criteria for HDR-BT and LDR-BT according to ABS and GEC-ESTRO are presented in Table **2**.

CONTRAINDICATIONS FOR BRACHYTHERAPY [36]

According to GEC/ESTRO-EAU-EORTC [4] the contraindications for HDR-BT are: life expectancy of less than 5 years, distant metastases, history of transurethral resection of the prostate (TURP) with chronic, significant damage to the gland (in a period of 3 months before brachytherapy), recurrent haematuria. Regular anticoagulation treatment should be interrupted at least 7 days prior to the implantation of radiation sources. The volume of the gland should not exceed 60 cm^3 (part of the gland lies closer to the pubic symphysis, which makes it harder to position the sources appropriately). It is possible to reduce the volume of the gland by administering hormone therapy for 3-6 months, which will enable a reduction of the volume of the gland in approximately 30% of the patients [17,54]. Transurethral resection of the prostate (TURP) is another relative contraindication for brachytherapy and is associated with higher rate (~50%) of urinary incontinence after procedure. Nevertheless, several publications did not confirmed these data and proved that risk of this kind of complication is less than 10% [55]. Contraindications for HDR-BT and LDR-BT according to ABS and GEC-ESTRO are presented in Table **3**.

DOSES IN BRACHYTHERAPY OF PROSTATE CANCER

According to ABS recommendations, patients with organ–confined prostate cancer are to be treated with monotherapy, others – with combined treatment (EBRT in 40-50 Gy dose with BT boost of 110 Gy and 100 Gy depending on which EBRT dose was administered (LDR-BT) or different HDR-BT schemas. The HDR-BT procedure is performed once or repeated several times, depending on the fractionating schema assumed. The ABS proposes three fractionating schemas for HDR-BT monotherapy and four schemas for combined treatment [3], however other schemas are also applied (Table **4**). Depending on the mode of fractioning, the fractionated doses are administered in one session at time intervals (e.g. every 6 hours) or are repeated in the course of subsequent procedures. Some centres use the 3 x 10.5-11 Gy fractioning schema with a 1-2 week interval between fractions [4,17,45]. Many different fractionations schema make difficult to compare treatment results.

Table 2: Patient Selection Criteria for HDR-BT and LDR-BT According to ABS and GEC-ESTRO [3,4,40,53]

ABS Prostate High-Dose Rate Task Group	ABS Prostate Low-Dose Rate Task Group	GEC-ESTRO – High -Dose-Rate, Low-Dose-Rate
Monotherapy		
Clinical T1b-T2b and Gleason score ≤ 7 and PSA ≤ 10 ng/mL	Clinical stage T1b-T2b and Gleason score ≤ 6 and PSA ≤ 10 ng/mL, Select higher risk patients, Salvage of select radiation therapy failures.	Clinical stage T1b-T2a iPSA≤ 10 ng/ml, Gleason max. 6)
Boost		
Patients with high risk features such as T3-T4, Gleason score 7-10, and/or PSA > 10 ng/mL Selected patients with “bulky” T1-2b tumor (inadequate information exists to clearly define bulky tumor based on DRE, TRUS, percentage positive biopsies)	≥ clinical stage T2c and/or Gleason score ≥ 7 and/or PSA > 10 ng/mL	Stages T1b–T3b Any Gleason score Any iPSA without distant metastases
	Special clinical situations Inadequate information exists to recommend supplemental EBRT based on perineural invasion, percent positive biopsies and/or MRI-detected extracapsular penetration	

DRE - digital rectal examination; TRUS – transrectal ultrasound; EBRT – external beam radiation therapy; MRI - magnetic resonance imaging.

Table 3: Contraindications for HDR-BT and LDR-BT According to ABS and GEC-ESTRO [3,4,40,53]

ABS Prostate High-Dose-Rate Task Group	ABS Prostate Low-Dose-Rate Task Group	GEC-ESTRO – High -Dose-Rate, Low-Dose-Rate
Relative contraindications		
Severe urinary obstructive symptoms Extensive TURP defect or TURP within 6 month Collagen vascular disease	Severe urinary rritative/obstructive symptomatology Extensive TURP defect Substantial median lobe hyperplasia Prostate dimensions larger than the grid (i.e., > 60 mm in width and > 50 mm in height) Severe pubic arch interference Gross seminal vesicle involvement Prior pelvic radiotherapy Inflammatory bowel disease Pathologic involvement of pelvic lymph nodes	Volume > 60 cm3 TURP within 6 months Infiltration of the external sphincter of the bladder neck Significant urinary obstructive symptoms Pubic arch interference Rectum-prostate distance on TRUS < 5 mm Lithotomy position or anaesthesia not possible
Absolute contraindications		
Unable to undergo anesthesia (general, spinal, epidural, or local) Unable to lay flat	Distant metastases Life expectancy < 5 years	

TURP – transurethral resection of the prostate.

Table 4: Doses for HDR-BT and LDR-BT According to ABS and ESTRO/EAU/EORTC [3,40,53]

ABS Prostate High-Dose Rate Task Group	ABS Prostate Low-Dose Rate Task Group and ESTRO/EAU/EORTC Low-Dose Rate
Monotherapy	
10.5 Gy x 3 8.5-9.5 Gy x 4 6.0-7.5 Gy x 6	^{103}Pd - median 125 Gy (110-120 Gy) ^{125}I – median 145 Gy (140-160 Gy) ^{131}Cs - 115 Gy
BT + EBRT	
15 Gy x 1 (with 36-40 Gy EBRT) 9.5-10.5 Gy x 2 (with 40-50 Gy EBRT) 5.5-7.5 Gy x 3 (with 40-50 Gy EBRT) 4.0-6.0 Gy x 4 (with 36-50 Gy EBRT)	^{103}Pd Boost (with 41.4 – 50.4 Gy EBRT) 90-100 Gy ^{125}I Boost (with 41.4 – 50.4 Gy EBRT) 108-110 Gy

BT – brachytherapy; EBRT – external beam radiation therapy.

DOSIMETRY

The V_{100} indicator is used for assessment of the HDR-BT treatment plan for prostate cancer - it provides a percentage value of the treated volume covered by the izodose of the fractionated dose. The American Brachytherapy Society recommends that the fractionated dose should cover >90% of the planning target volume (PTV), i.e. V_{100} > 90%. In the urinary bladder and the rectum the volume which receives 75% of the reference dose should be less than 1 cm^3 (V_{75} of the rectum and V_{75} of the urinary bladder < 1 cm^3). The volume of the urethra covered by 125% of the reference dose should be smaller than 1 cm^3 [3]. GEC/ESTRO-EUA-EORTC recommend the median target dose (MTD) in the urethra at a level of less than 120% per fraction and below 50 Gy of the total dose on the bulb of the penis in combination therapy with EBRT+HDR-BT in order to reduce the risk of impotency [4].

RESULTS

Several authors publishing their data in medical periodicals generally confirmed good results in prostate cancer treatment by LDR-BT alone. Implantation of low-dose-rate seeds in most cases is used as a single modality treatment with or without concurrent androgen deprivation. The main reason of problems in comparison between published series are: selection

criteria, nonuniformity of end points, different follow-up times and hormonal therapy used by medical centers worldwide. Publication data with longer follow-up are known as the most authoritative results (about 5 years) [56]. Authors from Memorial Sloan-Kettering Cancer Center reported the 5-year tumor control and toxicity outcomes for patients with localized prostate treated with I-125 permanent implantation [57]. The amount of 2693 patients with prostate cancer were treated between January 1998 and June 2002 with LDR-BT alone by using real-time intraoperative treatment planning system. The 5-year PSA relapse-free survival rates for low and intermediate risk patients - according to the ASTRO definition - were 96% and 89%, respectively. The authors stated that D90 was correlated to 8 year PSA relapse free survival (PRFS). On multivariate analysis in patients with postimplant dosimetry D90 was a significant predictor for PRFS. There is an agreement that parmeter D90 needs to be reported in seed publication. Acute urinary symptoms had 38% of patients, but within a median time of 6 months, 63% of them have been relieved from these symptoms. The late rectal toxicity was noticed at 1%, late rectal bleeding (Grade 2) at 7%. Apart from good biochemical control outcomes this publication demonstrated that real-time planning methods can consistently and reliably deliver the intended dose distribution to achieve an optimal therapeutic ratio between the target and normal tissue [57].

Five European countries (France, Finland, Italy, Spain and the UK) have gathered their data in interstitial LDR treatment of prostate cancer as a monotherapy and published it in July 2006. Between May 1998 and August 2003, the number of 1050 patients with localised disease in stage T1-T2 were treated by brachytherapy [58]. They were divided into three main risk groups (ASTRO definition) with percent disposition of 63.6%, 28.3%, 6.3% respectively. Unfortunately from whole number of patients only 364 of them were evaluable by the Kaplan-Meier method for determining freedom from biochemical failure in 36

Table 5: Treatment Results of Monotherapy LDR-BT Published by Different Authors

Author	Number of patients	Risk group	Treatment schedules (monotherapy)	Follow up	Results
Guedea F *et al*. [58]	364	I,II,III	LDR BT (results of 4 centres)	36 months	BC 93,0% I 88,0% II 80,0 III
Bladou F *et al*. [59]	260	I,II,III	LDR BT (I- 125)	29,5 months	DFS 93,8% (all group) 97,7% (I).
Radge H *et al*. [60]	619	I, III	LDR BT I- 125 (I) Pd-103 (III)	13 years	DFS 76% I 80% III
Sharkey J *et al*. [61]	166	I	LDR BT Pd-103 + HT	5 years	FFPF 86%
Merrick GS *et al*. [62]	32	I,II,III	LDR BT	26,4 months	BC 100%
Kollmeier MA *et al*. [63]	243	I,II,III	LDR BT (I- 125, Pd-103) + HT	8 years	FFPF 88,0% I 81,0% II 65,0% III
Prada PJ *et al*. [64]	275	I,II,III	LDR BT (I- 125, Pd-103)	5 years	96% OS 97% DFS 99% BC
Merrick GS *et al*. [65]	119	I,II,III	LDR BT	7 years	BC 93,1% I 100,0% II 95,2% III
Stock RG *et al*. [66]	79	I, II	LDR BT (I- 125, Pd-103)	24 months	FFPF 76%

BC – biochemical control rate; DFS – progression free survival rate; OS – overall survival; FFPF– freedom from PSA failure rate; LDR - BT – Low Dose Rate Brachytherapy; HT – androgen deprivation therapy; Risk groups: I (TNM cT1- cT2a, Gl $\leq$ 6, PSA < 10 ng/ml); II (TNM cT2a-cT2c, Gl 7, PSA 10-20 ng/ml); III (TNM > cT3, Gl 8-10, PSA > 20 ng/ml).

months time. The biochemical progression-free rate at 3 years for each: low, intermediate and high risk groups, was noticed at 93%, 88%, 80% respectively. Although in this publication authors reports preliminary data, the outcomes of LDR monotherapy were gathered from different medical centers and after statistic evaluation, confirmed good results depending on stratification into risk groups [58]. In Table **5** treatment results of monotherapy LDR-BT published by different authors are presented.

Centres which use HDR-BT monotherapy have very good results despite a separate fractionating schema and needle application technique. Results of prostate cancer HDR-BT monotherapy are summarised in Table **6**.

For example, during 8 years of follow-up of 298 patients biochemical control was observed in 97% of the cases, local control in 99% of the cases and specific survival in 99% of the cases. The patients who were treated belonged to the high risk group with a PSA of 10-15 ng/ml, Gleason 7 [30]. Mark *et al*. reported biochemical control in 88% in a group of patients from all risk groups [69]. Rogers *et al*. observed 94% biochemical control after 3 years in the intermediate risk group [32]. In 2006 Yoshioka *et al*. obtained 100% biochemical control in the low risk group, 89% in the intermediate group and 70% in the high risk group [33]. This and other studies show that HDR monotherapy is an effective method of treating prostate cancer patients in the low risk group and also in some patients from the intermediate risk group, as well as selected cases from the high risk group with the disease located in the prostatic gland. It is necessary to stress, however, that some patients select this method of treatment due to the shorter treatment time and agree to continue hormone therapy for 2-3 years after completing brachytherapy. At present there is no study available which would follow-up patients for 10-15 years and allows comparison with brachytherapy, surgical treatment and EBRT. Follow-up of the response to treatment with HDR-BT monotherapy until now indicates that the cure rate is similar to other methods of treatment, which justifies the assumption that this is an equivalent method of treatment.

In Table **7** results of treatment combination (EBRT plus LDR-BT) published by different authors are summarized (Table **7**).

SIDE EFFECTS

Despite the modern techniques and computer treatment planning systems applied, we are unable to avoid post-radiation complications. A properly conducted treatment results in a low percentage of third degree side effects, which amount to below 5% [4]. Some of the patients report complaints from the urinary system (radiation-induced reaction in the urethra) which begin several days after the procedure and in some cases may go on for as long as 6 to 9 months. Treatment with ionizing radiation may also cause a reaction and oedema of the gland and lead to

Table 6: The Results of HDR Brachytherapy of Prostate Cancer Patients

Study	N	Number of fraction	Gy/fr	TD (Gy)	Follow-up (Median)	Survival (risk group)	Lack of biochemical failure (%)	(DFS) (%)	(OS) (%)
Yoshioka *et al*. [33]	111	6	9	48-54	2.3	100% low 89% intermediate 70% high	100 (5 yrs follow-up - 97)	-	97 (5 yrs follow-up - 92)
Corner *et al*. [67]	110	4	8.5-9	36	1–2.5	100%	-	-	-
		3	10.5	31.5		100%			
Ghadjar *et al*. [68]	36	4	9.5	38	3	100% low and intermediate	-	-	100
Rogers *et al*. [32]	284	4	9	36	3	94% intermediate	-	100	-
Mark *et al*. [69]	301	6	9.5	45	8	88% intermediate	-	-	84
Demanes *et al*. [30]	298	6	7	38-42	5.2	97% low and intermediate	99	99	95
		4	9.5						

TD – Total Dose; DFS - Disease Free Survival; OS - Overall Survival.

Table 7: Results of Combined Treatment (EBRT Plus LDR-BT) Published by Different Authors

Author	Number of patients	Risk group	Treatment schedules (monotherapy)	Follow up	Results
Wallner K *et al*. [70]	112 (I risk group)	I,II,III	EBRT (44 Gy) + Pd 103 (90 Gy) v EBRT (20 Gy) + Pd-103 (115 Gy)	3 years	84% DFS 94%DFS
Sylvester JE *et al*. [71]	223	I,II,III	EBRT (45 Gy) + I-125, Pd-103	15 years	BFFS 88% (I) 80% (II) 53% (III)
Sherertz T *et al*. [72]	156	II,III	EBRT (44 Gy) + Pd 103 (90 Gy) v EBRT (20 Gy) + Pd-103 (115 Gy)	3 years	ovarall DFS 86%
Stock RG *et al*. [73]	43	III	HT + EBRT + Pd-103	4 years	FFPF 74%
Orio P *et al*. [74]	179	II,III	EBRT + Pd-103	3 years	ovarall DFS 79%
Peschel RE *et al*. [75]	68	I,II,III	EBRT (45 Gy) + I 125 (110 Gy) v EBRT (45 Gy) + Pd-103 (98 Gy)	5 years	72% DFS 74%DFS
Merrick GS *et al*. [76]	668	I,II,III	HT + EBRT + Pd-103, I-125	8 years	DFS 98,2% (I) 98,4% (II) 88,2% (III)

FFPF– freedom from PSA failure rate; DFS – progression free survival rate; FFPF– freedom from PSA failure rate; BFFS- biochemical failure survival rate; EBRT – external beam radiation therapy; HT – androgen deprivation therapy; Risk groups: I (TNM cT1- cT2a, Gl $\leq$ 6, PSA < 10 ng/ml); II (TNM cT2a-cT2c, Gl 7, PSA 10-20 ng/ml); III (TNM > cT3, Gl 8-10, PSA > 20 ng/ml).

acute urine retention and the need to maintain a catheter in the urinary bladder after the procedure [18,39]. Urinary incontinence is observed sporadically and most often concerns patients who have undergone previous TURP [18,77]. Quite severe, though rare post-radiation complications are necrosis and narrowing of the urethra caused by lack of proper optimization of the dose rate in the area of the middle lobe. Some patients may experience bleeding in the urinary tract. The problem of rectal bleeding concerns between 2% and 10% of patients, whereby only approximately 1% experience chronic ulcerations [18]. Few patients have been diagnosed with urogenital fistulas [18,28,39,78]. It seems that the potential risk of bowel complications results from the advanced age of most of the patients, circulatory disorders and the presence of inflammatory diseases of the end portion of the gastrointestinal tract. A significant complication in the case of 15-30% patients will be potency-related problems, however it has been proven that 80% of the patients in this group regain full sexual functions within five years [18,39]. Pharmacological treatment is usually also helpful in this aspect. Infertility is not a frequent consequence of brachytherapy, however, in several reports it has been reported that the volume of the ejaculate in the seminal vesicles was reduced [16,18].

In the case of small intensity of the post-radiation symptoms in the urinary tract good therapeutic effect is ensured by alpha-blockers and NSAIDs. Cases of possible late toxicity should be treated conservatively. TURP should be avoided at least of 1 year after treatment in order to reduce the risk of urinary incontinence [4].

CONCLUSIONS

For the radiation treatment of prostate cancer high dose should be delivered for optimal biochemical control. Radiobiological models support the current clinical evidence for equivalent outcomes in localized prostate cancer with either LDR or HDR brachytherapy using current dose regimens. At present, the available clinical data with these two techniques suggests that

they are equally effective, stage by stage, in providing high tumor control rates. Several houndred thousands of patients have been treated with LDT-BT, with experience over 15 years and more in major centres in the US and Europe. Results are mature and well established, and mainly related to the risk group of the patient. LDR-BT has been a gold standard for prostate brachytherapy in low risk patients for many years in a lot of countries. It is a convenient technique for a patient. On the other hand HDR-BT is more cost effective with reimbursement in many countries and results for HDR monotherapy are very promising.

Concluding, brachytherapy is a highly effective method of prostate irradiation, with higher concentration of the dose within the organ, which affects the reduction in the risk of complications in OaRs, like impotence (5-15%), and urinary incontinence (<5%). It is also the most cost-sparing technique of all prostate cancer treatment counting all costs, including diagnostic, treatment and social ones, after treatment.

REFERENCES

[1] Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011; 61(2): 69-90. http://dx.doi.org/10.3322/caac.20107

[2] Bracarda S, de Cobelli O, Greco C, Prayer-Galetti T, Valdagni R, Gatta G, *et al*. Cancer of the prostate. Crit Rev Oncol Hematol 2005; 56(3): 379-96. http://dx.doi.org/10.1016/j.critrevonc.2005.03.010

[3] Hsu I-C, Yamada Y, Vigneault E, Pouliot J. American Brachytherapy Society Prostate High-Dose Rate Task Group." Retrieved 15-03-2010, 2010, from http://www.americanbrachytherapy.org/guidelines/index.cfm.

[4] Kovács G, Pötter R, Loch T, Hammer J, Kolkman-Deurloo IK, de la Rosette JJ, *et al*. GEC/ESTRO-EAU recommendations on temporary brachytherapy using stepping sources for localised prostate cancer. Radiother Oncol 2005; 74(2): 137-48. http://dx.doi.org/10.1016/j.radonc.2004.09.004

[5] Mohler J, Bahnson RR, Boston B, Busby JE, D'Amico A, Eastham JA, *et al*. NCCN clinical practice guidelines in oncology: prostate cancer. J Natl Compr Canc Netw 2010; 8(2): 162-200.

[6] Erickson BA, Demanes DJ, Ibbott GS, Hayes JK, Hsu IC, Morris DE, *et al*. American Society for Radiation Oncology (ASTRO) and American College of Radiology (ACR) Practice Guideline for the performance of High-Dose-Rate Brachytherapy. Int J Radiat Oncology Biol Phys 2011; 79: 641-49. http://dx.doi.org/10.1016/j.ijrobp.2010.08.046

[7] Katz M S, Efstathiou JA, D'Amico AV, Kattan MW, Sanda MG, Nguyen PL, *et al*. The 'CaP Calculator': an online decision support tool for clinically localized prostate cancer. BJU Int 2010; 105(10): 1417-22. http://dx.doi.org/10.1111/j.1464-410X.2010.09290.x

[8] Horwich A, Parker C, Bangma C, Kataja V. ESMO Guidelines Working Group. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2010; (Suppl 5): 129-33. http://dx.doi.org/10.1093/annonc/mdq174

[9] Thompson I, Thrasher JB, Aus G, Burnett AL, Canby-Hagino ED, Cookson MS, *et al*. Guidelines for the management of clinically localized prostate cancer: 2007 update. J Urol 2007; 177(6): 2106-31. http://dx.doi.org/10.1016/j.juro.2007.03.003

[10] Heidenreich A, Bellmunt J, Bolla M, Joniau S, Mason M, Matveev V, *et al*. EAU Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Treatment of Clinically Localised Disease. Eur Urol 2011; 59(1): 61-71. http://dx.doi.org/10.1016/j.eururo.2010.10.039

[11] Haustermans KM, Hofland I, Van Poppel H, Oyen R, Van de Voorde W, Begg AC, *et al*. Cell kinetic measurements in prostate cancer. Int J Radiat Oncol Biol Phys 1997; 37(5): 1067-70. http://dx.doi.org/10.1016/S0360-3016(96)00579-2

[12] Crook JM, Gomez-Iturriaga A, Wallace K, Ma C, Fung S, Alibhai S, *et al*. Comparison of health-related quality of life 5 years after SPIRIT: Surgical Prostatectomy Versus Interstitial Radiation Intervention Trial. J Clin Oncol 2011; 29(4): 362-68. http://dx.doi.org/10.1200/JCO.2010.31.7305

[13] Talcott JA, Manola J, Clark JA, Kaplan I, Beard CJ, Mitchell SP, *et al*. Time course and predictors of symptoms after primary prostate cancer therapy. J Clin Oncol 2003; 21(21): 3979-86. http://dx.doi.org/10.1200/JCO.2003.01.199

[14] Jo Y, Junichi H, Tomohiro F, Yoshinari I, Masato F. Radical prostatectomy versus high-dose rate brachytherapy for prostate cancer: effects on health-related quality of life. BJU Int 2005; 96(1): 43-47. http://dx.doi.org/10.1111/j.1464-410X.2005.05564.x

[15] Ferrer M, Suárez JF, Guedea F, Fernández P, Macías V, Mariño A, *et al*. Health-related quality of life 2 years after treatment with radical prostatectomy, prostate brachytherapy, or external beam radiotherapy in patients with clinically localized prostate cancer. Int J Radiat Oncol Biol Phys 2008; 72(2): 421-32. http://dx.doi.org/10.1016/j.ijrobp.2007.12.024

[16] Halperin EC, Perez CA, Eds. Perez and Brady's Principles and Practice of Radiation Oncology 2008; 5th ed, Lippincott Williams & Wilkins.

[17] Kanikowski M, Skowronek J, Milecki P, Kubaszewska M, Chicheł A. Brachyterapia HDR raka gruczołu krokowego. Urol Pol 2007; 2: 5-11. [in Polish].

[18] Leibel SA, Phillips TL. Textbook of Radiation Oncology, Second Edition 2004, Chapter 45, 988-1000.

[19] Ragde H, Korb LJ, Elgamal AA, Grado GL, Nadir BS. Modern prostate brachytherapy. Prostate specific antigen results in 219 patients with up to 12 years of observed follow-up. Cancer 2000; 89(1): 135-41. http://dx.doi.org/10.1002/1097-0142(20000701)89:1<135::AID-CNCR18>3.0.CO;2-#

[20] Sylvester JE, Grimm PD, Wong J, Galbreath RW, Merrick G, Blasko JC. Fifteen-Year Biochemical Relapse-Free Survival, Cause-Specific Survival, and Overall Survival following I-125 Prostate Brachytherapy in Clinically Localized Prostate Cancer: Seattle Experience. Int J Radiat Oncol Biol Phys 2011; 81(2): 376-81. http://dx.doi.org/10.1016/j.ijrobp.2010.05.042

[21] Saibishkumar EP, Borg J, Yeung I, Cummins-Holder C, Landon A, Crook J. Sequential comparison of seed loss and prostate dosimetry of stranded seeds with loose seeds in 125I permanent implant for low-risk prostate cancer. Int J Radiat Oncol Biol Phys 2009; 73(1): 61-68. http://dx.doi.org/10.1016/j.ijrobp.2008.04.009

[22] Chicheł A. Brachyterapia HDR raka gruczołu krokowego - analiza zależności między czynnikami prognostycznymi a parametrami optymalizacyjnymi w obszarze leczonym i narządach krytycznych. Zeszyty Naukowe Wielkopolskiego Centrum Onkologii 2009; 6(3): 105-34. [In Polish].

[23] Chicheł A, Kanikowski M, Skowronek J, Dymnicka M, Piotrowski T. 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 Brachytherapy 2009; 1: 11-17.

[24] Seppenwoolde Y, Kolkman-Deurloo I-K, Sipkema D, de Langen M, Praag J, Jansen P, *et al*. HDR prostate monotherapy – dosimetric effects of implant deformation due to posture change between TRUS- and CT-imaging. Radiother Oncol 2008; 86: 114-19. http://dx.doi.org/10.1016/j.radonc.2007.11.004

[25] Martin T, Baltas D, Kurek R, Röddiger S, Kontova M, Anagnostopoulos G, *et al*. 3-D conformal HDR brachytherapy as monotherapy for localized prostate cancer. A pilot study. Strahlenther Onkol 2004; 180: 225-32. http://dx.doi.org/10.1007/s00066-004-1215-4

[26] Galalae RM, Kovacs G, Schultze J, Loch T, Rzehak P, Wilhelm R, *et al*. Long-term outcome after elective irradiation of the pelvic lymphatics and local dose escalation using high-dose-rate brachytherapy for locally advanced prostate cancer. Int J Radiat Oncol Biol Phys 2002; 52(1): 81-90. http://dx.doi.org/10.1016/S0360-3016(01)01758-8

[27] Martinez AA, Gustafson G, Gonzalez J, Armour E, Mitchell C, Edmundson G, *et al*. Dose escalation using conformal high-dose-rate brachytherapy improves outcome in unfavorable prostate cancer. Int J Radiat Oncol Biol Phys 2002; 53(2): 316-27. http://dx.doi.org/10.1016/S0360-3016(02)02733-5

[28] Demanes DJ, Rodriguez RR, Altieri GA. High dose rate prostate brachytherapy: the California Endocurietherapy (CET) Method. Radiother Oncol 2000; 57: 289-96. http://dx.doi.org/10.1016/S0167-8140(00)00291-7

[29] Demanes DJ, Rodriguez RR, Schour L, Brandt D, Altieri G, *et al*. High-dose-rate intensity-modulated brachytherapy with external beam radiotherapy for prostate cancer: California endocurietherapy's 10-year results. Int J Radiat Oncol Biol Phys 2005; 61(5): 1306-16. http://dx.doi.org/10.1016/j.ijrobp.2004.08.014

[30] Demanes DJ, Martinez AA, Ghilezan M, Hill DR, Schour L, Brandt D, *et al*. High-Dose-Rate monotherapy: safe and effective brachytherapy for patients with localized prostate cancer. Int J Radiat Oncol Biol Phys 2011; 81: 1286-92. http://dx.doi.org/10.1016/j.ijrobp.2010.10.015

[31] Martinez AA, Demanes J, Vargas C, Schour L, Ghilezan M, Gustafson GS. High-dose-rate prostate brachytherapy: an excellent accelerated-hypofractionated treatment for favorable prostate cancer. Am J Clin Oncol 2010; 33(5): 481-88. http://dx.doi.org/10.1097/COC.0b013e3181b9cd2f

[32] Rogers L, Rogers LI. Extended followup of high-dose-rate brachytherapy as monotherapy for intermediate- risk prostate cancer. Brachytherapy 2010; 9(Suppl 1): S55-S56. http://dx.doi.org/10.1016/j.brachy.2010.02.080

[33] Yoshioka Y, Konishi K, Oh RJ, Sumida I, Yamazaki H, Nakamura S, *et al*. High-dose-rate brachytherapy without external beam irradiation for locally advanced prostate cancer. Radiother Oncol 2006; 80(1): 62-68. http://dx.doi.org/10.1016/j.radonc.2006.06.011

[34] Yoshioka Y, Konishi K, Sumida I, Takahashi Y, Isohashi F, Ogata T, *et al*. Monotherapeutic High-Dose-Rate brachy-therapy for prostate cancer: five-year results of an extreme hypofractionation regimen with 54 Gy in nine fractions. Int J Radiat Oncol Biol Phys 2011; 80: 469-75. http://dx.doi.org/10.1016/j.ijrobp.2010.02.013

[35] Martinez AA, Pataki I, Edmundson G, Sebastian E, Brabbins D, Gustafson G. Phase II prospective study of the use of conformal high-dose-rate brachytherapy as monotherapy for the treatment of favorable stage prostate cancer: a feasibility report. Int J Radiat Oncol Biol Phys 2001; 49: 61-69. http://dx.doi.org/10.1016/S0360-3016(00)01463-2

[36] Skowronek J. Low-dose-rate or high-dose-rate brachytherapy in treatment of prostate cancer – between options. J Contemp Brachytherapy 2013; 1: 33-41. http://dx.doi.org/10.5114/jcb.2013.34342

[37] Nag S, Beyer D, Friedland J, *et al*. American Brachytherapy Society (ABS) recommendations for transperineal permanent brachytherapy of prostate cancer. Int J Radiat Oncol Biol Phys 1999; 44(4): 789-99. http://dx.doi.org/10.1016/S0360-3016(99)00069-3

[38] Porter AT, Blasko JC, Grimm PD, *et al*. Brachytherapy for Prostate Cancer. Cancer J Clin 1995; 45: 165-78. http://dx.doi.org/10.3322/canjclin.45.3.165

[39] Garbaulet A, Potter R, Mazeron JJ, *et al*. The GEC ESTRO Handbook of Brachytherapy, Brussels, 2002, Chapter 20, 473-480.

[40] Ash D, Flynn A, Battermann J, de Reijke T, *et al*. ESTRO/EAU/EORTC recommendations on permanent seed implantation for localized prostate cancer. Radioth Oncol 2000; 57: 315-21. http://dx.doi.org/10.1016/S0167-8140(00)00306-6

[41] Skowronek J, Kanikowski M, Zwierzchowski G, *et al*. Brachyterapia LDR w leczeniu raka gruczołu krokowego. Wsp Onkol 2009; 13(6): 316-329. [In Polish]

[42] Grimm P, Billiet I, Bostwick D, *et al*. Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group. BJU Int 2012; 109(Suppl 1): 22-29. http://dx.doi.org/10.1111/j.1464-410X.2011.10827.x

[43] Polascik TJ, Pound CR, DeWeese TL, *et al*. Comparison of radical prostatectomy and iodine 125 interstitial radiotherapy for the treatment of clinically localized prostate cancer: a 7-year biochemical (PSA) progression analysis. Urology 1998; 51(6): 884-9; discussion 889-90.

[44] Machtens S, Baumann R, Hagemann J, *et al*. Long-term results of interstitial brachytherapy (LDR-Brachytherapy) in the treatment of patients with prostate cancer. World J Urol 2006; 24(3): 289-95. http://dx.doi.org/10.1007/s00345-006-0083-1

[45] Burchardt W, Skowronek J, Łyczek J. Samodzielna brachyterapia HDR raka gruczołu krokowego – alternatywa we wczesnym stopniu zaawansowania. Przegl Urol 2012; 4: 33-38. [in Polish].

[46] Sylvester JE, Blasko JC, Grimm PD, Meier R, Malmgren JA. Ten-year biochemical relapse-free survival after external beam radiation and brachytherapy for localized prostate cancer: the Seattle experience. Int J Radiat Oncol Biol Phys 2003; 57(4): 944-52. http://dx.doi.org/10.1016/S0360-3016(03)00739-9

[47] Lee LN, Stock RG, Stone NN. Role of hormonal therapy in the management of intermediate- to high-risk prostate cancer treated with permanent radioactive seed implantation. Int J Radiat Oncol Biol Phys 2002; 52(2): 444-52. http://dx.doi.org/10.1016/S0360-3016(01)02598-6

[48] D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Fondurulia J, Chen MH, *et al*. Clinical utility of the percentage of positive prostate biopsies in defining biochemical outcome after radical prostatectomy for patients with clinically localized prostate cancer. J Clin Oncol 2000; 18(6): 1164-72.

[49] King CR. LDR vs HDR brachytherapy for localized prostate cancer- the view from radiobiological models. Brachytherapy 2002; 1: 219-28. http://dx.doi.org/10.1016/S1538-4721(02)00101-0

[50] Grills IS, Martinez AA, Hollander M, *et al*. High dose rate brachytherapy as prostate cancer monotherapy reduces toxicity compared to low dose rate palladium seeds. J Urol 2004; 171(3): 1098-104. http://dx.doi.org/10.1097/01.ju.0000113299.34404.22

[51] Yoshioka Y, Nose T, Yoshida K, Inoue T, Yamazaki H, Tanaka E, *et al*. High-dose-rate interstitial brachytherapy as a monotherapy for localized prostate cancer: treatment description and preliminary results of a phase I/II clinical trial. Int J Radiat Oncol Biol Phys 2000; 48: 675-81. http://dx.doi.org/10.1016/S0360-3016(00)00687-8

[52] Corner C, Rojas AM, Bryant L, Ostler P, Hoskin P, *et al*. A Phase II study of high-dose-rate afterloading brachytherapy as monotherapy for the treatment of localized prostate cancer. Int J Radiat Oncol Biol Phys 2008; 72(2): 441-46. http://dx.doi.org/10.1016/j.ijrobp.2007.12.026

[53] Merrick GS, Zelefsky M, Sylvester K, *et al*. American Brachytherapy Society Prostate Low-Dose Rate Task Group. http://www.americanbrachytherapy.org/guidelines/prostate_low-doseratetaskgroup.pdf

[54] Kucway R, Vicini F, Huang R, Stromberg J, Gonzalez J, Martinez A, *et al*. Prostate volume reduction with androgen deprivation therapy before interstitial brachytherapy. J Urol 2002; 167(6): 2443-47. http://dx.doi.org/10.1016/S0022-5347(05)65001-X

[55] Wallner K, Lee H, Wasserman S, *et al*. Low risk of urinary incontinence following prostate brachytherapy in patients with a prior transurethral prostate resection. Int J Radiat Oncol Biol Phys 1997; 37: 565-69. http://dx.doi.org/10.1016/S0360-3016(96)00570-6

[56] Kanikowski M, Skowronek J, Kubaszewska M, Chicheł A, Milecki P. Permanent implants in treatment of prostate cancer. Rep Pract Radioth Oncol 2008; 3: 150-67. http://dx.doi.org/10.1016/S1507-1367(10)60006-5

[57] Zelefsky MJ, Yamada Y, Cohen GJ, *et al*. Five-year outcome of intraoperative conformal permanent I-125 interstitial implantation for patients with clinically localized prostate cancer. Int J Radiat Oncol Biol Phys 2007 1; 67(1): 65-70.

[58] Guedea F, Aguilo F, Polo A, *et al*. Early biochemical outcomes following permanent interstitial brachytherapy as monotherapy in 1050 patients with clinical T1-T2 prostate cancer. Radioth Oncol 2006; 80(1): 57-61. http://dx.doi.org/10.1016/j.radonc.2006.06.004

[59] Bladou F, Salem N, Simonian-Sauve M, *et al*. Permanent iodine 125 implant brachytherapy in localized prostate cancer: results of the first 4 years of experience. Prog Urol 2004; 14(3): 345-52.

[60] Radge H, Grado GL, Nadir BS. Brachytherapy for clinically localized prostate cancer: thirteen-year disease-free survival of 769 consecutive prostate cancer patients treated with permanent implants alone. Arch Esp Urol 2001; 54(7): 739-47.

[61] Sharkey J, Chovnick SD, Behar RJ, *et al*. Minimally invasive treatment for localized adenocarcinoma of the prostate: review of 1048 patients treated with ultrasound-guided palladium-103 brachytherapy. J Endourol 2000; 14(4): 343-50. http://dx.doi.org/10.1089/end.2000.14.343

[62] Merrick GS, Butler WM, Wallner K, *et al*. Permanent prostate brachytherapy-induced morbidity in patients with grade II and III obesity. Urology 2002; 60(1): 104-8. http://dx.doi.org/10.1016/S0090-4295(02)01638-2

[63] Kollmeier MA, Stock RG, Stone N. Biochemical outcomes after prostate brachytherapy with 5-year minimal follow-up: importance of patient selection and implant quality. Int J Radiat Oncol Biol Phys 2003; 57(3): 645-53. http://dx.doi.org/10.1016/S0360-3016(03)00627-8

[64] Prada PJ, Hevia M, Juan G, *et al*. I-125 low dose rate brachytherapy in localized prostate cancer. Preliminary results after 5 years. Arch Esp Urol 2005; 58(3): 213-26.

[65] Merrick GS, Butler WM, Wallner KE, Galbreath RW, Adamovich E. Permanent interstitial brachytherapy in younger patients with clinically organ-confined prostate cancer. Urology 2004; 64(4): 754-9. http://dx.doi.org/10.1016/j.urology.2004.04.054

[66] Stock RG, Stone NN, De Wyngaert JK, Lavagnini P, Unger PD. Prostate specific antigen findings and biopsy results following interactive ultrasound guided transperineal brachytherapy for early stage prostate carcinoma. Cancer 1996; 77(11): 2386-92. http://dx.doi.org/10.1002/(SICI)1097-0142(19960601)77:11<2386::AID-CNCR30>3.0.CO;2-R

[67] Corner C, Rojas AM, Bryant L, Ostler P, Hoskin P, *et al*. A Phase II study of high-dose-rate afterloading brachytherapy as monotherapy for the treatment of localized prostate cancer. Int J Radiat Oncol Biol Phys 2008; 72(2): 441-46. http://dx.doi.org/10.1016/j.ijrobp.2007.12.026

[68] Ghadjar P, Keller T, Rentsch CA, Isaak B, Behrensmeier F, Stroux A, *et al*. Toxicity and early treatment outcomes in low- and intermediate-risk prostate cancer managed by high-dose-rate brachytherapy as a monotherapy. Brachytherapy 2009; 8(1): 45-51. http://dx.doi.org/10.1016/j.brachy.2008.09.004

[69] Mark RJ, Anderson PJ. Interstitial High-Dose-Rate Brachytherapy as Monotherapy for Early Stage Prostate Cancer: Median 8-Year Results in 301 Patients. Brachytherapy 2010; 9(Suppl 1): S76. http://dx.doi.org/10.1016/j.brachy.2010.02.127

[70] Wallner K, Merrick G, True L, *et al*. 20 Gy versus 44 Gy supplemental beam radiation with Pd-103 prostate brachytherapy: preliminary biochemical outcomes from a prospective randomized multi-center trial. Radiother Oncol 2005; 75(3): 307-10. http://dx.doi.org/10.1016/j.radonc.2005.03.019

[71] Sylvester JE, Grimm PD, Blasko JC, *et al*. 15-Year biochemical relapse free survival in clinical Stage T1-T3 prostate cancer following combined external beam radiotherapy and brachytherapy; Seattle experience. Int J Radiat Oncol Biol Phys 2007; 67(1): 57-64. http://dx.doi.org/10.1016/j.ijrobp.2006.07.1382

[72] Sherertz T, Wallner K, Merrick G, *et al*. The prognostic significance of Gleason pattern 5 in prostate cancer patients treated with Pd 103 plus beam radiation therapy. Cancer J 2004; 10(5): 301-6. http://dx.doi.org/10.1097/00130404-200409000-00007

[73] Stock RG, Stone NN. Preliminary toxicity and prostate-specific antigen response of a Phase I/II trial of neoadjuvant hormonal therapy, 103Pd brachytherapy, and three-dimensional conformal external beam irradiation in the treatment of locally advanced prostate cancer. Brachytherapy 2002; 1(1): 2-10. http://dx.doi.org/10.1016/S1538-4721(02)00006-5

[74] Orio P, Wallner K, Merrick G, *et al*. Dosimetric parameters as predictive factors for biochemical control in patients with higher risk prostate cancer treated with Pd-103 and supplemental beam radiation. Int J Radiat Oncol Biol Phys 2007; 67(2): 342-6. http://dx.doi.org/10.1016/j.ijrobp.2006.09.010

[75] Peschel RE, Colberg JW, Chen Z, Nath R, Wilson LD. Iodine 125 versus palladium 103 implants for prostate cancer: clinical outcomes and complications. Cancer J 2004; 10(3): 170-4. http://dx.doi.org/10.1097/00130404-200405000-00006

[76] Merrick GS, Butler WM, Wallner KE, *et al*. Impact of supplemental external beam radiotherapy and/or androgen deprivation therapy on biochemical outcome after permanent prostate brachytherapy. Int J Radiat Oncol Biol Phys 2005; 61(1): 32-43. http://dx.doi.org/10.1016/j.ijrobp.2004.05.003

[77] Kanikowski M, Skowronek J, Chicheł A. HDR brachytherapy of prostate cancer – two years experience in Greater Poland Cancer Centre. J Contemp Brachytherapy 2009; 1, 3: 137-44.

[78] Chicheł A, Kanikowski M, Skowronek J. Vital role of volume and number of needles in HDR brachytherapy (HDR-BT) of prostate cancer. J Contemp Brachytherapy 2009; 1, 3: 145-50.

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