

Prostate

# Salvage external beam radiotherapy for locally recurrent prostate cancer after definitive brachytherapy

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## ABSTRACT

**PURPOSE:** Patients with locally recurrent prostate cancer after definitive prostate brachytherapy have few evidence-based salvage options. We evaluate the efficacy and treatment-related side-effects of salvage external-beam radiotherapy (EBRT) after definitive prostate brachytherapy (PBT). **METHODS AND MATERIALS:** Eleven patients previously treated with definitive PBT and with biopsy-proven local-only recurrence received salvage reirradiation with EBRT. Genitourinary (GU) function was assessed with International Prostate Symptom Scores. Treatment-related toxicities were graded using CTCAE v 4.03.

**RESULTS:** Median follow-up was 26.5 months (range, 1–53.6 months); median age at EBRT salvage was 67 years (range, 61–81 years). Salvage EBRT included the whole pelvis in 8 patients. Two patients were treated with 3D-CRT; 9 underwent IMRT. Five patients (45%) received androgen deprivation therapy concurrent with salvage EBRT as part of long- or short-course hormone therapy. The median prostate dose was 70.2 Gy (range, 64.8–75.6 Gy). Actuarial 3-year overall and biochemical failure-free survival were 77% and 69%, respectively. Five patients (45%) had worsening GU symptoms, and 9 (82%) experienced a decline in erectile function. One patient experienced acute grade 2 GU toxicity. Four patients (36%) experienced late grade  $\geq 2$  GI/GU toxicities, including 2 who experienced grade 3 toxicities (rectourethral fistula/incontinence, bladder outlet obstruction). No grade 4/5 toxicities were noted.

**CONCLUSIONS:** Our data suggest that salvage EBRT can provide similar disease control and treatment-related toxicity to more established salvage therapies. This approach warrants further investigation on a larger scale. © 2016 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

## Keywords:

Salvage external beam radiotherapy; Reirradiation; Prostate brachytherapy

## Introduction

Prostate cancer is the most common noncutaneous malignancy affecting men, with an incidence of more than 220,000 cases annually in the United States (1). It is estimated that only 4% of those diagnosed have metastatic disease; therefore, most men undergo curative treatment, with a large number treated with definitive radiotherapy (2). In studies using the

Cancer of the Prostate Strategic Urologic Research Endeavor database, nearly one-fourth of men diagnosed with localized prostate cancer elected to undergo radiotherapy (either external beam radiotherapy [EBRT] or brachytherapy) (3, 4). Approximately 15% of low-/intermediate-risk and as many as 75% of high-risk prostate cancer patients will experience biochemical recurrence after definitive

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Table 1  
Patient and initial treatment characteristics

Patient no.	Age at initial BT (y)	Initial cT stage	Initial PSA	Initial GS	Initial risk category	Initial tx (dose)	Time to BF (mo)	Age at salvage EBRT (y)
1	65	T1c	9.8	5 (2 + 3)	Low	<sup>125</sup> I (144 Gy)	31	73
2	59	T1c	4.98	6	Low	<sup>125</sup> I (145 Gy)	18	61
3	60	T1c	3	6	Low	<sup>125</sup> I (145 Gy)	55	65
4	59	T1c	5.3	6	Low	<sup>125</sup> I (NA)	45	67
5	56	T1c	7.39	6	Low	<sup>125</sup> I (145 Gy)	97	65
6	65	T2a	4.9	6	Low	<sup>125</sup> I (144 Gy)	72	72
7	58	T2c	7.3	6	High	<sup>125</sup> I (145 Gy)	136	71
8	69	T2a	4.5	7 (4 + 3)	Intermediate	<sup>125</sup> I (144 Gy)	42	73
9	69	T1c	6.2	6	Low	<sup>125</sup> I (145 Gy)	79	81
10	56	T1c	8.1	7 (3 + 4)	Intermediate	<sup>125</sup> I (NA)	13	62
11	57	T1c	6.5	6	Low	<sup>125</sup> I (145 Gy)	49	62

BT = brachytherapy; cT = clinical T stage; PSA = prostate-specific antigen; GS = Gleason score; tx = therapeutic; BF = biochemical failure (Phoenix definition); EBRT = external beam radiotherapy; <sup>125</sup>I = iodine-125; NA = data not available.

radiotherapy (5). Most recurrences after definitive radiotherapy occur within 5 years of treatment; however, recurrences are seen 10 years after treatment and beyond (6, 7). Approximately one-quarter of patients with biochemical recurrence will have local clinical disease progression within 5 years, whereas half of the patients will have distant metastatic recurrence (8). It has been estimated that more than 30,000 men will develop biochemical recurrence after definitive primary radiotherapy, among whom ~25% will have biopsy-proven local-only disease (9).

After a negative metastatic workup and biopsy confirmation of local disease recurrence, patients have several options for aggressive local salvage therapy, including radical prostatectomy (RP), reirradiation, cryotherapy, and high-intensity focused ultrasound. Each comes with significant risk of side effects (5, 10, 11). Other management options include observation and androgen deprivation therapy (ADT). The option for salvage reirradiation has been limited to patients initially treated with EBRT salvaged with prostate brachytherapy (PBT). Several single-institution series describe the outcomes of salvage brachytherapy after EBRT, and recently the Radiation Therapy Oncology Group (RTOG)/NRG Oncology protocol investigated PBT for salvage reirradiation in a multiinstitutional cooperative group setting (RTOG 0526).

For patients with local prostate cancer recurrence after initial brachytherapy, however, salvage reirradiation has not been widely used. In the present study, we describe patients treated with salvage reirradiation using EBRT following recurrence after definitive PBT. We evaluate survival and disease control outcomes and treatment-related side effects.

## Methods and materials

### Patient characteristics

This is an institutional review board–approved retrospective study that included 11 consecutive patients treated from 2000 to 2013 with salvage EBRT after initial treatment for localized prostate cancer with low-dose-rate

(LDR) brachytherapy. All patients had biopsy-proven local recurrence with negative staging studies for distant metastatic disease. Table 1 includes patient characteristics and details of initial therapy. Initial diagnoses included low-risk ( $n = 8$ ), intermediate-risk (as a result of small-volume Gleason score [GS] 7 disease [GS 3 + 4 and GS 4 + 3]) ( $n = 2$ ), and high-risk (GS 6, prostate-specific antigen [PSA] 7.3, cT2c) ( $n = 1$ ) prostate cancer. Before salvage therapy, all patients underwent metastatic workup, including PSA measurement, chest/abdomen/pelvis CT, and bone scan. Median time to failure after initial brachytherapy (Phoenix definition) was 49.2 months (range, 12.9–135.5). Median PSA before salvage EBRT was 4.7 ng/mL (range, 3.6–15.3). Median age at time of salvage treatment was 67 years (range, 61–81). Nine of 10 patients with GS available at time of recurrence had an increase in GS compared with their original diagnoses. For 1 patient, the GS remained the same (GS 7, 4 + 3), and in another patient, the GS was indeterminate because of the radiation treatment effect from initial brachytherapy.

### Treatment characteristics

LDR iodine-125 (<sup>125</sup>I) brachytherapy was the initial treatment for 11 patients. The initial brachytherapy dose was 145 Gy for 6, 144 Gy for 3, and unavailable for 2 patients (Table 1). LDR brachytherapy treatment planning was generally consistent with our institutional guidelines as follows: patients received intraoperatively planned LDR brachytherapy using nonstranded <sup>125</sup>I using the Mick applicator (Mick RadioNuclear Instruments, Inc., Mount Vernon, NY). The prostate was defined using transrectal ultrasound, and a planning target volume was generated using the prostate plus a 3-mm isotropic expansion (no expansion posteriorly). Dosimetric goals were  $V_{100} > 90\%$  and  $D_{90} > 90\%$  at the minimum. Table 2 details patient and treatment characteristics at the time of EBRT salvage. Median total salvage dose for EBRT was 70.2 Gy (range, 64.8–75.6). Salvage EBRT included the whole pelvis in 8, prostate and proximal seminal vesicles in 1, and prostate

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