Case report

Second salvage high-dose-rate brachytherapy for radiorecurrent prostate cancer

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Abstract

Purpose: Salvage treatments for localized radiorecurrent prostate cancer can be performed safely when a focal and image guided approach is used. Due to the low toxicity, the opportunity exists to investigate a second salvage treatment when a second locally recurrent prostate cancer occurs. Here, we describe a second salvage treatment procedure of 4 patients.

Material and methods: Four patients with a pathologically proven second local recurrence were treated in an outpatient magnetic resonance imaging (MRI)-guided setting with a single fraction of 19 Gy focal high-dose-rate brachytherapy (HDR-BT). Delineation was performed using choline-PET-CT or a ^{68}Ga-PSMA PET in combination with multiparametric 3 Tesla MRI in all four patients. Toxicity was measured using common toxicity criteria for adverse events (CTCAE) version 4.0.

Results: With a median follow-up of 12 months (range, 6-15), there were 2 patients with biochemical recurrence as defined by the Phoenix-definition. There were no patients with grade 3 or more toxicity. In all second salvage HDR-BT treatments, the constraints for rectum, bladder, and urethra were met. Median treatment volume (GTV) was 4.8 cc (range, 1.9-6.6 cc). A median of 8 catheters (range, 6-9) were used, and the median dose to the treatment volume (GTV) was a D_{95}: 19.3 Gy (SD 15.5-19.4 Gy).

Conclusions: Second focal salvage MRI-guided HDR-BT for a select group of patients with a second locally recurrent prostate cancer is feasible. There was no grade 3 or more acute toxicity for these four patients.

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Key words: HDR brachytherapy, MRI guided, recurrent prostate cancer, second salvage treatment.

Purpose

Local recurrent prostate cancer after primary radiotherapy is a significant clinical problem. Approximately, half of all patients with high-risk prostate cancer experience a recurrence within 10 years post treatment [1,2]. Androgen deprivation is the most common treatment for biochemical recurrence post radiotherapy [3], as whole gland salvage treatments are associated with significant side effects resulting in a negative impact on the quality of life [4,5].

New imaging techniques, like ^{18}F choline positron emission tomography (PET) and ^{68}Ga-prostate specific membrane antigen (PSMA) PET-computed tomography (CT) [6,7], enable early detection of true local prostate cancer recurrences [8]. When registering this information with multiparametric (mp) magnetic resonance imaging (MRI) [9], which has a higher resolution compared to PET, safe local salvage treatment is possible [8,10,11].

As primary salvage low-dose-rate brachytherapy (LDR-BT) has shown to be safe and feasible [10], one can consider to perform a second salvage treatment in a selected group of patients (> 3-year interval between treatment, prostate-specific antigen [PSA] doubling time > 1 year and acceptable toxicity after 1st salvage treatment) [4,12]. With the added damage from the primary and salvage treatment to the normal tissue, a third treatment obviously has an increased risk of side effects.

The aim of this study is to describe a 2nd focal salvage 19 Gy single fraction HDR-BT in 4 patients, together with data on toxicity and biochemical outcome.

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Material and methods

Patients

Institutional review board approval for this analysis was obtained. Between May 2015 and January 2016, four patients with a second locally recurrent prostate cancer were treated in an outpatient setting with an MRI-guided focal HDR-BT technique. Patient characteristics are depicted in Table 1. All four patients received 145 Gy using ^{125}I as first salvage treatment. The treatment volume was approximately hemi-gland in all four patients.

Prior to the second salvage HDR-BT treatment, no patient received any hormonal therapy. All patients underwent choline PET-CT or ^{68}Ga-PSMA-PET-CT, to exclude regional and/or distant metastasis and a cross sectional mp-MRI. The diagnostic mp-MRI protocol included a T1-weighted fast gradient echo sequence (THRIVE), T2-weighted turbo spin echo sequence (TSE), balanced turbo gradient echo sequence with spectral fat suppression (bTFE SPAIR), diffusion weighted imaging (DWI), and a dynamic contrast enhanced (DCE) sequence. All primary and secondary recurrences were pathologically proven through biopsies (systematic TRUS-guided biopsies for primary recurrences and guided biopsies through fusion of diagnostic mp-MRI and ultrasound images for secondary recurrences). At the time of salvage treatment, PSA was below 10 ng/ml, PSA doubling time was one year or more, and the interval between 1st and 2nd salvage treatment was 3 years or more. All patients showed gastrointestinal (GI) or genitourinary (GU) toxicity rates of ≤ 2 (CTCAE version 4.0) from the previous treatments.

Treatment procedures

The pre-treatment mp 3T MRI (sequences described above) was used to delineate the prostate, gross tumor volume (GTV), and surrounding organs at risk (OAR). As opposed to the first salvage prostate brachytherapy, no margins around the GTV were applied to reduce the risk of inducing toxicity. A pre-plan was made to estimate whether the salvage procedure would be feasible with regards to the risk of severe toxicity. The pre-plan was considered feasible if dose of OAR was below the prescription (D_{1cc} rectum/bladder < 12 Gy, $D_{10\%}$ urethra < 17.7 Gy), independent of any overlap with the first or second treatment.

All patients were treated with a single fraction of 19 Gy in a shielded room, equipped with a 1.5 T MR scanner that was suited for salvage MRI-guided HDR-BT.

On the day of treatment, patients received spinal anesthesia on the MRI table and a urinary catheter was inserted to optimize urethra visualization. With the patient in lithotomy position, the regions of interest of the diagnostic 3T mp-MRI were registered (using rigid fusion) with the intraoperative ultrasound. This procedure helps to better visualize the GTV on the ultrasound images. Next, brachytherapy catheters were inserted into the target area (GTV) under ultrasound guidance with a transperineal approach.

Subsequently, the ultrasound equipment was removed and an intra-operative 1.5 T MRI was made for treatment planning. The intra-operative MRI consisted of a transversal T2-weighted turbo spin echo (TSE) images and 2 series of 3D balanced turbo gradient echo images, one with SPAIR (spectral attenuated inversion recovery) and one with SPIR (spectral presaturation with inversion recovery). Delineation adjustments for prostate and OAR movement were made. Next, an intra-operative simulation of dose distribution to the GTV and OAR was made. If constraints for the OAR were met, patients received a single fraction of 19 Gy to > 95% of the GTV. However, if the dose constraints for the OAR were exceeded, the dose to the GTV was reduced. As no literature on second salvage dose prescription is available, dose constraints based on Holly *et al*. were used [13], for rectum and bladder a D_{1cc} < 12 Gy, for urethra a $D_{10\%}$ < 17.7 Gy. Also, post-implant MRI sequences (same sequences as the intra-operative MRI) were performed to assess dose differences caused by intra-operative catheter shifts.

Endpoints and follow-up

Primary endpoint was the occurrence of severe toxicity (≥ grade 3). Toxicity was reported according to the Common Toxicity Criteria of Adverse Events (CTCAE) version 4. Clinical outcome was monitored using PSA measurements.

Follow-up, toxicity assessment, and PSA measurements were performed at 1 month and every 3 months during the first year after treatment, every 6 months during the second year after treatment, and annually thereafter.

Results

Baseline characteristics

The median follow-up time for patients treated with a second focal salvage HDR-BT was 12 months (range, 6-15 months) (Table 1). No patient was lost to follow-up. The age of the treated patients ranged from 63 to 72 years. At time of primary treatment, two patients had a T1c, one patient a T2, and one patient a T3a disease. Three patients received ^{125}I brachytherapy, and one patient external beam radiation therapy (EBRT) as primary treatment. The median time to the first relapse was 7 years, with a range of 5-8 years. At time of first salvage treatment, all patients had local recurrences within the prostate. For the first salvage treatment, all patients were treated with focal salvage ^{125}I brachytherapy [10]. Median time to second salvage was 4 years (range, 3-6 years). At the time of secondary salvage treatment, all 4 patients had locally recurrent prostatic cancer. However, for one patient there was seminal vesicle extension (iT3b). At time of secondary salvage treatment, median PSA was 3.75 ng/ml (range, 3.0-5.3 ng/ml).

Dosimetry

Prostate volumes ranged from 25.7-47.0 cc, GTV ranged from 1.9 to 6.6 cc. For 3 of the 4 patients, the prescribed D_{95} GTV of 19 Gy was reached. In one patient, the D_{95} GTV was lower (15.5 Gy) because the GTV was in close proximity to the rectal wall. This structure had al-

ready received a high cumulative dose from earlier radiation treatments. The constraints for rectum, bladder, and urethra were met for all four patients. Dosimetry results are shown in Table 2.

Toxicity

At baseline (before second salvage treatment), 2 patients had GI grade 1 toxicity, and 2 patients had GI grade 0 toxicity. One patient had grade 1 GU toxicity, and 3 patients grade 0 GU toxicity. Regarding erectile dysfunction (ED), one patient had grade 0, one grade 1, one grade 2, and one grade 3 toxicity. All baseline toxicity scores prior to second focal salvage HDR-BT did not worsen during follow-up, except for one patient who developed grade 1 ED after treatment. For both GU and GI toxicity, the toxicity score decreased from grade 1 to grade 0 in one patient. None of the patients developed ≥ grade 2 GU or GI toxicity after treatment.

Biochemical outcomes

Prostate-specific antigen curves of all 4 patients are shown in Figure 1. For 3 patients, the PSA increased during follow-up. Two patients had a biochemical recurrence as per the Phoenix definition (PSA rise of 2 ng/ml above nadir). In one of these patients, a lymph node metastasis was detected during follow-up using ^{68}Ga-PSMA. In the other two patients, so far no local recurrences or distant metastasis have been detected. In the one patient who did not receive the prescribed GTV dose of 19 Gy, no local recurrence has been detected up till now.

Discussion

This study shows that a second salvage treatment is feasible with regards to acute toxicity. However, median follow-up is limited to 12 months and late toxicity may be underestimated. To our knowledge, there is no literature regarding secondary salvage treatments performed by other treatment modalities.

^{68}Ga-PSMA scans or choline PET scans are considered to have a high sensitivity to detect a local recurrence [6,7]. The mp-MRI has optimal soft tissue contrast, and also has a high negative and positive predictive value for clinically significant prostate cancer [9,14]. Beside these aspects, the mp-MRI has superior resolution when compared to the ^{68}Ga-PSMA scan. A high resolution is of great importance when delineating the target area (GTV) and the OAR in preparation for focal salvage HDR-BT. Furthermore, there is high conformity between the area of recurrence and the treated primary index lesion [15]. By reducing the rectum and bladder dose through focal salvage brachytherapy, it can be expected that toxicity will decrease when compared to whole gland salvage treatments [5,10]. Focal salvage LDR-BT showed very limited toxicity and good biochemical outcomes [10].

As results for salvage modalities for both tumor control and toxicity are promising, a second salvage treatment can be considered in a highly selected group of patients with locally recurrent prostate cancer [16]. In the same light as the first salvage treatment, the goal of

Table 1. Patient characteristics. The different parameters are described at time of primary treatment (1), first salvage (2) or second salvage (3). BT – brachytherapy, EBRT – external beam radiotherapy, IMRT – intensity modulated radiotherapy, # – fractions. NB. All primary and secondary recurrences were pathologically proven through biopsies (systematic TRUS-guided biopsies for primary recurrences and guided biopsies through fusion of diagnostic mp-MRI and ultrasound images for secondary recurrences). Staging before primary treatment was based on (staging 1) digital rectal examination and transrectal ultrasound. Staging of the first and second recurrences (staging 2 and 3) were based on MRI

Patient	Age (3) (years)	T-stage (1)	T-stage (2)	T-stage (3)	Gleason score (1)	PSA (1) (ng/ml)	PSA (2) (ng/ml)	PSA (3) (ng/ml)	Treatment (1)	Treatment (2)	Time (1-2) relapse (years)	Time (2-3) relapse (years)
1	72	T1c	T2a	T3a	6	5.4	10.0	5.3	2001; ^{125}I BT; 145 Gy; Whole gland	2010; ^{125}I BT; 145 Gy; Focal	8	6
2	72	T1c	T2a	T2a	6	5.2	2.2	3.0	2006; ^{125}I BT; 145 Gy; Whole gland	2012; ^{125}I BT; 145 Gy; Focal	7	3
3	71	T3a	T2a	T3b	7	13.2	3.4	3.7	2007; EBRT (IMRT); 77 Gy (35$^{\#}$); Whole gland	2011; ^{125}I; 145 Gy; Focal	5	4
4	63	T2	T2a	T2a	5	5.8	4.4	3.8	2006; ^{125}I; 145 Gy; Whole gland	2012; ^{125}I; 145 Gy; Focal	7	4

Table 2. Treatment characteristics

Patient number	Prostate volume (cc)	GTV (cc)	D_{95} GTV (Gy)	Rectum D_{1cc} (Gy)	Bladder D_{1cc} (Gy)	Urethra $D_{10\%}$ (Gy)	Catheters (number)
1	29.7	1.9	19.4	6.5	4.6	1.7	6
2	32.3	5.5	15.5	7.2	4.9	10.0	9
3	47.0	6.6	19.2	5.4	8.6	5.3	8
4	25.7	4.1	19.3	6.6	3.9	5.8	8
Median	31.0	4.8	19.3	6.6	4.8	5.6	8

Cc – cubic centimeter, Gy – Gray, GTV – gross tumor volume, D_{95} GTV – dose in 95% of the GTV, D_{1cc} – dose in 1 cc of the bladder/rectum, $D_{10\%}$ – dose in 10% of the urethra volume

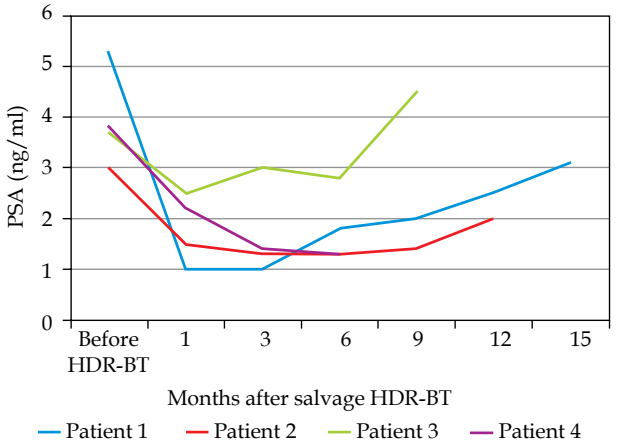

Fig. 1. Prostate-specific antigen curves of all 4 patients

a second salvage treatment is to further postpone androgen deprivation therapy, with its known deterioration on the quality of life [4,17,18]. The current availability of ^{68}Ga-PSMA scans also plays a key role in the selection of true locally recurrent prostate cancer in patients with a low PSA [8]. This allows for earlier treatment of these patients with possible smaller chance of metastasis from the index lesion. Prognostic factors are known for outcome after first (whole-gland) salvage treatment [19]. In multivariable analysis, disease-free survival interval (DFSI) after primary therapy and pre-salvage PSA-doubling time were predictors of biochemical failure [19]. These factors may be used for second salvage treatment, since the literature does not describe predictors for outcomes in this scenario.

In this study, no margin was applied to the GTV, as rectum and bladder already received radiation twice. It is not known whether there was microscopic spread around the GTV, but such a microscopic spread seems likely [2]. With a margin of 0 mm, we still expect some dose to be delivered to the first few mms around the GTV. As the area of microscopic spread will need less dose compared to the GTV due to a lower tumor density, we agreed on reducing the CTV and PTV margin to 0 mm around the GTV. Longer follow-up is necessary to determine if prostate cancer will recur adjacent, or perhaps even within the GTV after second salvage treatment.

For the 1st salvage LDR-BT treatment, dose restrictions for bladder, urethra, and rectum have been published to minimize the risk of late severe toxicity [20,21], namely a bladder D_{2cc} < 70 Gy, a urethral V_{100} < 0.4 cc and a rectal $D_{0.1cc}$ < 160 Gy. Unfortunately, no such restrictions are available for salvage HDR-BT [11]. As an accurate spatial dose delivery in salvage treatments is essential, many clinical groups prefer HDR-BT for treatment delivery [22]. ^{125}I seeds have the tendency to migrate from their original position and this phenomenon may have a negative effect on the intended dose delivery to the GTV. A shift in catheters in focal HDR-BT will also contribute to a suboptimal dose to the GTV, especially since in BT there is a steep dose gradient. With self-anchoring catheters, there is minimal displacement of the catheter tips, and it seems that these shifts have a minimal impact on dosimetry [23]. An advantage of HDR-BT compared to LDR-BT is that the dwell positions and times of the source can be regulated. With HDR-BT, more homogeneous dose to the GTV can be delivered and it is often possible to better modulate the dose around the adjacent OAR when compared to LDR-BT. There is literature suggesting adding of radiosensitizers, e.g. hyperthermia, may be considered [24].

There is a need for second salvage HDR-BT dose restriction values, since it is questionable whether the first salvage dose restriction parameters can be used for a second salvage treatment. In the current situation, this will be difficult to accomplish, as events (grade ≥ 3 GU and GI toxicity) and number of treated patients are low. Furthermore, determination of the cumulative dose may be difficult, since a different treatment modality was used as primary treatment. We suggest that dose constraints based on Holly *et al.* (for rectum and bladder D_{1cc} < 12 Gy, for urethra $D_{10\%}$ < 17.7 Gy) may be considered in clinical practice for both 1st and 2nd salvage HDR-BT [25].

The area of recurrence for the four 2nd salvage patients described in this study was 1 infield and 3 out of field. For each patient, the infield or out of field recurrences were determined based on the MRI used for planning of the first salvage treatment. The infield recurrence after the primary salvage treatment may have been caused by inadequate spacing of the ^{125}I seeds and/or by an aggressive tumor. The out of field recurrences may be explained by the fact that PSMA scans were not yet available at the time when patients underwent a primary salvage treatment. Out of field recurrences treated with a 2nd salvage HDR-BT will most probably have less impact on the OAR, since the accumulated dose for the specific OAR

will generally be lower than with an infield recurrence. Perhaps in or out of field 2nd recurrences can be taken into account when contemplating a 2nd salvage HDR-BT, and it may be an important selection criteria in future predictive models.

In 2 of 4 patients, there was a biochemical recurrence (Phoenix criteria) during follow-up (Figure 1). Although follow-up is still limited, it cannot be concluded whether patient selection had been appropriate. One patient showed a single nodal distant metastasis on a PSMA scan after biochemical recurrence, which was not present on the pre-treatment PSMA scan. For the other patient, further diagnostics will follow. One patient did not receive the prescribed dose to the GTV, and also shows PSA increase after treatment, although biochemical recurrence according to the Phoenix definition has not been reached. The increasing PSA in two of the patients may also be explained by a PSA bounce, as the median follow-up in this study is only 12 months. In the study of Mehta *et al.* [26], PSA bounce was noticed after an average of 9 months. There is no literature that describes PSA bounce after a 2nd salvage treatment.

Conclusions

Concluding, focal second salvage HDR-BT for locally recurrent prostate cancer is feasible in a highly selected group of patients, with a secondary local recurrence, minimal GI and GU toxicity, low PSA values at time of second salvage, and an interval of more than 3 years after earlier treatments. Confirmation in larger studies is needed. This approach may be used in the future to postpone hormonal therapy and positively influence the quality of life for patients with a 2nd locally recurrent prostate cancer.

Disclosure

Authors report no conflict of interest.

References

1. Zumsteg ZS, Spratt DE, Romesser PB et al. The natural history and predictors of outcome following biochemical relapse in the dose escalation era for prostate cancer patients undergoing definitive external beam radiotherapy. *Eur Urol* 2015; 67: 1009-1016.
2. Menard C, Iupati D, Publicover J et al. MR-guided prostate biopsy for planning of focal salvage after radiation therapy. *Radiology* 2015; 274: 181-191.
3. Tran H, Kwok J, Pickles T et al. Underutilization of local salvage therapy after radiation therapy for prostate cancer. *Urol Oncol* 2014; 32: 701-706.
4. Nguyen PL, D'Amico AV, Lee AK et al. Patient selection, cancer control, and complications after salvage local therapy for postradiation prostate-specific antigen failure, a systematic review of the literature. *Cancer* 2007; 110: 1417-1428.
5. Peters M, Moman MR, van der Poel HG et al. Patterns of outcome and toxicity after salvage prostatectomy, salvage cryosurgery and salvage brachytherapy for prostate cancer recurrences after radiation therapy: a multi-center experience and literature review. *World J Urol* 2013; 31: 403-409.
6. Umbehr MH, Müntener M, Hany T et al. The role of 11C-choline and 18F-fluorocholine positron emission tomography (PET) and PET/CT in prostate cancer: A systematic review and meta-analysis. *Eur Urol* 2013; 64: 106-117.
7. Breeuwsma AJ, Pruim J, van den Bergh AC et al. Detection of local, regional, and distant recurrence in patients with PSA relapse after external-beam radiotherapy using (11)C-choline positron emission tomography. *Int J Radiat Oncol Biol Phys* 2010; 77: 160-164.
8. Morigi JJ, Stricker PD, van Leeuwen PJ et al. Prospective Comparison of 18F-Fluoromethylcholine Versus 68Ga-PSMA PET/CT in Prostate Cancer Patients Who Have Rising PSA After Curative Treatment and Are Being Considered for Targeted Therapy. *J Nucl Med* 2015; 56: 1185-1190.
9. Barentsz JO, Richenberg J, Clements R et al. ESUR prostate MR guidelines 2012. *Eur Radio*l 2012; 22: 746-757.
10. Peters M, Maenhout M, van der Voort van Zyp JR et al. Focal salvage iodine-125 brachytherapy for prostate cancer recurrences after primary radiotherapy: a retrospective study regarding toxicity, biochemical outcome and quality of life. *Radiother Oncol* 2014; 112: 77-82.
11. Zamboglou C, Rischke HC, Meyer PT et al. Single fraction multimodal image guided focal salvage high-dose-rate brachytherapy for recurrent prostate cancer. *J Contemp Brachytherapy* 2016; 8: 241-248.
12. Claren A, Gautier M, Feuillade J et al. Second salvage treatment for local recurrence of prostate cancer using high-dose-rate brachytherapy: a case report. *J Contemp Brachytherapy* 2015; 7: 244-247.
13. Holly R, Morton GC, Sankreacha R et al. Use of cone-beam imaging to correct for catheter displacement in high dose-rate prostate brachytherapy. *Brachytherapy* 2011; 10: 299-305.
14. Fütterer JJ, Briganti A, De Visschere P et al. Can Clinically Significant Prostate Cancer Be Detected with Multiparametric Magnetic Resonance Imaging? A Systematic Review of the Literature. *Eur Urol* 2015; 68: 1045-1053.
15. Arrayeh E, Westphalen AC, Kurhanewicz J et al. Does local recurrence of prostate cancer after radiation therapy occur at the site of primary tumor? results of a longitudinal MRI and MRSI study. *Int J Radiat Oncol Biol Phys* 2012; 82: 787-793.
16. Duijzentkunst DA, Peters M, van der Voort van Zyp JR et al. Focal salvage therapy for local prostate cancer recurrences after primary radiotherapy: a comprehensive review. *World J Urol* 2016; 34: 1521-31.
17. Nguyen PL, Chen MH, Clark JA et al. Patient-reported quality of life after salvage brachytherapy for radio-recurrent prostate cancer: a prospective phase II study. *Brachytherapy* 2009; 8: 345-352.
18. Nguyen PL, Alibhai SM, Basaria S et al. Adverse effects of androgen deprivation therapy and strategies to mitigate them. *Eur Urol* 2015; 67: 825-836.
19. Peters M, van der Voort van Zyp JR, Moerland MA et al. Development and internal validation of a multivariable prediction model for biochemical failure after whole-gland salvage iodine-125 prostate brachytherapy for recurrent prostate cancer. *Brachytherapy* 2016; 15: 296-305.
20. Peters M, Hoekstra CJ, van der Voort van Zyp JR et al. Rectal dose constraints for salvage iodine-125 prostate brachytherapy. *Brachytherapy* 2016; 15: 85-93.
21. Peters M, van der Voort van Zyp J, Hoekstra C et al. Urethral and bladder dosimetry of total and focal salvage Iodine-125 prostate brachytherapy: Late toxicity and dose constraints. *Radiother Oncol* 2015; 117: 262-269.
22. Buchser D, Gomez-Iturriaga A, Melcon JI et al. Salvage high-dose-rate brachytherapy for histologically confirmed macroscopic local relapsed prostate cancer after radical prostatectomy. *J Contemp Brachytherapy* 2016; 8: 477-483.

23. Pieters BR, van der Grient JN, Blank LE et al. Minimal displacement of novel self-anchoring catheters suitable for temporary prostate implants. *Radiother Oncol* 2006; 80: 69-72.
24. Kukiełka AM, Strnad V, Stauffer P et al. Salvage brachytherapy in combination with interstitial hyperthermia for locally recurrent prostate carcinoma following external beam radiation therapy: a prospective phase II study. *J Contemp Brachytherapy* 2015; 7: 254-258.
25. Holly R, Morton GC, Sankreacha R et al. Use of cone-beam imaging to correct for catheter displacement in high dose-rate prostate brachytherapy. *Brachytherapy* 2011; 10: 299-305.
26. Mehta NH, Kamrava M, Wang PC et al. Prostate-specific antigen bounce after high-dose-rate monotherapy for prostate cancer. *Int J Radiat Oncol Biol Phys* 2013; 86: 729-733.