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Institutional long-term outcomes at the first Canadian center performing intraoperatively planned low-dose-rate brachytherapy alone in low- and intermediate-risk prostate cancer

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ABSTRACT

PURPOSE: The aim of this study is to report the long-term outcomes and toxicities from a large cohort of patients with localized prostate cancer treated with low-dose-rate intraoperatively planned brachytherapy.

METHODS AND MATERIALS: Prostate-specific antigen levels, urinary symptoms, and erectile function were recorded at baseline, and each followup visit was then entered into a prospective database. Urinary toxicity requiring procedural intervention was retrospectively verified using an integrated electronic medical system. A separate cross-sectional survey was performed to measure postimplant sexual function.

RESULTS: A total of 822 patients with low and favorable intermediate-risk prostate cancer were treated at our institution between 2003 and 2013. The Kaplan−Meier estimates for biochemical recurrence for our cohort were 95% and 87% at 5 and 10 years, respectively. Cystoscopy, transurethral resection of prostate, or dilatation was required for 7.1% of 720 patients with more than 2 years of followup. At a median followup of 3.7 years, 64.4% of patients retained adequate erectile function for intercourse, with 54% of patients who were no longer sexually active postimplant reporting social factors as the primary reason.

CONCLUSIONS: Our institutional experience with intraoperative low-dose-rate prostate brachytherapy yielded excellent long-term results with a low incidence of urinary and sexual toxicity.

Keywords: Prostate neoplasm; Brachytherapy; Intraoperative; Biochemical recurrence; Erectile function

Introduction

Multiple series have demonstrated the efficacy of brachytherapy in treating localized prostate cancer with excellent long-term outcomes (1−7). Many centers use a preplanned template-based approach that was first introduced in the 1980s and first adopted in North America by Blasko *et al.* (8) in Seattle. This approach involves a two-stage procedure including a transrectal ultrasound (TRUS)−based planning study to capture images of the prostate from which an individualized treatment plan is generated and a separate TRUS-based delivery. To deliver the planned treatment accurately, the patient's position must be identical to the initial TRUS study. Achieving this can be difficult as the patient may be awake for the initial TRUS but under anesthetic for the implant procedure, which causes relaxation of the pelvic floor musculature (9). Prostate size and shape can also change in the interim for patients on antiandrogen therapy (9). Any deviation

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from the original plan requires intraoperative modification (e.g., additional seeds and changes in seed position within the template) without immediate feedback on the impact on the overall dosimetry (9).

Intraoperative planning occurs at the time of the implant using a real-time image of the prostate. Our center was one of the first to use this technique in North America. An advantage of this approach is that the prostate is in the same position during planning and implantation (9). A patient can be treated in a single visit, which is more convenient particularly for those traveling long distances. The urethra and rectum are also visualized in real time to more accurately spare these organs at risk. Needle tracking and automated seed deployment further increase the accuracy in seed position (10). The proposed advantages of the intraoperative planning compared with the preplanned technique have been debated (11, 12). There are few published reports on long-term clinical results using an intraoperative planning system. This is a report of long-term biochemical relapse−free survival (bRFS) and toxicity for patients with low and low-tier intermediate-risk prostate cancer (IRPCa) treated with low-dose-rate intraoperatively planned prostate brachytherapy (LDR-IOBT).

Methods and materials

Patient selection

Patients were treated between May 2003 and December 2013. From 2003 to 2005, only patients with low-risk prostate cancer (prostate-specific antigen [PSA] <10 ng/mL, Gleason ≤6, and clinical stage ≤T2a) were eligible. After 2005, select patients with a single intermediate-risk factor (PSA, 10−20, Gleason 7, or clinical stage T2b−T2c) were offered treatment. The prostate gland size was first assessed on TRUS at time of biopsy and reassessed by CT or ultrasound, and if greater than 50 cc, patients received a minimum of 3 months of androgen deprivation therapy (ADT) before implant.

Treatment

Patients were planned and treated with an intraoperative technique using the Nucletron SPOT system (Elekta, Inc., Stockholm, Sweden) for planning inside the operating room (OR) and the FIRST system (Elekta, Inc., Stockholm, Sweden) for remote seed delivery. Full details of intraoperative planning techniques have been described elsewhere (10, 13). In brief, each patient was prepared and draped in the lithotomy position under anesthesia. A motorized TRUS probe was used to generate a three-dimensional reconstructed image. Contours of the prostate gland, urethra, and anterior rectal wall were done at the computer console in the OR on the sagittal views and confirmed on axial and coronal reconstructions of the prostate. The base of the seminal vesicles was included in the prostate contour for patients with intermediate-risk disease as long as dosimetric limits for organs at risk were met. In all cases, the treatment volume to which the 100% isodose was prescribed was defined as the prostate contour plus a 5-mm margin in all directions except posteriorly where a maximum 3-mm margin trimmed to rectum was used. The dose constraints used to guide prostate brachytherapy planning were as follows: prescribed dose to target 144 Gy, prostate D_{90} (dose received by 90% of the prostate) 180−200 Gy, prostate V_{100} (volume of the prostate contour receiving 100% of the prescribed dose) >96%, prostate V_{150} 74−85%, and prostate V_{200} 37−48%; urethral V_{140} <24%, urethral V_{150} <3%, and urethral V_{160} <1%; and rectal V_{100} <0.3 cc. Before 2005 (83 cases), forward planning was used exclusively to generate plans that met the dose constraints mentioned previously. These constraints were chosen based on a trend in intraoperatively planned prostate brachytherapy of dose loss when intraoperative plans are compared with Day 30 dosimetry (14). This trend is particularly apparent when prostate swelling occurs (14). After 2005 (740 cases), inverse planning using SPOT PRO v3 (Elekta, Inc., Stockholm, Sweden) was used to generate a preliminary plan, which met the predefined dose constraints (15, 16). Although these plans would provide adequate D_{90} coverage, the dose distribution in some cases was considered inferior by the treating radiation oncologist. Hence, the plans were reviewed jointly by the treating physician and planner, and then modified to either reduce the number of needles delivering a single seed or further distribute dose according to the treating physician's personal preferences provided the aforementioned constraints were still met. In all cases, our center's practice has been used to ensure that areas of the prostate with biopsy-proven disease do not receive dose less than 190 Gy. Seed activity was 0.439 U for prostate size < 30 cc and 0.555 U for >30 cc. This practice was built on experience, and it allowed faster planning in the OR and more flexibility to manually sculpt dose with the increased number of seeds. Overall total activity implanted was proportional to gland volume as seen in Supplementary Fig. 1.

Needles were placed using a template-based system with a computer-guided technique in the sagittal view plane. Needles were implanted one by one and connected to the remote delivery system systematically using an ultrasound-based guidance system.

Followup

All patients had a postimplant CT scan at 4 weeks. The American Urology Association symptom scores, PSA, and erectile function were recorded at baseline and at each followup appointment (every 3 months for the first 2 years, then every 6 months from years 2 to 5, then annually). Before implant, each patient signed an institutional research ethics board−approved consent for personal information to be used for research purposes, and these data were entered into a prospective database. In followup, patients who had biochemical relapse were re-evaluated with