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### Pulsed-dose rate brachytherapy in prostate cancer

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**MINIMAL DISPLACEMENT OF NOVEL SELF-ANCHORING  
CATHETERS SUITABLE FOR TEMPORARY PROSTATE IMPLANTS**

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## ABSTRACT

Catheters were developed that can be fixed in the prostate gland by self-expanding parts for use in PDR brachytherapy. Daily CT-scans were made to investigate the magnitude of catheter displacement.

The mean absolute displacement during the 3 days treatment was 1.2 mm. The resulting minor alterations in dose-volume parameters were of no clinical importance.

## INTRODUCTION

Data from phase III studies show that high dose radiotherapy is necessary to control prostate cancer, especially in intermediate and high risk cancers [9, 11, 12]. However, increasing dose with external beam radiotherapy leads to a higher risk of normal tissue damage. This can be partly overcome by giving a boost with brachytherapy [2]. Ragde et al. reported long-term survival rates with a 45 Gy external beam dose followed by a 120 Gy iodine-125 permanent seed boost [10]. Implants can also be performed with a temporary needle or catheter implant and stepping-source brachytherapy. Several investigators have used high-dose rate (HDR) brachytherapy boost to improve tumor control in intermediate- to high-risk patients [3, 7].

Needle displacement between fractions is the main technical problem that occurs with a perineal temporary prostate implant which necessitates a needle position check with fluoroscopy or CT-scan before each HDR treatment [1, 4, 6, 8]. In our institute we have chosen to deliver the brachytherapy boost by pulsed-dose rate (PDR). Because of the higher number of fractions during day and night it is not acceptable to check the position of the needles before each pulse. For that reason we developed a catheter that can be fixed in the prostate gland and therefore could reduce catheter displacement. We describe the implantation procedure, analyzed catheter displacement, and its consequences on dose distribution.

## MATERIALS AND METHODS

### General

From May 2003 to March 2005 43 patients were entered in a study to investigate prospectively the feasibility of PDR boost for histologically proven adenocarcinoma of the prostate. The Medical Ethics Committee of the hospital approved this study and written informed consent was obtained from all patients. Thirty-one patients were included in this analysis to assess the usability of the novel catheters. The other patients are part of a toxicity analysis, which will be reported separately.

### External beam radiotherapy

Radiotherapy started with external irradiation of the lower pelvic lymph nodes, prostate, and base of the seminal vesicles. A CT-scan of the pelvis was made to perform virtual simulation (AcQsim, Philips Medical Systems, The Netherlands). Patients who did not undergo a pelvic lymph node dissection (pN0), were irradiated on the prostate and base of the seminal vesicles (Clinical Target Volume (CTV)) only. With 3-dimensional conformal techniques a radiotherapy plan was obtained on the CTV with 1 cm margin. The dose in the ICRU reference point [5] was 46 Gy in daily fractions of 2 Gy.

### Implantation technique and treatment planning

The implantation was performed according to a pre-plan. Treatment planning was performed with BPS 14.2 software (Nucletron B.V., The Netherlands) on ultrasound images, obtained with a multiplane 7.5 MHz transducer (Hitachi, Japan), in lithotomy position and with a transurethral catheter in place. Most source tracks, resembling planned catheter positions, were placed at the periphery of the prostate in order to cover the prostate gland completely and to spare the urethra. Dwell positions were 5 mm apart. Dwell-time optimization to improve the dose distribution was carried out on the pre-plan.

The implantation was done the week following the end of external beam radiotherapy. Implantations were performed under general or spinal anesthesia with the patient in lithotomy position and under antibiotic coverage (ciprofloxacin), starting the evening before. The endorectal ultrasound probe was placed similarly as during the preplan. Before the reconstruction of the preplan TRUS, a transurethral balloon-catheter was introduced and the bladder filled with 150 ml saline. First a 7F needle covered by a synthetic splitsheat (Optimed, Germany) was inserted transperineally into the prostate. In transverse ultrasound view the needle was placed at any desired position by using a template enabling movement of the needle-guidance arm in lateral and ventro-dorsal direction, according to the preplan. In the sagittal view the needle was advanced up into the seminal vesicles or bladder wall. After withdrawing the needle a 6F catheter (ELLA-CS, Czech Republic) could be placed through the splitsheat. Finally, the splitsheat was withdrawn and the catheter was fixed into the prostate by a self-anchoring mechanism at the outside tip of the catheter (Fig. 1). By opening the needle-guidance arm the catheter could be freed from the template. All consecutive catheters were placed accordingly (Fig. 2). Three



**Figure 1.** The catheter consists of an inner and outer luminal part. By pulling the outer part at the entrance end of the catheter, the umbrella anchoring mechanism unfolds itself over the inner part. This situation can be fixed with a closing knob (black arrow in figure 2) incorporated into the catheter. The radioactive sources go into the inner part.



**Figure 2.** Some catheters already placed. Note the free movable needle-guidance arm of the template (white arrow), which can be placed in any desired position. By opening the arm catheters can be freed from the template.

non-radiating iodine seed-markers, two at the base and one at the apex, were placed in the prostate to help with the recognition of these structures on CT-scan. Positioning of the seeds was done with the use of ultrasound guidance, as well as measurement of the distances between the prostate contour and the tip of each catheter.

The antibiotic treatment was continued from one day before until three days after removal of the catheters at the end of the brachytherapy treatment. Catheters were removed by relaxation of the anchoring mechanism and subsequent retraction.

Following the implantation a CT-scan was made with the catheters in situ, using 2-mm slice thickness and 2-mm slice spacing, resulting in a center to center slice distance of 2-mm. On the CT slices the prostate gland without margin (= PTV), urethra, rectum and bladder were delineated. The seed-markers placed into the prostate and the measured length of the prostate along each catheter helped with delineation of the prostate. The urethra and rectum were delineated from 2 slices above to 2 slices below the prostate. Only the part of the bladder adjacent to the prostate (5 slices) was delineated, being the volume that receives the highest dose from the implant.

With the PTV and all organs at risk delineated, dose planning was performed with dwell-time optimization. The first source position starts at 6 mm from the tip of the catheter.

The reference dose (RD) was 2496 cGy in 24 pulse doses of 104 cGy covering 95% of the PTV. The period time (time between start of two consecutive pulses) was 2.2 hours. The total treatment lasted 50.6 hours.

### Catheter displacement and the influence on dose distribution

Thirty-one patients received a second CT-scan on the day after the implantation (day 2) and 26 patients also on the second day after the implantation (day 3). The position of the prostate on these repetitive CT-scans was matched to the first CT-scan using the seed-markers and the part of the Foley catheter inside the prostate. To correct for prostate movements we have chosen not to match on bony structures. By comparing the two images, displacement of catheters relative to the prostate can be measured.

Assessment of the influence of catheter displacements on alteration of the dose distribution was performed by comparing the situation approximately 48 hours after the implant (day 3) to the situation on the day of the implant. The catheter displacements were entered in the planning system and a recalculation of the dose distribution was performed. From a cumulative dose-volume histogram (CDVH) the volumes of the PTV receiving a dose equal to or higher than 100% ( $V_{100}$ ), and 150% ( $V_{150}$ ) of the RD were obtained. Also the dose to 90% of the PTV ( $D_{90}$ ), the dose to 0.5 ml of the urethra volume ( $D_{0.5\text{ml-u}}$ ), 2 ml of the bladder volume ( $D_{2\text{ml-b}}$ ), and the rectum volume ( $D_{2\text{ml-r}}$ ) were calculated.

### Statistical considerations

Implantation of the prostate was performed according to a standard geometry of 12 catheters for the majority of patients. The position of the catheters were coded and used in the analysis to investigate if there were positions where catheters moved most. One-way analysis of variance (One-way ANOVA) of the absolute displacement of catheters was used for this analysis, only for patients with 12 catheters implanted.

Paired comparison of dose-volume parameters was used to investigate the impact of catheter movement on dose distribution. For hypothesis testing the paired  $t$  test was used.  $V_{150}$  and  $D_{2\text{ml-b}}$  values were logarithmically transformed to get a Normal distribution.  $D_{90}$  could not be transformed to a Normal distribution so a non-parametrical test was used. All

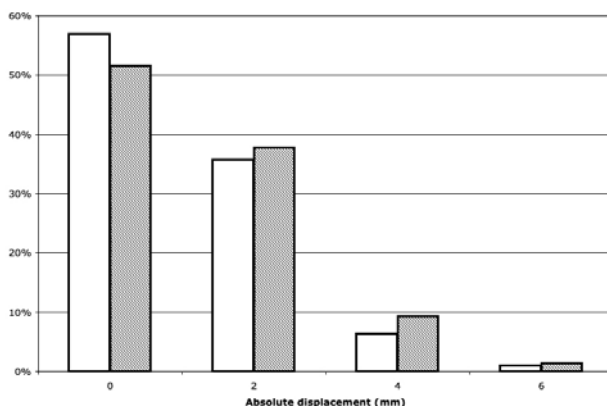


Figure 3. Absolute displacements of catheters on day 2 (white bars) and day 3 (shaded bars).

**Table 1.** Paired differences of dose-volume parameters on day 1 compared to day 3.

Dose-volume parameters	Mean difference day 1-3	95% CI	P
$V_{100}$	0.25 ml	0.05 to 0.46	0.02°
$\text{Ln}(V_{150})$	0.04 ml	-0.002 to 0.08	0.06°
$D_{0.5\text{ml-u}}$	0.99 cGy/pulse	0.02 to 1.96	0.05°
$D_{2\text{ml-r}}$	0.93 cGy/pulse	0.31 to 1.56	0.01°
$\text{Ln}(D_{2\text{ml-b}})$	-0.01 cGy/pulse	-0.05 to 0.03	0.63°
$D_{90}$			0.002*

° Paired t-test

\* Wilcoxon signed ranked sum test

tests were two-sided and a P-value  $\leq 0.05$  was considered significant. Statistical analysis was performed with Statistical Package for the Social Sciences, version 11.0 for Mac OS X (SPSS, Chicago, IL, USA).

## RESULTS

### Catheter displacement and the influence on dose distribution

In total 602 catheter positions compared to the initial position were measured. The mean absolute catheter displacement on day 2 and 3 were 1.0-mm (range 0-6) and 1.2-mm (range 0-6), respectively (Fig. 3).

One-way ANOVA could not identify any location in the prostate at which catheters moved more;  $P = 0.27$  on day 1 and  $P = 0.95$  on day 2.

The displacement of catheters caused some minor differences of dose-volume parameters after two days of treatment (Table 1).

## DISCUSSION

The flexible catheters used in this study were well tolerated. The major advantage of the catheters is the anchoring mechanism into the prostate gland, making external fixation unnecessary. Catheter movements with an absolute mean distance of only 1 mm were found, which is considerably smaller than displacements in HDR of up to 40 mm as reported by others [1, 4, 6, 8]. The magnitude of displacement did not depend on catheter localization in the prostate, even for the catheters placed into the seminal vesicles.

The displacements of the catheters had no relevant effect on the dose distribution during the treatment period. The  $V_{100}$  decreased significantly (0.25 ml), but this is probably of no clinical relevance. Also, the  $D_{90}$  decreased significantly, but still the mean  $D_{90}$  on the last the day of treatment was higher than the reference dose (108%). A  $D_{90}$  of at least the reference dose has also been reported by others performing temporary implants [6]. Mullokandov and Gejerman assessed the influence of catheter movement on the dose

distribution in a similar way as we did [8]. The catheters were fixed into a perineal template and sutured to the skin. In this study the median  $D_{90}$  decreased by up to 35% resulting in a median  $D_{90}$  of 62% of the reference dose. Therefore, they advised to evaluate catheter or needle position before each fractionated treatment. With the novel anchoring catheters displacement is not a major problem anymore, which is essential in multifractionated PDR because verification of catheter position before each fraction is not feasible. These catheters can also be used for fractionated HDR brachytherapy.

One limitation of the flexible catheter technique is the possibility of conduct problems due to kinking of the catheter. We have only observed serious problems resulting in cancellation of the treatment particularly at the beginning of the study period. It is our experience that these problems are not occurring any more because of better care of the catheters and instruction to the nursing staff.

## REFERENCES.

1. Damore SJ, Syed N, Puthawala AA, Sharma A. Needle displacement during HDR brachytherapy in the treatment of prostate cancer. *Int J Radiat Oncol Biol Phys.* 2000; 46:1205-1211.
2. Dattoli M, Wallner K, True L, Cash J, Sorace R. Long-term outcomes after treatment with external beam radiation therapy and palladium 103 for patients with higher risk prostate carcinoma. Influence of prostatic acid phosphatase. *Cancer.* 2003; 97:979-983.
3. Galalae RM, Kovács G, Schultze J, 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; 52:81-90.
4. Hoskin PJ, Bownes PJ, Ostler P, Walker K, Bryant L. High dose rate afterloading brachytherapy for prostate cancer: catheter and gland movement between fractions. *Radiother Oncol.* 2003; 68:285-288.
5. ICRU. Prescribing, recording and reporting photon beam therapy (supplement to ICRU report 50), ICRU report 62. Bethesda, MD, 1999.
6. Martinez AA, Pataki I, Edmundson G, et al. 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.
7. Martinez AA, Gustafson G, Gonzalez J, et al. Dose escalation using conformal high-dose-rate brachytherapy improves outcome in unfavorable prostate cancer. *Int J Radiat Oncol Biol Phys.* 2002; 53:316-327.
8. Mullokandov E, Gejerman G. Analysis of serial CT scans to assess template and catheter movement in prostate HDR brachytherapy. *Int J Radiat Oncol Biol Phys.* 2004; 58:1063-1071.
9. Pollack A, Zagras GK, Starkschall G, et al. Prostate cancer radiation dose response: Results of the M.D. Anderson phase III randomized trial. *Int J Radiat Oncol Biol Phys.* 2002; 53:1097-1105.
10. Ragde H, Elgamal AA, Snow PB, et al. Ten-year disease free survival after transperineal sonography-guided iodine-125 brachytherapy with or without 45-gray external beam irradiation in the treatment of patients with clinically localized, low to high Gleason grade prostate carcinoma. *Cancer.* 1998; 83:989-1001.
11. Shipley WU, Verhey LJ, Munzenrider JE, et al. Advanced prostate cancer: The results of a randomized comparative trial of high dose irradiation boosting with conformal protons compared with conventional dose irradiation using photons alone. *Int J Radiat Oncol Biol Phys.* 1995; 32:3-12.
12. Zietman AL, DeSilvio ML, Slater JD, et al. Comparison of conventional-dose vs high-dose conformal radiation therapy in clinically localized adenocarcinoma of the prostate. *JAMA.* 2005; 294:1233-1239.