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Penile brachytherapy—Retrospective review of a single institution

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ABSTRACT

PURPOSE: To analyze the results of exclusive brachytherapy (BT) to treat patients with penile squamous cell carcinoma confined to the glans or prepuce.

METHODS AND MATERIALS: Retrospective analysis of 25 patients treated for T1–T2 penile cancer with exclusive interstitial BT between July 1989 and March 2014 at our institution.

RESULTS: Median followup was 9.2 years (range, 0–19). The mean patient age was 65.3 years (range, 51–80). Most patients underwent exclusive low-dose-rate BT (56%; $n = 14$) or pulsed-dose-rate BT (40%; $n = 10$). Only 1 patient received high-dose-rate BT (4%). The median prescribed dose was 60 Gy. Eight patients died during follow-up because of systemic progression (one case) and other intercurrent causes (seven cases). Two failures were recorded (one local and one regional), both at 4 months after BT. The remaining patients continued follow-up at our institution and maintained response. Two patients underwent partial phallectomy for toxicity. At the time of this report, 12 of the 25 patients are alive and free of disease. The most common late toxicities were telangiectasia, urethral stenosis, and atrophy, in 48%, 43%, and 17.4% of patients, respectively.

CONCLUSIONS: BT with low dose rate/pulsed dose rate provides excellent locoregional control for small (≤4 cm) T1–T2 squamous cell carcinoma of the penile glans.

Keywords: Penile cancer; Brachytherapy; Retrospective analysis

Introduction

Penile cancer (PC) is a rare tumor, accounting for about 1% of tumors in males and less than 0.5% of all cancers (1). The average age at diagnosis is 68 years, with an increased risk for males older than 50 years (2). PC occurs most frequently in uncircumcised men and is associated with risk factors, including phimosis, poor hygiene, and human papilloma virus type 16. Additional risk factors include balanitis, chronic inflammation, penile trauma, treatments with psoralen plus ultraviolet A, tobacco use, and lichen sclerosus (3). The most commonly affected areas are the glans, followed by the prepuce and penile shaft (2). Penile tumors generally present as palpable visible lesions, which may be associated with pain, discharge, or bleeding. The vast majority (95%) of PCs are squamous cell carcinomas (SCCs) and can either be exophytic (most of which are located in the glans and are well differentiated) or endophytic (tend to be located in the glans or prepuce and poorly differentiated). Metastatic spread occurs most commonly to the inguinal lymph nodes.

Because of the low incidence rate of PC, no prospective randomized trials have been performed to assess the available therapeutic options. Approaches to early stage noninvasive tumors include laser therapy, topical 5-fluorouracil, imiquimod, or local surgical resection. T1 tumors may be amenable to a partial glans-sparing penectomy, although larger tumors (≥T2) typically require total penectomy. Understandably, given the important functional loss and impotence associated with surgery, the psychological trauma of total or partial penectomy can be immense. For this reason, interest in alternatives is high (4–6).

Brachytherapy (BT) is an effective alternative to surgery for treatment for SCC–PC in early stage disease (T1–T2 N0 tumors located in the glans without extension to the

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balanopreputial sulcus). For eligible patients, BT is an attractive alternative to surgery because it allows for penile conservation, with survival outcomes that are similar to surgery (7).

According to the American Brachytherapy Society–Groupe Européen de Curitherapie–European Society of Therapeutic Radiation Oncology guidelines (8), low-dose-rate (LDR) and pulsed-dose-rate (PDR) iridium-192 (^{192}Ir) BT are the preferred BT modalities for treating PC. High-dose-rate (HDR) BT has also been used to treat PC, although only a few studies have been reported (9, 10). Although solid evidence exists to support the use of LDR and PDR BT for PC, only approximately 20 studies have been performed, and all but two of those included fewer than 80 patients (11).

Given the rarity of this disease and the relatively small number of published studies, it seems clear that more evidence would be useful to further confirm the reported benefits of BT in PC. Here, we report our single-institution experience with exclusive BT to treat 25 patients diagnosed with penile SCC confined to the glans or prepuce.

Methods and materials

We retrospectively analyzed all patients who underwent exclusive interstitial BT for PC between July 1989 and March 2014 at our institution. A total of 25 patients were identified and included in this study (Table 1).

Table 1
Patients and treatment characteristics

Patient	BT type	Treatment date	Dose (Gy)	Age
1	PDR	February 18, 2008	60	60
2	PDR	May 25, 2009	50	61
3	PDR	January 12, 2009	50	76
4	PDR	May 19, 2008	65	73
5	PDR	June 30, 2008	60	81
6	LDR	June 03, 2003	65	62
7	PDR	July 03, 2006	65	60
8	LDR	April 24, 2006	65	77
9	LDR	September 05, 2005	65	51
10	PDR	July 01, 2013	60	79
11	PDR	January 23, 2012	50.4	62
12	PDR	February 21, 2011	65	57
13	PDR	March 17, 2014	50	66
14	HDR	February 11, 2008	20	62
15	LDR	August 29, 2005	65	58
16	LDR	November 04, 1998	65	58
17	LDR	January 16, 1995	65	75
18	LDR	November 05, 1990	60	63
19	LDR	December 18, 1995	55	68
20	LDR	November 19, 1990	60	71
21	LDR	November 20, 1989	60	80
22	LDR	February 08, 1993	60	60
23	LDR	October 25, 1993	60	61
24	LDR	July 31, 1989	60	41
25	LDR	January 13, 1997	60	70

BT = brachytherapy; PDR = pulsed dose rate; LDR = low dose rate; HDR = high dose rate.

No patient presented nodal or metastatic disease. All patients were given detailed information regarding the treatment process and its advantages and disadvantages.

Description of implant technique

In all cases, treatment begins with circumcision, performed at least 15 days before the implant, to allow for optimal tumor assessment and better determination of target volume. The implant is performed under spinal or local anesthesia, and a Foley catheter is inserted to determine the urethral position and to avoid penetrating the urethra. The urinary catheter remains in place during the surgical procedure and for the duration of treatment. A physical examination is performed to assess the target volume (Fig. 1). After the gross tumor volume has been determined, a margin of 0.5–1 cm is added to create the clinical target volume.

In most cases, a Gerbaulet Glans Applicator is used (Fig. 2). The Gerbaulet Glans Applicator consists of two square plates of plastic, perforated by multiple holes separated at 1 cm intervals, which form squares and equilateral triangles. This applicator is modified for PDR treatments, and the holes are separated by 1.2 cm.

Next, the Paris system is used to determine the number of needles needed and their arrangement. The needles are inserted transverse to the penile axis, and their length will vary according to tumor size and penile thickness. After the needles are inserted, they are secured with buttons (Figs. 1 and 2). The patient is then transferred to the CT scanner for image acquisition. In some cases, especially in the early years of the study period, a theoretical dosimetry was used (i.e., the active and inactive distances of each needle were measured). For LDR BT (used at our institution until 2005), we used 65 Gy of LDR delivered via manually loaded ^{192}Ir wires in 5–6 days. The activity used was between 4 and 6 $\mu Gy/m^2.h.cm$, with an active length of 3.5–4 cm, and 6–8 needles in three or four planes. The dose rate was approximately 0.5–0.7 Gy/h between 92.8 and 119.1 h. For exclusive BT with PDR (LDR was replaced by PDR at our institution in 2006), most patients received approximately 16 Gy/d until the total prescribed dose (60–65 Gy) was reached (0.7 Gy/h). The dose is prescribed to the 85% isodose according to the Paris system.

The treatment takes place in an adapted bunker with the patient supine in bed. The length of each fraction varies according to the number of implanted vectors and the activity of the radioactive source at the time of treatment. The patients remain hospitalized under bed rest during the duration of the treatment period, although they can be disconnected between pulses to have a shower or to walk around the unit. After the final irradiation session, all the needles are removed, along with the urinary catheter.

Medication

Before the implant, all anticoagulant therapy is suspended, and anxiolytics are prescribed. During the implant,