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BRACHYTHERAPY

High-dose-rate brachytherapy as a monotherapy for prostate cancer—Single-institution results of the extreme fractionation regimen

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ABSTRACT

PURPOSE: We report a single-institution retrospective analysis of the outcomes, disease control, and toxicity of high-dose-rate (HDR) brachytherapy used as the only treatment modality (monotherapy) for localized prostate cancer.

METHODS: Between 2006 and 2012, 77 patients with diagnosed prostate cancer were treated with HDR brachytherapy as a monotherapy. The prescribed dose was 45 Gy in three separate implants 21 days apart, with single fraction per implant. Of the 77 patients, 67 (87%) received hormonal therapy. Prostate-specific antigen failure was defined according to Phoenix consensus, as nadir + 2 ng/mL. Toxicity was scored according to Common Terminology Criteria for Adverse Events, version 4.03.

RESULTS: The median followup time was 57 months (4.75 years). The 5-year actuarial overall survival was 98.7%, biochemical control 96.7%, local control 96.9%, and metastasis-free survival 98.4%. Younger age at the beginning of brachytherapy predicted the onset of bounce phenomenon. There were no Grade 3 or higher acute toxicities detected, and Grade 2 genitourinary acute toxicity developed in 19 patients (24.6%). There were no Grade 2 gastrointestinal complications. No Grade 4 or 5 late toxicity was detected. There were also no Grade 3 gastrointestinal toxicities detected. One patient (1.3%) underwent transurethral resection of the prostate because of Grade 3 urethral stenosis and urinary retention. A total of 26 patients (33.8%) developed Grade 2 late toxicity.

CONCLUSIONS: HDR brachytherapy as monotherapy for localized prostate cancer was feasible, effective, and had acceptable toxicity profile.

Keywords: Prostate cancer; High-dose-rate brachytherapy; Monotherapy; Toxicity; Outcomes

Introduction

Radiotherapy is a well-established treatment option of localized prostate cancer. There are several radiation therapy modalities available, including external beam radiotherapy (EBRT), low-dose-rate brachytherapy (LDRBT), high-dose-rate brachytherapy (HDRBT), and a combination of EBRT and brachytherapy (1). HDRBT has several advantages over LDRBT in the treatment of prostatic adenocarcinoma, such as greater ability to treat extracapsular extension and seminal vesicles, or possibility to implant large-volume glands (1–3). HDRBT improves the distribution of radiation dose because—in contrast to LDRBT—the iridium-192 source dwell time and positions are adjustable. Several radiobiological reports suggest low α/β ratio of prostate cancer, which favors this type of brachytherapy (4–6).

HDRBT was introduced into clinical practice as a boost after EBRT (7). Growing clinical experience for HDRBT resulted in National Comprehensive Cancer Network recommendations in 2014 that it can be used as monotherapy or in combination with EBRT instead of LDRBT (8). Consensus guidelines of American Brachytherapy Society published in 2012 (9) and recommendations of Groupe Européen de Curiethérapie/European Society for Radiotherapy and Oncology dated 2013 (10) were still cautious

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in defining the role of HDRBT as a sole modality in treating prostate cancer.

There are many dose fractionation schemes in HDRBT monotherapy. Several single-center series of patients with long-term results have been published to date. In Centrum Onkologii - Instytut im. M. Skłodowskiej-Curie, Krakow Branch (COK), we have launched HDR brachytherapy for prostate cancer in 2006, both as monotherapy, boost after EBRT, and as salvage treatment. The first regimen of monotherapy was 45 Gy in three implants, separated by 3 weeks, each with a single fraction of 15 Gy. This scheme was common in Poland (11). Now this scheme is in use for patients at intermediate and high risk opting for HDR monotherapy, and in patients with low-risk group, we introduced new regimen with total dose of 36 Gy in three fractions each of 12 Gy. In the present study, we report our experience with HDR brachytherapy as monotherapy in patients with localized prostate cancer, as well as toxicity rates and patient outcomes.

Methods and materials

Patient characteristics and selection criteria

Between May 2006 and July 2012, a total of 77 patients were treated with HDR brachytherapy as monotherapy for clinically localized prostate cancer. All patients had histologically proven disease and had staging, including at least digital rectal examination (DRE), transrectal ultrasound (TRUS), abdominal and pelvic ultrasound, CT and/or MRI, and bone scan.

The eligibility criteria were (*1*) biopsy-proven prostatic adenocarcinoma, (*2*) clinical TNM stage T1c−2c without nodal or distant metastases, (*3*) Gleason score ≤7, (*4*) no contraindications for spinal anesthesia, (*5*) gland size less than 60 cc, (*6*) if transurethral resection of the prostate (TURP) was performed, at least 6 months should pass to qualification, (*7*) the distance between rectal mucosa and rear edge of prostate >5 mm, (*8*) no pubic arch interference, (*9*) International Prostate Symptom Score <20 points, and (*10*) informed consent obtained. Patients were considered ineligible for monotherapy for various reasons, including nodal or distant metastases, Gleason score 8 and higher, a broad pelvic inlet, or severe urinary symptoms.

The National Comprehensive Cancer Network definition of risk group was used to stratify patients into groups of low risk, intermediate risk, or high risk (8). Low-risk patients were defined as those with prostate-specific antigen (PSA) ≤10 ng/mL, local stage T1−T2a, and Gleason score of ≤6; intermediate-risk patients were PSA level of 10−20 ng/mL, local stage T2b−T2c, and Gleason score of 7; high-risk patients were those with PSA level above 20 ng/mL, stage T3a−T3b, and Gleason score of 8 and above.

A total of 67 patients (87%) received hormonal therapy. Androgen deprivation therapy (ADT) was initiated by clinical oncologists in COK or urologists referring patients. Usually, ADT consisted of antiandrogen (flutamide or bicalutamide) and luteinizing hormone−releasing hormone agonist (leuprolide, goserelin, or triptorelin). Sixty-four patients receiving ADT finished their hormonal therapy at least 2 years before the last followup visit. Patient and tumor characteristics are shown in Table 1.

Brachytherapy protocol

HDR brachytherapy procedure at our institution does not differ from that reported in the literature (1, 12) but will be briefly presented. The procedure starts with a Foley catheter insertion into the bladder (or in exceptional cases, we use Tiemann catheter) to facilitate visualization of the urethra and bladder wall. Then, the patient is anesthetized spinally and laid in lithotomy position. Axial cross sections of the prostate with craniocaudal 10−15 mm margins are acquired in continuous probe movement technique into the treatment planning software (Nucletron SWIFT; or its successor Oncentra Prostate; Nucletron BV, Veenendaal, The Netherlands). Based on this set of images, radiation oncologist contours the prostate, urethra, and rectum and physicist performs virtual plan. The clinical target volume for stage T1c−2c includes the whole prostate gland without any margins. The planning target volume (PTV) is equal to the clinical target volume. Radiation oncologist (TW, AMK, or TD) implants steel applicators, subsequently

Table 1
Patient and tumor characteristics

Characteristic	Median (range) or *n* (%)
Followup time (mo)	56.5 (11.4−92.6)
Age at treatment (y)	67 (49−79)
Pretreatment PSA (ng/mL)	7.6 (0.512−32.14)
Pretreatment PSA level	
≤10	58 (75.3)
11−20	16 (20.8)
≥20	3 (3.9)
Local stage	
T1c	43 (55.8)
T2a	23 (29.9)
T2b	3 (3.9)
T2c	8 (10.4)
Gleason score	
≤6	71 (92.2)
7	4 (5.2)
≥8	0
Unknown	2 (2.6)
Risk group	
Low	47 (61.1)
Intermediate	27 (35)
High	3 (3.9)
Androgen deprivation therapy	
n (%)	67 (87)
Median duration (range)	17 (7−75)
Prostate gland volume (cc)	
Before treatment	25.7 (12−49)
At first implant	30.3 (10.6−57)
At second implant	32.6 (16.7−56.6)
At third implant	32.6 (14.6−59.3)

PSA = prostate-specific antigen.