

Contemporary Role of Radiotherapy in the Management of Primary Penile Tumors and Metastatic Disease



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KEYWORDS

- Penile cancer • Radiotherapy • Brachytherapy • Surface mold radiotherapy
- Radiotherapy management of regional lymph nodes • Postoperative radiotherapy
- Combined chemoradiotherapy • Penile cancer clinical trials

KEY POINTS

- Squamous cell cancer of the penis is a radiocurable malignancy all too often managed by partial or total penectomy.
- External radiotherapy and brachytherapy have a role to play in the definitive management of the primary tumor, with 5-year penile preservation rates reported at 60% and 85%, respectively.
- Nodal staging remains a cornerstone of management because it is the strongest predictor of survival and inguinal status determines pelvic management.
- Postoperative radiotherapy of the regional nodes for high-risk pathology is indicated.
- Chemoradiotherapy should be considered as neoadjuvant treatment for unresectable nodes or as definitive management.

INTRODUCTION

The vast majority of penile cancers are squamous cell carcinoma (SCC), a radiosensitive and radio curable malignancy. There is consistent evidence across other SCC sites, including head and neck, cervix, vulva, and anal canal, that radiotherapy and the combination of sensitizing chemotherapy and radiotherapy are effective treatment. Furthermore, all these sites share a common pathway in human papillomavirus causation in a significant percentage of cases. Human papillomavirus positivity is associated with a better outcome and higher response rates to chemoradiation, and in penile cancer has been associated with improved 5-year survival.^{1,2}

Largely owing to the relative rarity of penile cancer in Western societies, there is a paucity of level 1 evidence to guide treatment. The incidence of approximately 1 per 100,000 in North America and the developed countries of Western Europe is an obstacle to completion of randomized studies to compare surgery with radiotherapy or radiation to chemoradiation.³

The traditional surgical approach to penile cancer has been partial or total penectomy. Because of the impact on sexual function, quality of life, and mental health,^{4,5} recent advances in surgery toward maximizing penile preservation, such as glansectomy and glans resurfacing, have attempted to address these issues but are not widely

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adopted.^{6,7} There are obvious quality of life advantages to organ preservation that can be provided by nonsurgical alternatives.

In localized disease, various forms of radiotherapy, including external beam, interstitial brachytherapy, and surface mold brachytherapy, offer a high chance of cure with organ preservation, reserving surgery for local recurrence. When there is a significant risk of regional node involvement by virtue of the stage or grade of the primary tumor, management with radiation can be combined with surgical staging of the nodes. The indications for postoperative adjuvant radiation to regional lymphatics following nodal staging are well-established from other anogenital SCC sites and include:

- Multiple node involvement,
- Extracapsular/extranodal extension, and
- Positive surgical margins.

For men presenting with locally and/or regionally advanced disease, chemoradiotherapy may render the disease resectable or can be instituted as a definitive treatment.

RADIOTHERAPY FOR THE PRIMARY TUMOR

Penile preservation should always be considered for the primary tumor. Although not always possible, especially in more locally advanced T3 to T4 disease, quality of life advantages include maintenance of erectile and sexual function and preserved sense of manliness. Delaunay and colleagues⁸ published results of a self-reported questionnaire administered to 21 men at an average of 80 months after penile brachytherapy. Seventeen of 18 men potent before brachytherapy reported maintenance of erections and 10 were still in an active sexual relationship. Although the capacity for erection and ejaculation can be maintained after partial penectomy, the lack of a glans and small penile size are cited as reasons for cessation of sexual activity.⁹ Emotional and mood disorders, anxiety, depression,^{10,11} and even suicide or attempted suicide are reported.⁵ Radiation therapy is associated with better global sexual scores than partial penectomy or local excision.¹² An analysis of 128 patients from 6 studies of surgical management of penile carcinoma reported impaired well-being in up to 40%, with psychiatric symptoms in approximately 50%. Additionally, up to 75% of patients report a reduction in sexual function after surgery.¹⁰

CARCINOMA IN SITU

SCC in situ may be adequately treated with circumcision if confined to the foreskin. Topical therapies

such as 5-fluoro-uracil cream or imiquoid provide excellent cosmetic results but careful follow-up is mandatory as recurrence is not uncommon. Other penile-sparing options include laser ablation, preferably Nd-YAG lasers, which penetrate up to 6 mm, have shown good tumor control (7% local failure [LF] at 4 years) with satisfactory function and cosmesis; 75% of men resume sexual activity.^{13–15} Mohs micrographic surgery or surgical excision with frozen section for intraoperative margin verification may permit local excision, but local recurrence remains a risk after any penile-sparing procedure, reported in up to one-third of patients.^{16,17} External beam radiation therapy may be used with a report of 100% local control for in situ disease,¹⁸ but the preferred radiation may be mold plesiotherapy (**Box 1**).

INVASIVE CANCER

Curative radiotherapy of the primary tumor can be delivered either through external beam radiation, interstitial brachytherapy, or surface mold plesiotherapy. For external beam radiotherapy, the 5-year local control and penile preservation rates are about 60%. For low dose rate (LDR) interstitial brachytherapy both local control and penile preservation are about 85% at 5 years and 70% at 10 years.^{19,20} Local recurrence is salvageable by surgery and does not affect disease-specific mortality. Each of these modalities is considered in turn.

External Beam Radiotherapy

External beam radiotherapy for early stage localized T1 to T2 SCC of the penis presents challenges with supporting and isolating the organ from adjacent normal structures while positioning it for treatment. Full bolus must be applied to eliminate the skin-sparing characteristics of modern megavoltage beams. With the patient supine, the penis is supported vertically in a split block of tissue-equivalent material with a central chamber to encase the penis (**Fig. 1**). Initially, wax blocks

Box 1

Options for squamous cell carcinoma in situ

- Circumcision (if confined to foreskin)
- Topical 5-fluoro-uracil/imiquoid
- Nd-YAG laser ablation
- Local excision with margin verification
- External beam radiotherapy
- Surface mold plesiotherapy

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