

Salvage brachytherapy for recurrent prostate cancer

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ABSTRACT

PURPOSE: To evaluate the role of salvage prostate brachytherapy for locally recurrent prostate cancer after external beam radiation alone.

METHODS AND MATERIALS: Sixty-nine consecutive patients treated with salvage brachytherapy after a local failure were analyzed. All patients were found to have pathologic proven recurrent prostate cancer at least 2 years after initial therapy and no regional or distant disease on imaging studies. Pd-103 was used with a prescribed pD_{90} of 100 Gy. In total, 89.9% of patients received androgen suppression (AS) as part of their salvage therapy. Patients whose prostate-specific antigen >5.0 ng/mL while on AS were considered to have castration resistant prostate cancer (CRPC). Patients on AS >6 months before salvage brachytherapy were considered to have delayed therapy. Patients retreated within 5 years after their initial treatment were considered to have early failures.

RESULTS: Total median followup after salvage therapy was 5.0 years (0.6–13.7). From the date of salvage, 5-year biochemical control for low-risk patients was 85.6%, intermediate-risk patients 74.8%, and high-risk patients 66%. Five-year biochemical control was 73.8% for non-CRPC and 22% for CRPC cases (<0.001). Including and excluding CRPC cases, early treatment after failure vs. delayed treatment was significantly better ($p < 0.05$). Chronic adverse events were seen in few patients, with genitourinary Grade 3 toxicity of 8.7% and no genitourinary Grade 4 or gastrointestinal Grade 3 or higher toxicities.

CONCLUSIONS: A subset of failures after definitive radiation is local in nature, and excellent control is possible with salvage brachytherapy. © 2014 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords:

Prostate cancer; Salvage therapy; Brachytherapy; Local failure; Outcome; Castration resistant; Biochemical control; Biochemical failure; Androgen suppression; Radiation therapy

Introduction

The management of patients with a rising prostate-specific antigen (PSA) after initial local management has been controversial. PSA failures may represent local or distant disease and androgen suppression (AS) is considered first line for its management (1). However, more recent studies have shown that after radical prostatectomy the predominant mode of failure is local, and localized radiation will dramatically change the natural history of the disease

(2). Published data showed improved outcomes, with a decrease in both distant metastasis and local failure after local adjuvant radiation (3–6).

Biochemical failures are the consequence of a localized or a distant prostate cancer failure. A proportion of biochemical failures may ultimately harbor residual localized cancer only. Furthermore, distant failures at least partially result from a second wave of metastatic disease from an initial local failure (7, 8). Therefore, isolated locally recurrent disease may benefit from local salvage therapy.

Salvage therapy for a biochemical failure after radiation is rarely performed. Few publications have explored the role of salvage brachytherapy for this subset of patients (9, 10). This series is the largest experience for salvage brachytherapy for prostate cancer patients and one of the largest series for salvage therapy (11, 12). Our manuscript helps explore

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the possibility of successful local salvage therapy for locally recurrent prostate cancer after definitive external beam radiation.

Methods and materials

Patient and treatment data were collected in our institutional review board–approved database. For this analysis, only patients treated for salvage for locally recurrent disease were selected ($n = 72$). Patients lost to followup ($n = 3$) were excluded. A total of 69 patients were available for review.

All patients treated had received external beam radiation therapy alone to a median dose of 68.4 Gy (63–77.4 Gy). The majority of these patients were treated with three-dimensional conformal radiation. However, eight cases were treated to doses of 77.4 Gy with intensity-modulated radiation therapy (IMRT) with or without image-guided radiation therapy (IGRT). We did not retreat patients treated previously with brachytherapy alone or combined with external beam. All patients required a positive prostate biopsy at least 2 years after the completion of external beam treatment. They were biopsied after a suspected local failure alone. This was defined by the American Society for Radiation Oncology definition or Phoenix definition. The median time to biopsy was 6.8 years (2.3–21 years). Digital rectal prostate findings remained the same with a persistent prostate abnormality in 27 of the 33 cases. Patients' initial characteristic and characteristics at the time of failure are seen in Table 1.

All patients were evaluated initially by a thorough history and physical examination (including digital rectal examination) followed by routine laboratory studies, including pelvic CT scans, bone scans, serum PSA levels, and Gleason score (GS). Prostate needle biopsies were done for all cases at least 2 years after the completion of definitive radiation. All patients were re-staged according to the American Joint Committee on Cancer staging system 7th edition.

Patients retreated within 5 years of initial definitive therapy are considered to have an early failure. Patients receiving AS for more than 6 months before salvage therapy are classified as having delayed therapy. Patients whose PSA was 5.0 ng/mL or higher while on AS were analyzed independently and considered to have castration resistant prostate cancer (CRPC) for the purpose of the analysis of this article. CRPC defines a continuous spectrum of disease on medical or surgical castration. CRPC can include a rising PSA alone to clinically progressive disease; a PSA >5.0 ng/mL on AS defined a subset within the overall population.

Treatment

All patients were implanted using palladium-103 and interactive ultrasound-guided transperineal technique described previously (13). Prescribed prostate D_{90} was 100 Gy. AS for at least 6 months was recommended for all cases starting

Table 1
Patient's characteristics

Characteristics	Initial	Salvage
Age (y)	63.9	72.5
Range	51–78	55–88
T-stage (%)		
T1	38.6	45.0
T2	55.7	50.8
T3	5.7	4.2
PSA (ng/mL) (%)		
<10	62.0	84.5
10–20	24.0	12.7
>20	14.0	2.8
Gleason score (%)		
≤6	50.7	32.4
7	29.6	40.9
8–10	19.7	26.8
Median	6	7
PNI (%)		8.5
Androgen suppression (%)	32.4	89
Median (y)		1.38
Range (y)		0.3–12.3
FU (y) median		
Median (y)	12.51	5.02
Range (y)	3.5–23.5	0.6–13.7

PSA = prostate-specific antigen; PNI = perineural invasion; FU = followup.

2 months before salvage radiation. Intraoperative and postoperative doses can be seen in Table 2.

Data collection and review

An ongoing prostate database has been available at our institution for the last 15 years; first salvage case was treated in January 1989 and the last case in September 2011. Information for salvage cases was prospectively collected in the database with additional fields added for these patients exclusively. Any adverse event (AE) found was recorded and defined in the database. For purpose of this review, the radiation oncology charts and urology charts were available for all cases and reviewed and compared with the information available in the database. Each chart was re-reviewed by the treating radiation oncologists, and special attention

Table 2
Intraoperative and postoperative pd-103 brachytherapy doses

Intraoperative doses			Postoperative doses		
IOP pD ₉₀ (Gy)	Minimum	79.95	POP pD ₉₀ (Gy)	Minimum	74.63
	Maximum	133.83		Maximum	124.54
	Median	108		Median	99.7
IOP UV 150 (cc)	Minimum	0	POP UV 150 (cc)	Minimum	0
	Maximum	0.42		Maximum	0.42
	Median	0		Median	0
IOP RV 100 (cc)	Minimum	0	POP RV 100 (cc)	Minimum	0
	Maximum	0.07		Maximum	0.59
	Median	0		Median	0

IOP Pd = intraoperative prostate dose; POP pD = postoperative prostate dose; IOP UV = intraoperative urethra volume; POP UV = postoperative urethra volume; IOP RV = intraoperative rectum volume; POP RV = postoperative rectum volume.

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