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Large prostate gland size is not a contraindication to low-dose-rate brachytherapy for prostate adenocarcinoma

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ABSTRACT

PURPOSE: Prostate volume greater than 50 cc is traditionally a relative contraindication to prostate seed implantation (PSI), but there is little consensus regarding prostate size and clinical outcomes. We report biochemical control and toxicity after low-dose-rate PSI and compare outcomes according to the prostate size.

METHODS AND MATERIALS: A total of 429 men who underwent low-dose-rate PSI between 1998 and 2009 were evaluated. Median followup was 38.7 months. Patients were classified by prostate volume into small, medium, and large subgroups. Differences were analyzed using the Mann–Whitney and Pearson's χ^2 tests for continuous and categorical variables, respectively. Cox proportional hazards regression models were used to evaluate effect of prostate size on outcomes.

RESULTS: Patient pretreatment factors were balanced between groups except for age ($p = 0.001$). The 10-year actuarial freedom from biochemical failure for all patients treated with PSI was 96.3% with no statistically significant difference between large vs. small/medium prostate size (90% vs. 96.6%, $p = 0.47$). In a multivariate analysis, plan type (hazard ratio [HR] = 0.25, $p = 0.03$), dose to 90% of the gland (D_{90}: HR = 0.98, $p = 0.02$), volume receiving 200 Gy (V_{200}: HR = 0.98, $p = 0.026$), and biologic effective dose (HR = 0.99, $p = 0.045$), but not prostate size (HR = 2.27, $p = 0.17$) were significantly associated with freedom from biochemical failure. Prostate size was not significantly associated with time to maximum American Urologic Association score.

CONCLUSION: In men with large prostates, the PSI provides biochemical control and temporal changes in genitourinary toxicity that are comparable with men having smaller glands. Accurate dose optimization and delivery of PSI provides the best clinical outcomes regardless of gland size. Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: Prostate cancer; Brachytherapy; Low-dose rate; Biochemical control

Introduction

Prostate cancer is the second most prevalent solid tumor diagnosed in men from the United States and Europe (1). Treatment options for men with low- and intermediate-risk prostate cancer as defined by National Comprehensive Cancer Network (NCCN) guidelines (2) include radical prostatectomy, external beam radiation therapy (EBRT), and prostate seed implantation (PSI). The data suggest that long-term outcomes of patients with organ-confined prostate cancer are equally favorable after radical prostatectomy, EBRT, or PSI (3, 4); however, in terms of cost-effectiveness, PSI is the economically favorable approach (5).

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Historically, the physicians have been reluctant to offer PSI to patients with large prostate gland size owing to difficulty with the technique of seed implantation and concerns for potential pubic arch interference and excess toxicity. These patients are routinely offered more costly alternatives of treatment. In a survey evaluating practice patterns among physicians performing brachytherapy in the United States, approximately a third of responders would implant a prostate gland size greater than 50 cc, and only 9% would implant a gland with size greater than 60 cc (6). Several studies evaluating clinical outcomes and toxicity profile of PSI in patients with large prostate gland size have generated conflicting results (7–10). We sought to determine whether large prostate gland size negatively impacted long-term clinical outcomes and genitourinary (GU) toxicity. To do so, we analyzed our single-institutional retrospective database consisting of men with low- and intermediate-risk prostate cancer treated with PSI and report on long-term outcomes in men with large-sized glands compared with small- or medium-sized glands.

Methods and materials

Patient characteristics

After approval by the Institutional Review Board, 429 men who underwent low-dose-rate (LDR) PSI at a single institution between 1998 and 2009 were identified. Patients eligible for study inclusion had clinical, technical, and dosimetric details of the implant available for review. All patients cases were initially discussed in a multidisciplinary tumor board and evaluated by a thorough history and physical examination (including digital rectal examination), routine laboratory studies, pelvic computed tomography, nuclear medicine bone scan, serum prostate-specific antigen (PSA), and needle biopsy to determine the Gleason score. All patients were staged according to the 1992 American Joint Committee on Cancer staging system (11). Patients were further classified into risk groups according to NCCN guidelines (2). Patients with American Urological Association (AUA) Prostate Symptom Score greater than 15, large transurethral resection of prostate defects, and those with high operative risk were ineligible for PSI. There was no systematic evaluation of gland size as long as patients met criteria for AUA score of 15 or lower and ability to receive anesthesia. Most patients had a postvoid residual and urodynamic evaluation performed by our urologist colleagues before referral. In selected cases of eligible patients who had severe urinary symptoms, a more extensive workup including transurethral incision of prostate was performed to relieve symptoms before PSI; however, this was not common practice.

Prostate brachytherapy and combined therapies

Before PSI, a volume study was performed to assess prostate volume and anatomy to develop a preliminary seed distribution plan for seed ordering.

The LDR-PSI procedures were performed under general anesthesia with patients in the dorsal lithotomy position. When pubic arch interference was a concern, the patients were placed in the dorsal lithotomy position with extended hip flexion. Using sterile technique, a Foley catheter was inserted to identify the urethra during treatment planning and an ultrasound probe was inserted into the rectum for real-time image guidance. Transverse images were acquired covering the entire extent of the prostate. Next, the prostate target volume was contoured and the rectum, urethra, and bladder were identified as organs at risk. Since 2004, dosimetry has been planned intraoperatively including an interactive planning technique (VariSeed, Varian Medical Systems, Inc., Palo Alto, CA). A modified peripheral loading pattern was used for seed implantation to deliver adequate dose to the prostate while also minimizing dose to the bladder and urethra. Needles were placed using a perineal template and ultrasound guidance. Loose seeds were placed using loaded Mick applicator (Mick Radio-Nuclear Instrument, Mount Vernon, NY) under fluoroscopy with a marker cable used to define the prostate base. The peripheral loading technique was used. All patients undergo immediate postimplant cystoscopy to evaluate bladder wall as well as fluoroscopy to verify seed placement.

Treatment guidelines include rectal 1 cc doses less than the prescription dose and maximum urethral doses less than 150% of the prescription dose. The goal dose to 90% of the prostate (D_{90}) is greater than 90%, and the volume receiving 100% of the prescription dose (V_{100}) is greater than 90%. Prescription dose is 145 and 125 Gy when ^{125}I and ^{103}Pd are used in monotherapy, respectively. Doses were decreased to 110 and 70–100 Gy for ^{125}I and ^{103}Pd, respectively, when used in combination with EBRT. Patients routinely return for a post-mplant imaging study approximately 30 days after PSI, after allowing for prostate gland edema to subside.

Although PSI may be used as a monotherapy in low-risk prostate cancer, combination therapy with brachytherapy, EBRT, and/or androgen deprivation therapy (ADT) was used in men with intermediate- and high-risk disease. The EBRT treatment was delivered using widely standardized methods including three-dimensional conformal techniques and routine use of intensity-modulated radiotherapy beginning in 2004. Gold fiducial markers or seed matching was used for daily position verification with orthogonal imaging or image-guided radiotherapy with conebeam CT beginning in 2006. Prescription dose was typically 45 Gy in 1.8 Gy daily fractions with elective coverage of the pelvic lymph nodes in high-risk disease. Dose was prescribed to the isodose line covering the planning treatment volume.

The ADT consisted of a gonadotropin-releasing hormone agonist (leuprolide acetate or goserelin acetate) with or without antiandrogen (flutamide or bicalutamide). When used, ADT was typically prescribed 3 months preimplantation and an additional 2–3 months postimplantation of seeds (12). In patients receiving ADT, post-ADT prostate volume was used for the analysis.