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BRACHYTHERAPY

Focal brachytherapy for localized prostate cancer: Urinary toxicity depends on tumor location

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ABSTRACT

PURPOSE: To evaluate whether patients with prostate cancer have worse functional urinary recovery with focal brachytherapy (FBT) at the base versus the apex of the prostate.

METHODS AND MATERIALS: The functional outcomes of patients treated with FBT at the base of the prostate were compared with those of patients treated with FBT at the apex. Urinary symptoms, continence, and erectile dysfunction were measured using the International Prostate Symptom Score (IPSS), International Continence Score (ICS), and International Index of Erectile Function (IIEF-5) questionnaires, respectively, at baseline and at 6, 12, and 24 months after treatment.

RESULTS: Twenty-eight and 13 patients were treated with FBT at the apex and the base, respectively, of the prostate. A significant difference between groups was found in the IPSS score at 6 months (mean IPSS: apex 6.4 ± 4.7, base 10.6 ± 5.7; $p = 0.02$), but not at baseline or at 12 and 24 months after treatment. On multivariate analysis, only FBT at the base of the prostate remained an independent predictor of worsening urinary symptoms (odds ratio, 5.8; $p = 0.04$).

CONCLUSIONS: At 6 months after FBT, significantly less urinary toxicity was found in patients who underwent FBT at the apex versus the base of the prostate. Continence and sexual side effects were minimal in all patients.

Keywords: Prostate cancer; Focal therapy; Brachytherapy; Urinary toxicity; Urinary symptoms

Introduction

Prostate cancer (PCa) is the most common tumor in men and accounts for 21% of newly diagnosed malignancies in North America (1). Because of the high incidence, PCa is a topic of major concern and continuous debate. The treatment of PCa has changed substantially over time with the development of new technologies. In this context, brachytherapy (BT) evolved to produce less toxicity while achieving optimal cancer control (2). Contemporary series reported 10-year cancer-specific survival rates of 87−96% for patients with low- and intermediate-risk PCa treated with BT (2, 3) and potency rates superior to those with surgery (4, 5). Nevertheless, patients may still have self-limited urinary and bowel symptoms. The long-term rates of relevant urinary and rectal toxicity (Radiation Therapy Oncology Group [RTOG] Grade > 2) are approximately 6% and 1%, respectively (6, 7). Furthermore, urinary−intestinal fistula may occur in 0.3% of patients, with devastating consequences (8).

This scenario motivated the development of a therapeutic strategy for tissue preservation. The association of MRI and template biopsy permits precise assessment of the PCa index lesion, which determines local progression and metastatic seeding (9). Focal BT (FBT) was developed to destroy the

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index lesion while possibly delivering less radiation to the prostate surroundings. Recent evidence suggests that this treatment approach decreases the effects of toxicity (10−12).

Our institution pioneered FBT, with the first treatment performed in 2010 (10). Through our experience, we observed that patients with treated tumors at the base of the prostate had severe urinary symptoms during early followup. This phenomenon was not seen in patients with treated tumors at the apex of the prostate. We investigated this association with the aim of better counseling patients undergoing FBT. The objective of this study was to analyze whether patients treated with FBT at the base of the prostate had worse functional recovery than those treated with FBT at the apex.

Methods and materials

A retrospective review was performed using our institutional PCa database to search for patients treated with FBT between January 2008 and August 2014. Focal treatment was defined as a target ablation of the index lesion with a security margin of 1 cm, respecting the rectal and urethral safety dose limits. Eligibility criteria for FBT included (*1*) Gleason score $\leq 3 + 4$, (*2*) prostate-specific antigen (PSA) $\leq$ 15 ng/mL, (*3*) clinical stage T2a or lower, (*4*) unilateral tumor, (*5*) life expectancy $\geq$ 10 years, (*6*) biopsy cores with less than 50% of tumor involvement, (*7*) cores involved $\leq$ 25% of the total, and (*8*) prostate volume $\leq$ 60 cm^3. All patients had at least one template perineal biopsy and MRI of the prostate. The cohort was treated with low-dose iodine-125 seeds, following a previously described technique by the same experienced radiotherapist (JMC) (10). Seed activity was 0.546 kerma units, with limited variations between patients. Number and location of the implanted seeds were chosen according to the real-time planned dynamic dose calculation for each patient. The target D_{90} was 145 Gy. Rectum and urethral dose limits were $D_{2cc} \leq 145$ Gy and $D_{10} \leq 150$ Gy, respectively. A previously inserted Foley catheter helped to outline the urethral limits with the transrectal ultrasound. Followup included use of the International Prostate Symptom Score (IPSS), International Continence Score (ICS), and International Index of Erectile Function (IIEF-5) validated questionnaires at baseline and at 6, 12, and 24 months after FBT. Briefly, the IPSS score is composed of seven questions related to urinary symptoms (incomplete empting, frequency, intermittency, urgency, weak stream, straining, and nocturia) and two questions related to quality of life. Symptom intensity was categorized as mild (score 0−7), moderate (score 8−19), or severe (score 20−35). The ICS and IIEF-5 assess urinary continence and sexual function, respectively. Inclusion criteria comprised FBT as primary treatment for PCa and complete followup with completed IPSS questionnaires within 24 months after treatment. Patients who had FBT at both the apex and the base of the prostate were excluded.

Questionnaire scores of patients who had FBT at the apex or the base of the prostate were compared. Patients with FBT target comprising both the apex and middle prostate were classified as the apex group. Patients with FBT target comprising both the base and middle prostate were classified as the base group (Fig. 1). The primary end point was worse urinary symptoms, as measured by the IPSS. Secondary end points were worse continence and erectile function, as measured by ICS score and IIEF-5, respectively.

Statistical analysis was performed using Stata 13.0 (StataCorp, College Station, TX). Demographic characteristics are shown as simple frequencies. The χ^2 test was used to compare categorical variables. The questionnaires scores were compared using the Student's t test. A multivariate analysis was performed to analyze risk factors associated with an IPSS $\geq$ 8 at 6 and 12 months after FBT. The forward selection model was used to estimate risk using odds ratios. A p-value < 0.05 was statistically significant.

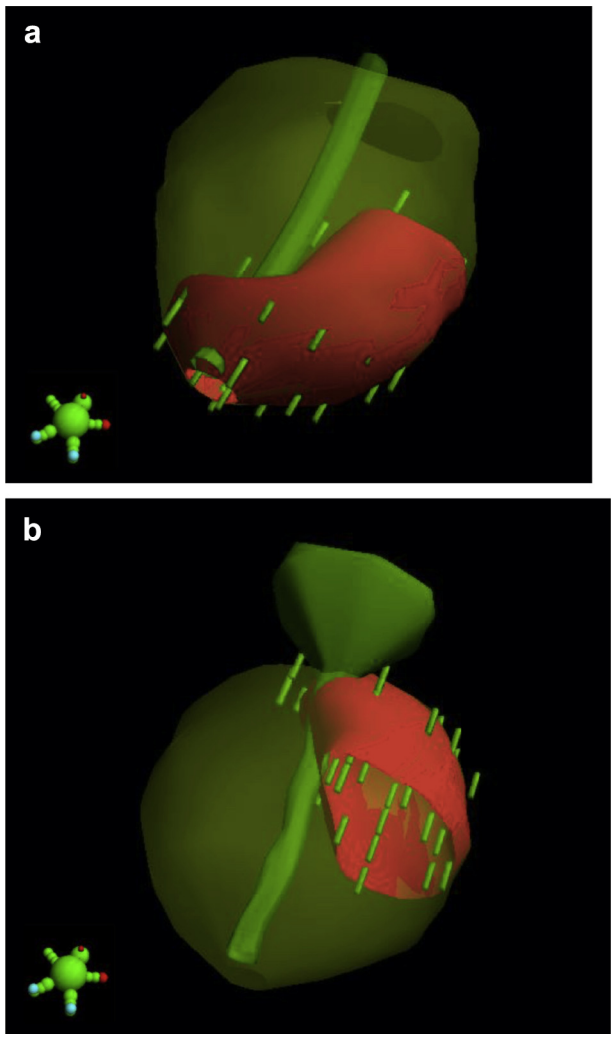

Fig. 1. (a) Focal brachytherapy of the left apex (treated volume in red and implanted seeds in green). (b) Focal brachytherapy of the left base (treated volume in red and implanted seeds in green). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)