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High-dose-rate brachytherapy with or without intensity modulated radiation therapy as salvage treatment for an isolated, gross local recurrence of prostate cancer post-prostatectomy

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ABSTRACT

PURPOSE: To evaluate the use of high-dose-rate (HDR) brachytherapy \pm intensity modulated radiation therapy (IMRT) as salvage therapy for patients with an isolated, gross local recurrence of prostate cancer after radical prostatectomy.

METHODS AND MATERIALS: Between October 2009 and May 2013, the authors treated six patients with salvage iridium-192 HDR brachytherapy ± IMRT for biopsy-proven, recurrent prostate cancer post-prostatectomy. In each patient, a pelvic MRI scan or CT scan demonstrated a nodule (range 1.6, 4.7 cm) in the prostate bed. Although prostate-specific antigen values were 0.2–9.5 ng/mL at the time of salvage brachytherapy, there was no pelvic adenopathy on CT or MRI scan, and a bone scan was negative in all cases. Five patients were treated with IMRT to 4500–5040 cGy in 25–28 fractions to the prostate bed followed by two 950 cGy HDR brachytherapy fractions separated by 1–2 weeks. A sixth patient underwent HDR brachytherapy monotherapy consisting of 3800 cGy in four fractions over 3 days. Toxicities were graded according to the Common Terminology Criteria for Adverse Events, version 4.0.

RESULTS: Median followup was 9 months (range 3, 40 months). All six patients have been free of androgen deprivation therapy and have an undetectable prostate-specific antigen. One patient developed late Grade 2 urinary incontinence. There was no late grade ≥ 2 gastrointestinal toxicity. **CONCLUSIONS:** HDR brachytherapy \pm IMRT is a safe and effective salvage therapy option for an isolated, gross local recurrence of prostate cancer after radical prostatectomy and merits further study. © 2014 Published by Elsevier Inc on behalf of American Brachytherapy Society.

invasion (3).

Keywords:

Iridium; Brachytherapy; Salvage therapy; Prostatic neoplasms; HDR; Prostatectomy

Introduction

Adverse pathologic findings at the time of radical prostatectomy include positive surgical margins, extraprostatic extension, or seminal vesicle invasion (1). In a large, community-based series of men in the United States undergoing radical prostatectomy, about one-third of prostate cancer patients had positive surgical margins (2). Also, approximately 35% of prostate cancer patients undergoing radical prostatectomy in the United States

According to the National Comprehensive Cancer Network, treatment options for an isolated local recurrence of prostate cancer after radical prostatectomy are radiation therapy \pm neoadjuvant/concomitant/adjuvant androgen deprivation therapy (ADT) vs. observation (8). Radiation therapy without ADT is the most common salvage therapy for a local recurrence of prostate cancer after radical prostatectomy (9). The American Urological Association

have extraprostatic extension and 9% have seminal vesicle

cancer patients is predominantly local (4). Radiation

therapy to the prostate bed reduces the risk of metastatic

The pattern of treatment failure in high-risk prostate

disease and biochemical failure (5–7). As a result, Swanson *et al.* (4) have suggested that improvements in local control are likely to have the greatest impact on outcome in prostate cancer patients with adverse pathologic features.

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Table 1 Salvage high-dose-rate brachytherapy patient characteristics

Patient#	PSA (ng/mL)	Lesion size (cm)	Imaging	Prostatectomy to HDR (mo)	ADT initiation to HDR (mo)	ADT effect (mo)	ADT following HDR (mo)	HDR dose (cGy)	IMRT dose (Gy)
1	0.2	1.6	MRI	156	5	3 then discontinued	0	950 × 2	50.4
2	9.5	4.1	MRI	90	None	None	0	950×2	50.4
3	3.5	1.6	MRI	113	None	None	0	950×2	50.4
4	2.3	4.7	MRI	116	89	48 then resistance, continued for 41	3	950 × 4	None
5	0.6	2.6	MRI	25	1	18 then discontinued	18	950×2	50.4
6	1.6	2	CT	194	144	132 then resistance and discontinued	0	950 × 2	45

PSA = prostatic-specific antigen; HDR = high-dose-rate; ADT = androgen deprivation therapy; IMRT = intensity modulated radiation therapy.

(AUA) and American Society for Radiation Oncology guidelines for salvage treatment of recurrent prostate cancer suggest that physicians "should offer salvage radiotherapy to patients with prostatic-specific antigen (PSA) or local recurrence after prostatectomy in whom there is no evidence of distant metastatic disease (10)."

In this study, the authors hypothesized that high-dose-rate (HDR) brachytherapy \pm intensity modulated radiation therapy (IMRT) could be used to safely deliver dose-escalated radiotherapy to patients with an isolated, gross local recurrence of prostate cancer after radical prostatectomy.

Methods and materials

Patient characteristics

After obtaining investigational review board approval, the authors reviewed electronic medical records on six patients with an isolated local recurrence of prostate cancer post-prostatectomy who were treated with salvage HDR brachytherapy \pm IMRT between October 2009 and May 2013. The following AUA definition of recurrent prostate cancer in the post-prostatectomy setting was used: a serum PSA level of \geq 0.2 ng/mL, with a second confirmatory PSA level of >0.2 ng/mL (11).

All patients initially underwent radical prostatectomy with negative margins. One patient had extraprostatic extension and a second patient had seminal vesicle invasion. Two patients had a PSA level that remained detectable (0.6–2.1 ng/mL) 4–6 weeks post-prostatectomy.

Patient characteristics are shown in Table 1. The median PSA value was 2.0 ng/mL (range 0.2, 9.5 ng/mL) at the time of salvage HDR brachytherapy. The median time from radical prostatectomy to salvage HDR brachytherapy was 114 months (range 25, 194 months). Four of six patients were treated with ADT before salvage HDR brachytherapy (range 1, 144 months before HDR) and two patients (#4 and #5) continued ADT during salvage HDR. Two patients were castrate-resistant, with a period of 4 and 11 years from ADT initiation to castrate resistance (#4 and #6, respectively); Patient #4 continued ADT for nearly 4 years following castrate resistance with an increasing PSA and then discontinued ADT 3 months following salvage HDR,

whereas Patient #6 discontinued ADT 1 year before salvage HDR. Two additional patients (#5 and #1) were placed on ADT at 1 and 5 months before salvage treatment, respectively; Patient #5 continued ADT for 18 months following HDR with 24 months of additional followup after discontinuing ADT, and Patient #1 had a single 3-month ADT treatment 5 months before salvage HDR, with his PSA responding to 0.2 ng/mL before initiating salvage treatment. All four patients treated with ADT had at least 6 months of followup from the last ADT treatment. A pelvic MRI (n = 5) or CT scan (n = 1) demonstrated a 1.6-4.7 cm (median, 2.3 cm) mass in the prostate bed in all cases. Following suspicious imaging findings, all recurrences were biopsied with pathologic confirmation of adenocarcinoma before salvage therapy. Although PSA values ranged from 0.6 to 9.5 ng/mL at the time of salvage HDR brachytherapy, there was no pelvic adenopathy on MRI or CT scan and a bone scan was negative in all cases. Five patients were treated with IMRT to 4500-5040 cGy in 25–28 fractions to the prostate bed using the European Organization for Research and Treatment of Cancer guidelines for target volume definitions (12) followed by two 950 cGy HDR brachytherapy fractions separated by 1-2 weeks. Another patient (#4) with a palpable, castrateresistant recurrence following post-prostatectomy external beam radiation therapy (EBRT) to 7000 cGy in 35 daily fractions in combination with ADT 8 years earlier underwent salvage HDR brachytherapy monotherapy consisting of 3800 cGy delivered in four fractions over 3 days with a single implant. Urinary symptoms at baseline and at last followup were assessed by a self-administered AUA Symptom Score (AUASS). Urinary and rectal toxicities were graded according to the Common Terminology Criteria for Adverse Events, version 4.0.

Prostate fiducial marker placement and HDR brachytherapy technique

Before initiation of EBRT, all patients underwent transrectal ultrasound (TRUS) guide placement of four fiducial markers in and around their nodular prostate bed recurrence. This was done with patients in the left lateral decubitus position using a transrectal approach without sedation. The fiducial markers made it possible to determine the

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