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High-dose-rate brachytherapy for large prostate volumes (≥50 cc)—Uncompromised dosimetric coverage and acceptable toxicity

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ABSTRACT

PURPOSE: The purpose of this study was to review our single-institution experience using high-dose-rate (HDR) brachytherapy in patients with large-volume prostate glands (≥50 cc).

METHODS AND MATERIALS: Fifty-four patients treated with HDR brachytherapy for prostate cancer at the Penrose Cancer Center between 2001 and 2006 were identified as having an ultrasound volume of at least 50 cc at the time of implant (range, 50–97.3 cc; mean, 61.5 cc; median, 57 cc; upper quartile, 83.3–97.3 cc). Neoadjuvant hormones (17 patients) were not routinely recommended unless the initial ultrasound volume suggested pubic arch interference or the patient's Gleason score or prostate specific antigen prompted use. All patients received HDR brachytherapy as a boost before or after conformal external beam radiation therapy to 4500 cGy. Boost brachytherapy doses ranged from 1600 to 1900 cGy, given in two to three fractions.

RESULTS: The median D_{90} (minimal dose to 90% of the prostate) was 109% of prescription dose (range, 95–115%) and the median V_{100} (volume receiving 100% of the dose) was 96% (range, 90–99%). V_{150} ranged from 10% to 35%, with a median value of 18.3%. Six patients (11%) required temporary placement of a urinary catheter for acute obstructive symptoms after brachytherapy. With a median followup of 1.8 years, there has been a single case of Grade 2 gastrointestinal toxicity and 1 patient has developed a bulbo-urethral stricture requiring dilation. There have been no cases of rectal bleeding.

CONCLUSIONS: Large prostate volume is not a contraindication to HDR brachytherapy. Excellent dosimetric coverage can be attained with acceptable acute toxicity.

Keywords: Prostate; Large volume; High-dose-rate brachytherapy; Pubic arch interference

Purpose

Low-dose-rate (LDR) brachytherapy with permanent radioactive seeds has become a standard treatment for localized prostate cancer over the past decade. Historically, patients with large-volume glands (>50–60 cc) have been considered suboptimal candidates for LDR brachytherapy. It has been shown that prostate volume correlates directly with the ability to perform an adequate permanent seed implant (1–3), post-treatment urinary symptoms (4–8), and pubic arch interference (PAI). A number of strategies have been used to alleviate the geometric difficulties of performing brachytherapy on a large prostate gland, ranging from downsizing with neoadjuvant hormonal therapy (9, 10) to procedural techniques designed to predict and avoid PAI (11–14). High-dose-rate (HDR) brachytherapy using a free-hand perineal template offers flexibility of needle trajectory intraoperatively and permits target coverage optimization through control of dwell position times. The purpose of this study was to review our single-institution experience using HDR brachytherapy in patients with large-volume prostate glands.

Methods and materials

Patient selection

The records of 315 patients treated with HDR brachytherapy for clinically localized prostate cancer at the Penrose Cancer Center between 2001 and 2006 were

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retrospectively reviewed under institutional review board approval. From the entire cohort of eligible patients, 54 were identified as having a preimplant ultrasound volume of at least 50 cc (range, 50–97.3 cc; mean, 61.5 cc; median, 57 cc; upper quartile, 83.3–97.3 cc). Neoadjuvant hormones (17 of 54 patients) were not routinely recommended unless the initial ultrasound volume at the time of biopsy suggested PAI or the patient's Gleason score or prostate specific antigen prompted use clinically. At our institution, patients with Gleason scores of $3+4$ are offered 6 months of androgen deprivation therapy, those with Gleason $4+3$ are offered 8–12 months, and those with Gleason scores $\geqslant 8$ are offered 2 years of androgen deprivation therapy. Patients treated with androgen deprivation for downsizing were included in the study population as long as the prostate volume measured by ultrasound at the time of the implant remained >50 cc. Analysis was based on the prostate volume at the time of implant in those receiving hormones. The median volume of glands requiring neoadjuvant hormone therapy specifically for downsizing to avoid PAI was 100 cc (range, 56–171). Those with large initial volumes who were hormonally downsized below 50 cc were excluded from analysis.

Treatment

Fifty-four patients receiving HDR brachytherapy as a boost before or after 3D conformal external beam radiation therapy (EBRT) to 4500 cGy in 25 fractions comprise the study cohort. Six patients receiving brachytherapy alone as monotherapy were excluded from analysis. EBRT was delivered using daily ultrasound guidance (Z-Med) for localization. Sequencing of brachytherapy and EBRT was primarily based on logistic constraints; 27 patients had brachytherapy before EBRT and 27 patients had brachytherapy after EBRT. For low-risk patients (Gleason $\leqslant 6$; prostate specific antigen $\leqslant 10$, Stage $\leqslant$T2a; 26 of 54 patients), the EBRT clinical target volume consisted of the prostate only expanded by 8 mm in all directions except posteriorly where the expansion was limited to 5 mm. For intermediate- and high-risk patients with an estimated risk of pelvic lymph nodes >15%, the clinical target volume included the prostate, seminal vesicles, and regional nodes. Boost brachytherapy doses ranged from 1600 to 1900 cGy, given in two to three fractions, with the most common fractionation schedule being 950 cGy in two daily fractions given on the same day as the implant. The first 9 patients in the series received three fractions of 600 cGy; thereafter, all patients had a single implant procedure with two fractions delivered at least 6 h apart on the same day. The duration between EBRT and brachytherapy was typically 2 weeks.

Implant technique

All patients underwent transrectal ultrasonography (by the same ultrasoundographer) in the dorsal lithotomy position to assess prostate size intraoperatively. Two gold marking seeds were placed at the base of the gland and one seed was placed at the apex. Seed location was assessed by ultrasound and fluoroscopy. Using a free-hand perineal template, a median of 16 (range, 14–20) 17-G closed-ended stainless steel needles were then placed under ultrasound guidance to cover a midgland axial slice using a modified peripheral loading pattern. Cystoscopy was performed and needles were serially advanced toward the base until tenting of the bladder wall was visualized. The perineal template was sutured to the perinium and the stainless steel needles remained in place until after the last HDR fraction was delivered.

Treatment planning

Computed tomography simulation with 1- to 3-mm slice thickness occurred immediately after the implant procedure and the three-dimensional data set was transferred to the BrachyVision (Varian Medical Systems, Charlottesville, VA) treatment-planning computer. A single physician (AVP) contoured the bladder, rectum, prostate, and urethra for each case. Plans were optimized for target coverage and normal tissue avoidance using variable dwell times per needle. Treatment goals included coverage of the prostate volume with 95–100% prescription dose while keeping the urethra and bladder neck <115% of prescription dose. Less than 1 cc of the rectum should receive >70% dose. These goals are based on adequate LDR coverage goals, but represent in-house treatment guidelines derived from initial clinical experiences.

Treatments were delivered using a HDR ^{192}Ir source with 5-mm dwell positions along each needle. All patients were treated twice per day with at least a 6-h interfraction interval. The same brachytherapy plan was used for the morning and afternoon fraction; the decision to use the same plan for each fraction arose from our initial experience with the first 50 patients, in whom a repeat computed tomography scan was performed before the afternoon session. The position of the needles with respect to reproducible bony landmarks was found to differ by <2 mm in all cases except for 1 patient who attempted to ambulate between fractions. Thereafter, we have confirmed implant integrity by measuring the distance between the template and needle hub before each treatment.

Statistical analysis

Statistical Analysis Systems software was used for all statistical analyses (15). Toxicity data were obtained from the medical record and telephone interviews with patients. American Urologic Association (AUA) symptom scores were collected prospectively at the time of consultation and periodically during followup visits. Baseline AUA scores were compared with those reported greater than 1 year after brachytherapy; an increase in AUA score of