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Dosimetric comparison between treatment plans of patients treated with low-dose–rate vs. high-dose–rate interstitial prostate brachytherapy as monotherapy: Initial findings of a randomized clinical trial

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ABSTRACT

PURPOSE: The aim of this study was to compare the dosimetry of intraoperative dose plans of prostate cancer patients treated with low-dose–rate (LDR) and high-dose–rate (HDR) interstitial brachytherapy (BT).

METHODS AND MATERIALS: A randomized clinical trial was initiated at our institution to compare the results and side effects of LDR and HDR BT as monotherapy in the treatment of early, organ-confined prostate cancer patients. Eighty-seven patients were randomly assigned to receive HDR afterloading BT with one fraction of 19 Gy or permanent LDR ^{125}I seed BT with 145 Gy. Inverse optimization algorithms were used for planning. Stranded seeds were implanted using live ultrasound imaging after preimplant treatment planning. Final dosimetry of HDR treatments was based on updated needle and contour positions. Statistical comparisons with nonparametric test were performed between the corresponding dose–volume parameters.

RESULTS: The V_{100} and V_{150} were 99% and 61%, respectively, for LDR, whereas 98% and 32% for HDR treatments. The D_{90} was less for HDR (122% vs. 110%). The dose distributions were more homogeneous and conformal with HDR technique (dose homogeneity index, 0.39 vs. 0.67; conformal index, 0.65 vs. 0.80). The urethra and rectum received significantly less dose with HDR. The D_{10} and D_{30} for urethra were 133% and 128%, respectively, for LDR and 114% and 111% for HDR treatments. The D_{2cm^3} for rectum was 68% and 55% for LDR and HDR technique, respectively.

CONCLUSIONS: Both techniques provided acceptable target volume coverage with a slightly higher value with the LDR technique. The dose distributions were more homogeneous and conformal, and both urethra and rectum were better protected with the HDR technique.

Keywords: Prostate cancer; Brachytherapy; Low-dose rate; High-dose rate; Dosimetry

Introduction

Brachytherapy (BT) plays an important role in management of localized prostate cancer. During BT, high dose can be delivered to target volume with low dose to surrounding normal tissues and organs at risk. For nonmetastatic prostate cancer, both low-dose–rate (LDR) and high-dose–rate (HDR) treatment techniques are used as curative treatment either as a boost to external beam radiation or as a monotherapy (1). Permanent implant LDR prostate BT with seeds is a well-established and proved method in the treatment of patients with low or selected intermediate risk, organ-confined prostate cancer (2–6). It has been used for nearly 30 years and has become a gold standard for prostate BT in low-risk patients. HDR prostate BT was initially introduced as a boost treatment to supplement dose given by external beam therapy (7–10). Since the late 90s, HDR BT with several fractions has been applied as monotherapy too, and there is good evidence in the literature that it is a safe and effective treatment method for prostate

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cancer (11−18). Regarding dosimetry, the HDR method has higher dose modulation potential compared with LDR seed BT. In the latter, the dose distribution can be shaped only with spatial arrangement of seeds with uniform activity. Although different seed activities can be used during one implantation with higher dose modulation possibility, this method is not used routinely in clinical practice. Whereas in HDR BT, in addition to spatial arrangements of sources, an additional option is existing for tailoring the dose distribution to target volume. With a stepping source (^{192}Ir) variable dwell times can be used in different source dwell positions, which provides another option to modulate the dose distribution. Another advantage of stepping source is that small geometrical miss or volume discrepancies can be compensated with increased or decreased dwell times in certain needles and/or source positions (19, 20).

At our institute, the HDR prostate BT program was implemented in 2001. At the beginnings, patients with intermediate- and high-risk prostate cancer were treated using the combination of three-dimensional conformal external beam radiotherapy and HDR BT as a boost treatment. Initially 8 Gy, later 10 Gy was delivered by BT with one fraction. Later, in 2008, our institution started the permanent prostate seed BT program with ^{125}I seeds as a monotherapy for patients with low- and intermediate-risk prostate cancer. The first 79 patients were implanted with loose seeds, and thereafter, all patients were treated with stranded seeds. Having obtained adequate experience in both prostate BT techniques, in 2015 a randomized clinical trial was initiated at our institution to compare the clinical results and side effects of LDR and HDR BT as monotherapy in the treatment of early, organ-confined prostate cancer patients.

Dosimetrical characteristics of both treatment techniques have been intensively investigated separately in many centers worldwide, and lots of articles are available in the literature with assessment of dosimetry. However, these studies included nonhomogeneous separate patient populations, which makes the direct dosimetric comparison challenging. The purpose of this study was to dosimetrically assess and compare the intraoperative treatment plans of prostate cancer patients treated with LDR and HDR interstitial BT in a randomized clinical trial.

Methods and materials

Our trial has been registered on ClinicalTrials.gov with an identifier of TC02258087. The treatments have been approved by the national and institutional ethics committees, and all patients signed an informed consent before the treatment. Patients with low- and selected intermediate-risk prostate cancer were randomly assigned to receive either HDR afterloading BT with one fraction of 19 Gy or permanent LDR ^{125}I seed BT with 145 Gy. Current analysis includes dosimetrical assessment of the first 87 patients enrolled into the study.

Implantation techniques

In both techniques, the implantation was performed with transrectal ultrasound (Pro Focus 2202; BK Medical ApS, Herlev, Denmark) guidance in spinal anesthesia. The urethra was visualized with Foley catheter. After preimplant treatment planning, stranded seeds (IsoSeed; Bebig-Theragenics, Berlin, Germany) with fixed separation of 1 cm were implanted into the prostate using live ultrasound imaging by means of a biplane probe (Type 8848). Axial and longitudinal planes were used for needle insertion. Finally, for verification purpose, an X-ray image was taken to count the seeds and check their positions. Before the HDR needle insertion, preimplant planning was also made, but the final dosimetry was always based on updated needle and contour positions. During HDR planning, only axial images were used. Before irradiation, the positions of needles were also confirmed with a verification X-ray image. Fixation needles to block prostate movement were used in HDR but not in LDR treatments. Because only single fraction was delivered with the HDR technique, the possible needle displacement observed in fractionated therapy could be avoided making the dose delivery more accurate.

Treatment planning

Treatment planning and dosimetry were based on intraoperative ultrasound images acquired on the implant day for both techniques. The prostate gland was outlined in axial planes as target volume. For low-risk patients, no margin was applied, but for intermediate risk patients a 3-mm margin was added around the prostate constrained to the anterior rectal wall as recommended by the Groupe Européen de Curiethérapie-European Society for Radiotherapy and Oncology (GEC-ESTRO) guidelines (21). The intratarget section of urethra was contoured as circles with 8-mm diameter around the catheter representing a periurethral volume. The rectum was outlined anterior to the water balloon placed around the ultrasound probe. For LDR treatments, the SPOT-PRO 3.1 and for HDR treatments the Oncentra Prostate 3.2.2 planning systems (both from Elekta, Brachytherapy, Veenendaal, The Netherlands) were used. Inverse optimization algorithms (inverse planning simulated annealing [IPSA] for LDR and Hybrid Inverse Planning and Optimization [HIPO] for HDR) were applied to define the source positions for both and the dwell times for HDR techniques (22−25). Our dose constraints for target, urethra, and rectum used during optimization are listed in Table 1 for inverse planning simulated annealing and HIPO. Table 2 includes our acceptance criteria of treatment plans for both treatment techniques. For both techniques, Day 0 US images were used for planning. Because in the intraoperative setting the anatomical