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Long-term outcome of magnetic resonance spectroscopic image–directed dose escalation for prostate brachytherapy

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ABSTRACT

PURPOSE: To report the long-term control and toxicity outcomes of patients with clinically localized prostate cancer, who underwent low-dose-rate prostate brachytherapy with magnetic resonance spectroscopic image (MRSI)–directed dose escalation to intraprostatic regions.

METHODS AND MATERIALS: Forty-seven consecutive patients between May 2000 and December 2003 were analyzed retrospectively. Each patient underwent a preprocedural MRSI, and MRS-positive voxels suspicious for malignancy were identified. Intraoperative planning was used to determine the optimal seed distribution to deliver a standard prescription dose to the entire prostate, while escalating the dose to MRS-positive voxels to 150% of prescription. Each patient underwent transperineal implantation of radioactive seeds followed by same-day CT for postimplant dosimetry.

RESULTS: The median prostate D_{90} (minimum dose received by 90% of the prostate) was 125.7% (interquartile range [IQR], 110.3–136.5%) of prescription. The median value for the MRS-positive mean dose was 229.9% (IQR, 200.0–251.9%). Median urethra D_{30} and rectal D_{30} values were 142.2% (137.5–168.2%) and 56.1% (40.1–63.4%), respectively. Median followup was 86.4 months (IQR, 49.8–117.6). The 10-year actuarial prostate-specific antigen relapse–free survival was 98% (95% confidence interval, 93–100%). Five patients (11%) experienced late Grade 3 urinary toxicity (e.g., urethral stricture), which improved after operative intervention. Four of these patients had dose-escalated voxels less than 1.0 cm from the urethra.

CONCLUSIONS: Low-dose-rate brachytherapy with MRSI-directed dose escalation to suspicious intraprostatic regions exhibits excellent long-term biochemical control. Patients with dose-escalated voxels close to the urethra were at higher risk of late urinary stricture.

Keywords: MR spectroscopy; Prostate; Brachytherapy; Dose escalation

Introduction

Dose escalation is a critical component in radiation therapy (RT) for prostate cancer. Randomized controlled trials (1, 2) and institutional series (3) have demonstrated a benefit in prostate-specific antigen (PSA) relapse–free survival for patients who underwent dose escalation during external beam RT. Institutional series have also suggested the existence of a dose–response relationship for low-dose-rate (LDR) brachytherapy (4–6). In addition, higher radiation doses have been associated with lower positive biopsy rates along with improved clinical outcomes for patients with negative biopsies after both external beam

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RT (7) and brachytherapy (8). However, dose escalation to the entire prostate gland can result in increased gastrointestinal and genitourinary toxicity (1).

Studies have shown that prostate cancer often recurs at the original site after RT (9, 10). As a result, investigators have been interested in developing methods for escalating radiation dose to intraprostatic regions, while both maintaining coverage of the entire prostate gland and respecting normal tissue dose constraints. This form of dose escalation would in theory lead to improved clinical outcomes without higher toxicity rates. However, intraprostatic dose escalation requires advanced imaging capabilities, which can detect intraprostatic tumor deposits with acceptable sensitivity and specificity. Furthermore, highly conformal RT techniques are needed for safe and effective treatment delivery.

In this report, we summarize our institutional experience with intraprostatic dose escalation using LDR brachytherapy and magnetic resonance spectroscopic imaging (MRSI). We used LDR brachytherapy with real-time ultrasound-based intraoperative treatment planning (11, 12) because this modality allows for highly conformal dose escalation to intraprostatic regions. We incorporated preoperative MRSI into treatment planning because this modality can identify regions suspicious for intraprostatic tumor deposits based on elevated choline plus creatine-to-citrate ratios (13, 14). We had previously explored the feasibility of generating MRS-optimized dose distributions for permanent prostate implants (15). We now present our long-term clinical outcomes for patients treated with this technique.

Table 1
Baseline clinical characteristics

Characteristics	Total, n (%)
Age	
Median (IQR)	66 (59−69)
Clinical stage	
T1c	33 (70)
T2a	12 (26)
T2b	2 (4)
Gleason score	
6 (3 + 3)	39 (83)
7 (3 + 4)	7 (15)
7 (4 + 3)	1 (2)
Pretreatment PSA	
Median (IQR)	5.1 (3.8−7.0)
NCCN risk	
Low	35 (74)
Intermediate	12 (26)
Pretreatment MRI	
Organ confined	39 (83)
Suspicious ECE	7 (15)
Definite ECE	1 (2)
Pretreatment MRI prostate volume (cc)	
Median (IQR)	26.0 (21.0−36.5)
Baseline IPSS (n = 24)	
Median (IQR)	6 (4−9)
Neoadjuvant ADT	8 (17)
Isotope used	
^{125}I (definitive, 144 Gy)	45 (96)
^{125}I (boost, 110 Gy) + EBRT (50.4 Gy)	1 (2)
^{103}Pd (definitive, 140 Gy)	1 (2)
Followup, mo	
Median (IQR)	86.4 (49.8−117.6)

ADT = androgen-deprivation therapy; ECE = extracapsular extension; EBRT = external beam radiation therapy; IQR = interquartile range; NCCN = National Comprehensive Cancer Network; PSA = prostate-specific antigen.

Methods and materials

Patient population

Forty-seven patients with clinically localized prostate cancer, who underwent LDR brachytherapy with MRSI-directed dose escalation between May 2000 and December 2003, were included in this retrospective analysis. As shown in Table 1, 35 patients (74%) had National Cancer Center Network low-risk disease (T1-T2a, Gleason 6, and PSA <10 ng/mL). The remaining 12 patients (26%) had intermediate-risk disease (T2b-T2c, Gleason 7, or PSA 10−20 ng/mL). Clinical T-stage was defined by digital rectal examination. The numbers of patients with suspicious and definite radiographic extracapsular extension, as assessed by MRI, were 7 (15%) and 1, respectively. The median International Prostate Symptom Score, which was available for 24 patients, was 6. The median pretreatment prostate volume, as assessed by MRI, was 26.0 cc among all patients. Eight patients received neoadjuvant androgen-deprivation therapy (ADT), primarily for cytoreduction, and MRI was obtained before ADT in six of these patients. With respect to brachytherapy, 45 patients received ^{125}I monotherapy with a prescription dose of 144 Gy. One patient underwent an ^{125}I boost to 110 Gy followed by 50.4 Gy external beam RT due to concern for suspicious extracapsular extension on MRI. This patient had also received neoadjuvant ADT. Another patient received ^{103}Pd monotherapy to 140 Gy.

MRSI imaging

Before the procedure, all patients were scanned on a General Electric Signa 1.5 T MR scanner with an endorectal radiofrequency probe inflated with 100 cc of air. Acquired sequences included T1-weighted images and T2-weighted axial images. Spectroscopic analysis was conducted on T2-weighted sequences using 0.12 cc (0.625 cm × 0.625 cm × 0.30 cm) voxels over a 50-mm field of view. Peak areas of choline, creatine, and citrate were then calculated on an offline workstation, and MRS-positive voxels that were suspicious for malignancy based on choline plus creatine-to-citrate ratios were identified based on previously established criteria (14, 16).

LDR brachytherapy with MRSI-directed dose escalation

The LDR brachytherapy and intraoperative planning technique have been previously described (15). Briefly,