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Short communication

Brachytherapy for conservative treatment of invasive penile carcinoma in older patients: Single institution experience

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ABSTRACT

Background: No study has examined the possibility to perform an organ sparing strategy in older patients with penile carcinoma, and amputation is frequently proposed. We report our experience of interstitial brachytherapy for the conservative treatment of penile carcinoma confined to the glans in patients aged of 70 years and more. **Methods:** A total of 55 patients candidates to conservative brachytherapy were identified. Median age was 73.8 years (range: 70–95 years). Patients underwent a circumcision then 3–4 weeks later, an interstitial brachytherapy was delivered, median dose of 65 Gy (range 55–74 Gy). Salvage surgery was discussed in patients with histological confirmation of residual/relapsed tumor.

Results: With median follow-up of 9.0 years, eight patients (14.5%) experienced a relapse, including five patients with local relapse. Three patients with local relapse only underwent salvage penile surgery, including two partial glansectomies and one total penectomy, and were in second complete remission at last follow-up. Among 55 patients analyzed for late side effects, seven patients (13.0%) presented pain or ulceration, 12 (22.2%) experienced urethral or meatal stenosis requiring at least one dilatation, two patients (3.7%) experienced both ulcerations and urethral complication. Three patients (5.5%) needed partial glansectomy for focal necrosis. At five years, estimated overall survival rate was 74.5% (95%CI: 62.0–87.0%) and local relapse free rate was 91.0% (95%CI: 82.6–99.4%). **Conclusion:** Brachytherapy is feasible in selected older patients with penile carcinoma, with efficacy and toxicity rates comparable to that of other series in younger patients.

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1. Introduction

Penile cancer is very rare entity (annual incidence rate of less than 1/100,000 in male European population) [1]. Most are squamous cell carcinoma, usually occurring in uncircumcised men and frequently associated with phimosis and with presence of human papillomavirus (HPV)-16. The incidence of penile cancer increases with age, with a peak incidence in men older than age 65 [1].

There is no randomized study to provide a high level of evidence on the optimal treatment in these patients, with only retrospective studies including usually few patients. Total amputation is frequently proposed as first intent treatment. Although radical surgery results in to high local control rates, the functional loss is major, associated with urinary

sequelae, and potentially a strong psychosexual impact. Therefore, alternative penile-sparing techniques have been proposed [2–4]. Interstitial brachytherapy delivers high irradiation doses directly inside the tumor, and its use has been associated with high probability of reaching complete remission while preserving the penis. Moreover, most local relapses can be salvaged by second-intent surgery [5–10]. However, no study has specifically examined the possibility to perform an organ sparing strategy in older patients, probably because it is frequently believed that those would be less interested in esthetic and preservation of function than their younger counterparts, although this assumption remains to be proven [5–10]. Older patients frequently present at an advanced stage of their disease, with a tumor that has been frequently neglected. Moreover, penile cancers occurring in older patients exhibit specific biological and histological features making it difficult to extrapolate data obtained in younger patients to the older population [11].

We report our institutional experience of interstitial brachytherapy for treatment of penile carcinoma confined to the glans or the prepuce in patients aged of 70 years and more. To our best knowledge, this is

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the first study examining the results of brachytherapy in this population. Patterns of relapse, toxicity rates, and prognostic factors were examined.

2. Materials and Methods

2.1. Patients and Tumors

We retrospectively examined clinical records of all consecutive patients treated by brachytherapy between March 1975 and June 2014 at our institution (Gustave Roussy, Villejuif, France) for a histologically confirmed invasive squamous cell carcinoma of the penile glans at age of 70 years or more. These patients were identified from a larger series of patients, all ages included, whose outcome was recently reported [10]. Patients with in situ carcinoma were excluded from analysis. A total of 55 patients were identified, including 11 patients aged 80 years or more. Median age at time of brachytherapy was 73.8 years (range: 70–95 years). Fifteen patients presented high blood pressure (36.4%), 8 (14.5%) had a history of cancer (rectal, cardia, prostate, head and neck (2), skin (3)), 7 (12.7%) patients had severe vascular diseases with 3 having a cardiac stroke history, 4 (7.3%) had arrhythmia, 4 (7.3%) had diabetes, and two patients had renal dysfunction.

The criterion for performing brachytherapy in these patients was that there was no tumor extension to the corpus cavernosum. A total of 55 patients fulfilled inclusion criteria for a conservative procedure and were examined for outcome. Eleven patients (20.0%) had been previously treated for a precancerous lesion of penile glans and nine patients (16.4%) had a history of phimosis. Median tumor largest diameter at time of brachytherapy was 20 mm (range: 5 to 50 mm).

After a comprehensive primary staging including clinical examination, computed Tomography, pelvis magnetic resonance imaging, 54 patients were staged clinically negative node involvement (cN0) status, including 12 patients who had a lymph node procedure confirming histologically negative inguinal lymph node status (pN0), and one (1.8%) patient had cytologically confirmed inguinal nodale metastases (pN+). He underwent a completing inguinal lymph node dissection.

Patients and primary tumors characteristics are provided in Table 1.

2.2. Treatment

If not done prior, a wide circumcision was routinely made three to four weeks prior to brachytherapy. The objective is to facilitate

brachytherapy and also to decrease its acute side effects. Brachytherapy was performed under general anesthesia as previously described [8,9]. Briefly, a urinary catheter was inserted to accurately determine the position of urethra and was kept during the brachytherapy process. The implantation of interstitial needles was done in order to appropriately cover the macroscopic tumor plus a 5–10 mm safety margin, according to the Paris system rules, as reported before [10]. The implant geometry was maintained using an applicator made of two perforated Plexiglas plates. A perforated sponge was used to keep the radioactive materials away from the testes (Fig. 1). Depending on the year of treatment, patients could receive either a low dose-rate (LDR) brachytherapy using iridium 192 wires delivering less than 10 Grays (Gy) per day or a pulse-dose rate (PDR) brachytherapy delivering continuous hourly pulses of 0.42 Gy. LDR brachytherapy (iridium 192 wires), is currently replaced with either PDR or high dose rate brachytherapy. PDR brachytherapy combines the theoretical radiobiological advantages of LDR brachytherapy but safer for radioprotection of the staff. However, the brachytherapy technique is nearly the same because using the implantation of interstitial needles. Contrary to LDR, dose delivering is pulsed with PDR. Median total prescription dose of brachytherapy was 65 Gy (range 55–74 Gy). Brachytherapy characteristics are shown in Table 1.

The only patient with inguinal metastases underwent inguinal lymph node external beam radiotherapy with a dose of 50 Gy in 2 Gy fractions.

2.3. Follow-up

Follow-up was scheduled at 4 to 8 weeks after brachytherapy completion and then every 4 months for the next 2 years, then every 6 months for the next 3 years, then annually. Salvage surgery (partial or total penectomy) was discussed in patients with histological confirmation of residual/relapsed tumor. Failures were classified according to the site of first tumor relapse: local (occurring in the penis), pelvic lymph node or metastatic. Survival times were estimated from the date of histological diagnosis with Kaplan–Meier method. Comparisons with log-rank student and Mann–Whitney tests were performed using SPSS software (IBM, Armonk, United State).

2.4. Ethics

The design of the study was approved by local ethic committee and follows French law about retrospective single center medical study.

Table 1
Patients, tumors, and treatments.

Characteristics	n (%) or (25%–75%)
Number of patients	55 (100%)
Median age (years)	73.8 (range: 70–95)
Past medical history	
Precancerous lesions	11 (20%)
Phimosis	9 (16.4%)
Median tumor diameter (mm)	20 (10–26)
Inguinal lymph node status	
Clinically N0	48 (87.3%)
pN0	11 (20%)
pN+	1 (2%)
Brachytherapy technique	
Low-dose rate	32 (58.2%)
Pulse dose rate	23 (41.8%)
Median number of catheters per implant	6 (3–8)
Median number of planes	2 (2–3)
Median brachytherapy dose (Gy)	65 (60–70)
Median treatment volume (cc)	26.4 (15–44)
Median total activity (cm)	23 (12–34)
Median dose rate (Gy.h ⁻¹)	0.46 (0.4–0.6)

mm: millimeters; N0: negative node involvement; pNx: histologically proven node status (0: negative, +: involvement); Gy: Gray; cm: centimeters; cc: cubic centimeters; Gy·h⁻¹: Gray per hour.

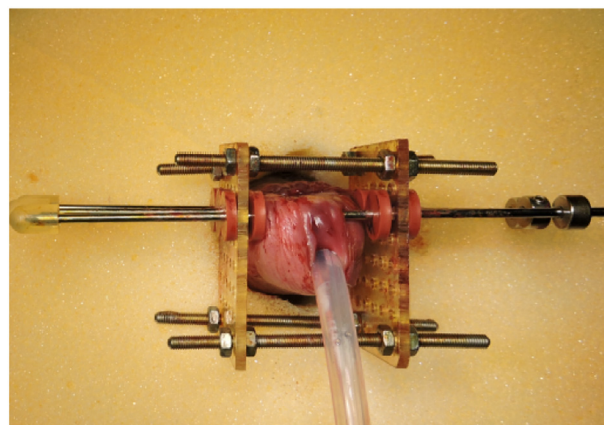


Fig. 1. Illustration of an implantation in a 75-year old patient treated for a tumor of the lateral part of penile glans (three needles used).

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