Primary penile cancer organ sparing treatment

Roman Sosnowski[1], Marcin Kuligowski[1], Olga Kuczkiewicz[2], Katarzyna Moskal[2], Jan Karol Wolski[1], Marc A. Bjurlin[3], James S. Wysock[4], Piotr Pęczkowski[5], Chris Protzel[6], Tomasz Demkow[1]

[1]Urooncology Department, Maria Sklodowska Curie, Memorial Cancer Hospital, Warsaw, Poland
[2]The Second Faculty of Medicine with the English Division and the Physiotherapy Division, Medical University of Warsaw, Warsaw, Poland
[3]Division of Urology, NYU Lutheran Medical Center, NYU Langone Health System, NYU School of Medicine, New York, USA
[4]Department of Urology, NYU Langone Medical Center, NYU School of Medicine, New York, New York USA
[5]Department of Radiotheraphy, Maria Sklodowska-Curie, Memorial Cancer Hospital, Warsaw, Poland
[6]Department of Urology, University of Rostock, Germany

Introduction Surgical treatment of penile cancer is usually associated with mutilation; alterations in self-esteem and body image; affecting sexual and urinary functions; and declined health-related quality of life. Recently, organ sparing treatment has appeared and led to limiting these complications.
Material and methods An extensive review of the literature concerning penile-preserving strategies was conducted. The focus was put on indications, general principles of management, surgical options and reconstructive techniques, the most common complications, as well as functional and oncological outcomes.
Results Analyzed methods, e.g.: topical chemotherapy, laser ablation therapy, radiotherapy, Moh's microscopic surgery, circumcision, wide local excision, glans resurfacing and glansectomy are indicated in low-stage tumors (Tis, Ta-T2). After glansectomy, reconstruction is also possible.
Conclusions Organ sparing techniques may achieve good anatomical, functional, and psychological outcomes without compromising local cancer control, which depends on early diagnosis and treatment. Penile sparing strategies are acceptable treatment approaches in selected patients with low-stage penile cancer after establishing disease-risk and should be considered in this population.

Corresponding author
Roman Sosnowski
1, Cyganeczki Street
02–928 Warsaw, Poland
phone: +48 601 623 018
roman.sosnowski@gmail.com

INTRODUCTION

Penile cancer is an uncommon malignancy in Europe and North America with a reported incidence of 0.1 to 0.9 per 100 000 men [1, 2]. However, in developing countries the incidence is higher and reaches 50 per 100 000 men in north-eastern Brazilian states [3]. This various worldwide distribution depends on age, circumcision practice, hygiene patterns and risk factors for penile cancer [2, 4]. Phimosis, human papillomavirus infection, chronic inflammatory conditions (balanoposthitis and balanitis xerotica obliterans), sexual history (multiple partners, early age at first intercourse), and treatment with psoralen and ultraviolet A photochemotherapy are strongly associated with risk of developing penile cancer [5–8].

The surgical management of penile cancer depends on the stage of the disease, TNM (tumor nodus tumor metastases) staging system, as well as the grade and lesion location, which is detailed in Table 1. The mainstay of surgical treatment relies upon wide excision including partial penectomy and total penectomy. More recently, a variety of operative techniques and therapeutic strategies have been developed to reconcile good functional and psychological outcomes with sufficient oncological control through organ sparing techniques [9, 10].
While large retrospective studies report a statistically higher local recurrence rate following organ-sparing techniques compared with penis amputation, repeat organ sparing resection for local recurrence appears to provide satisfactory outcomes which results in corresponding overall survival rates after

Table 1. *Conservative and organ sparing treatment options for penile cancer [8]*

Primary tumor	Conservative or organ sparing treatment
Tis	Topical chemotherapy, laser, WLE, glans resurfacing
Ta, T1a	Laser with/without circumcision, WLE with/without circumcision, glans resurfacing, glansectomy (partial), radiotherapy for lesion <4 cm
T1b and T2 confined to the glans	WLE with reconstructive surgery, Laser with circumcision, glansectomy, radiotherapy for lesion <4 cm
T2 with invasion of the corpora cavernosa	Partial penectomy and reconstruction, radiotherapy for lesion <4 cm
T3 with invasion of the urethra	No recommendation for organ sparing surgery
T4 with invasion of other adjacent structures	no recommendation for conservative treatment or organ sparing surgery
Local recurrence after conservative treatment	Salvage surgery with penis-sparing treatment in small recurrences or partial amputation Large or high-stage recurrence: partial or total amputation

WLE – wide local excision

preserving and radical treatment [10]. Penile amputation frequently results in unsatisfactory side effects of penile disfigurement or emasculation along with effects on corporal image, self-esteem and genital sensibility, frequently impairing sexual function or micturition. As a result, it is understandable why patients are afraid of the mutilating effects after total penectomy and are unwilling to undergo radical treatment [11]. Patients' preferences should be respected in the treatment decision-making process and psychological support should be provided while maintaining oncological outcomes. The aim of this article is to provide a contemporary review of the penile–sparing approaches in the management of primary penile cancer. Emphasis is placed on indications for appropriate stages, general principles of management, surgical options and reconstructive techniques, as well as functional and oncological outcomes.

Topical chemotherapy

Agents used for topical chemotherapy or immunotherapy of penile cancer are 5-flurouracil (5-FU) 5%, imiquimod 5% and interferon alfa-2a creams [11]. Indications for this treatment are premalignant and superficial lesions, such as carcinoma in situ (Erythroplasia of Queyrat, Bowen's disease) and bowenoid papulosis. 5-FU is frequently administered as a first line therapy [12, 13, 14]. There is no specific regimen for 5-FU therapy. The most common method is applying the medication directly onto the lesion for a 12-hour duration every other day for 4–6 weeks

[11, 14, 15], while other schemes suggest applying the cream twice daily for 3 weeks [13]. If necessary, the cycle can be repeated. As a second- line treatment, imiquimod 5% can be applied in a similar manner [4], although there are some reports of successful use as a first-line therapy [14, 16]. Toxicity and adverse events are relatively low. The most common side effects of topical chemotherapy include discomfort, erythema, irritation and soreness. Hypersensitivity or allergy to 5-FU are also possible and it can manifest as a severe allergic reaction- generalized dermatitis [15]. 5-FU has demonstrated good oncological outcome without evidence of recurrence in post treatment biopsy after a 5 year follow-up [17]. A larger retrospective study concerning the treatment of penile CIS with 5-FU as a first- and imiquimod as a second-line therapy, report complete response in 57% and partial response in 13.6% of patients [12].

Laser ablation therapy

Laser ablation of the superficial primary tumor offers a penile preservation strategy. Indications for treatment include in situ disease and, in some publications, also T1 tumors [11]. Contraindications are lesions with >6 mm depth invasion and T2 tumors [18]. The types of lasers which are most commonly used in clinical practice are the CO_2 laser and the neodymium-yttrium-aluminium-garnet (Nd:YAG) laser. These lasers differ from each other in wavelength, which is 10.6 μm for the CO_2 laser and 1.06 μm for the Nd:YAG laser [2, 15]. This is reflected in tissue penetration depth: 0.1 mm for CO_2 laser and 4.2 mm for Nd:YAG [11]. Because of its low penetration power, the CO_2 laser is an alternative to topical chemotherapy as a first-line treatment of penile cancer *in situ* [12]. The mechanism of tissue destruction differs between the two types of lasers. The CO_2 laser ablation leads to tissue carbonization and vaporization, while Nd:YAG causes protein denaturation, coagulative necrosis and also limited carbonization and vaporization [15]. When managing penile carcinoma with laser treatment, it is imperative to ablate the surrounding area of the tumor bed. A margin of 8–10 mm extending beyond the tumor site should be treated when using the CO_2 laser [19]. Usage of Nd:YAG laser requires a minimum 3 mm rim around the primary lesion ablation site [20, 21]. Peniscopy, microscopic examination of the penis with a colposcope after application of 5% acetic acid, can be helpful to detect lesions suspected of malignancy [22]. Complications after CO_2 laser treatment, which include bleeding and meatal stenosis, are rare, occurring in less than 1%. In one study, there were no urinary or sexual function complica-

tions observed after Nd:YAG laser application [8]. Recurrence of penile cancer after CO_2 laser ablation occurs in 10–26% of patients [13]. Results of Nd:YAG laser treatment depends on tumor stage with recurrence rates ranging from 3.1% to 48% [18, 20].

Mohs microscopic surgery

The Mohs microscopic surgical technique was developed in the 1930's for treatment of common skin cancers. Although mohs microscopic surgery (MMS) has been adopted for the treatment of penile cancer, few studies using the management option have been reported to date. During MMS, the tumor is excised in horizontal layers with concomitant multiple frozen sections and microscopic evaluation until the surgical bed is cancer free. This microscopic guidance allows for the removal of tumor tissue within clear resection margins and the preservation of uninvolved penile tissue for good cosmetic and functional results. According to Frederic Moh's data, this technique is very much stage-dependent, successful mainly in small (<1.0 cm) low stage, low grade lesions [23]. Tumor size has been shown to be an important predictor for local control with no recurrence in small lesions, <2 cm, and 50% recurrence with lesions >3 cm. In other series, overall recurrence rates were 32% after the first MMS procedure, apparently higher than after amputations; however, in those cases patients were suitable for further Mohs procedures [24]. Although complications are rare, meatal stenosis and organ disfigurement are reported, the latter mostly in larger high stage tumors.

While attractive because of negative margins reassurance and preservation of penile anatomy and function, careful patient selection for this technique remains crucial for treatment success. MMS may be offered to men with CIS or distal superficially invasive tumors who desire penile preservation for the best outcomes.

MMS has gained limited popularity among urologists as it is time consuming and requires a multidisciplinary team with close cooperation between urologist and pathologist.

Circumcisions

The majority of patients with penile cancer are uncircumcised. About 20% of new malignancies involve only the prepuce at presentation. In these cases, circumcision may be sufficient for curative treatment. Specifically, circumcision maybe be an acceptable treatment modality for lesions limited to distal prepuce that are low stage (Tis, Ta, T1) and low grade (G1,G2) [2, 25, 26]. When the tumor involves the basal prepuce, excision needs to be extended to the penile shaft to ensure negative surgical margins [27]. However, this simple procedure is related with poor local control and recurrence rates as high as 50% have been reported [2, 26]. Therefore, careful selection and close follow-up of patients is mandatory.

Wide local excision

Recent growing data on the oncological safety of negative surgical margins of only a few millimetres have encouraged urologists to perform local excision of penile carcinoma in select cases [28–31]. Wide local excision (WLE) is an approved local treatment modality for glans tumors of up to T2 and low stage and grade tumors of the shaft (up to T1 G2) [8]. In small lesions, primary closure of the wound is often possible. However, closing larger lesions may result in penile disfigurement or tilting, affecting micturition and erectile appearance. Consequently, in such cases grafting may be required, preferably with split thickness skin grafts. There are no strict limitations in the terms of lesion size for this management technique, but rather it is considered individually depending on the glans size or tumor location. Tumors covering more than half of the glans; close to the urethral meatus; urethral involvement; and concurrent CIS are contraindications for WLE. Local recurrence is not uncommon with the 5 year recurrence-free survival for T1 and T2 tumors being 63% [32]. Although local control is achieved in most cases with WLE, close follow up is required to monitor for recurrence which could signify regional lymph node spread and affect the patient's prognosis.

WLE is associated with less postoperative complications and leads to better sexual outcomes as comparing to glansectomy, which is often an alternative. Some authors consider WLE the best approach for treating primary penile tumors when feasible [33].

Glans resurfacing

Glans resurfacing is a relatively new procedure that was first described in 2000 by Depasquale and colleagues for the treatment of extensive balanitis xerotica obliterans and subsequently adapted for superficial glans cancers [34]. It is an acceptable treatment modality for Tis, Ta and T1a disease. Literature supports its use for extensive pre- malignant lesions and carcinoma in situ, where it can be performed as a primary procedure or when treatment with topical agents fails [15, 35, 36].

This procedure is performed under tourniquet control. After marking the glans quadrants, epithelium and subepithalial tissue is removed from the

Figure 1. *Initial step in glans resurfacing where the epithelium and subepithalial tissue is removed from the spongiosum by sharp dissection.*

Figure 2. *Split-skin graft is sutured with interrupted absorbable sutures to the meatal and shaft edges after removal of epithelium and subepithalial tissue during glans resurfacing.*

Figure 3. *Developing the plane to allow separation of the glans from corpora cavernosa during the intial step of glansectomy.*

spongiosum by sharp dissection, starting from the meatal edge and proceeding to the coronal sulcus and slightly over to the shaft skin (Figure 1). Next, the resection site is covered, typically with a split-skin graft (SSG) harvested from the lateral thigh, or alternatively with tunica vaginalis or buccal mucosa. The graft is trimmed to size and then carefully sutured with interrupted absorbable sutures to meatal and shaft edges (Figure 2). Quilting sutures are placed in a regular fashion to ensure graft adherence, occasionally complemented by small longitudinal incisions. After completion of the surgery a catheter is placed and compressive dressing is applied. Patients remain on bed-rest for usually 3–5 days, after which the catheter and bandage are removed and patients are discharged home. After 4–6 weeks the cosmetic outcome is usually excellent. In several studies no complications were reported, but there is a potential risk of graft loss and need for re-grafting [15].

In cases where lesions affect part of the glans (less than 50%), partial glans resurfacing is an option. The technique is analogous to total glans resurfacing, where a wedge excision of the tumor is performed. In these cases, peniscopy done prior to surgery may be helpful in assessing lesion occurrence and for better resection planning [37]. Shabbir et al. reported high positive margins rates of 28% for this technique with the need for further conservative treatment [35]. Other studies have used glans resurfacing for premalignant lesions with excellent results [15, 38]. However, patients should be informed of the risk of positive margins and need for secondary treatment. Overall recurrence rates at mid-term follow-ups were no higher than 6% [35] with no cases of local failure in other studies [15].
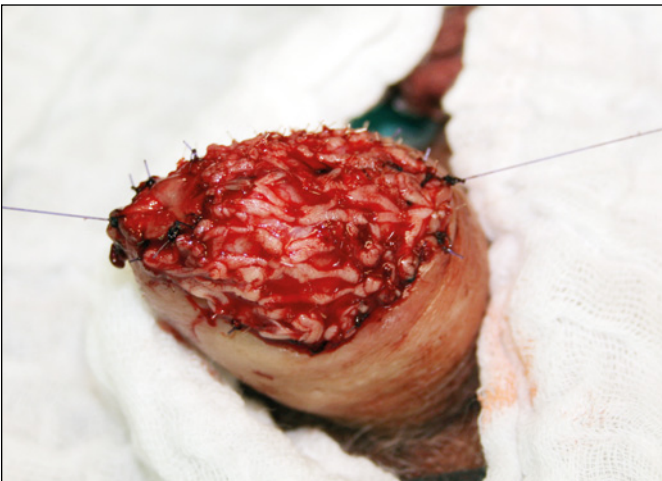
Glansectomy

Since penile cancer can occur in up to 80% of cases distally, either on the glans or prepuce, the majority of patients may be amenable to glansectomy [2, 39] which was first described by Austoni in 1996 [27]. Glansectomy is a treatment modality for glandular tumors Ta, T1 and T2 [26, 30]. Either total or partial glansectomy may be performed depending on cases, both with or without grafting.

Total glansectomy starts with catheter insertion and a tourniquet is placed at the penile base for bleeding control. A circular subcoronal incision is made down to the Buck's fascia. At this point a plane is developed in which the glans is separated from the corpora cavernosa (Figure 3). Neurovascular bundles are sectioned and the urethra is divided, freeing it from the specimen. Next the urethra is ventrally spatulated and a new meatus is formed by fixing
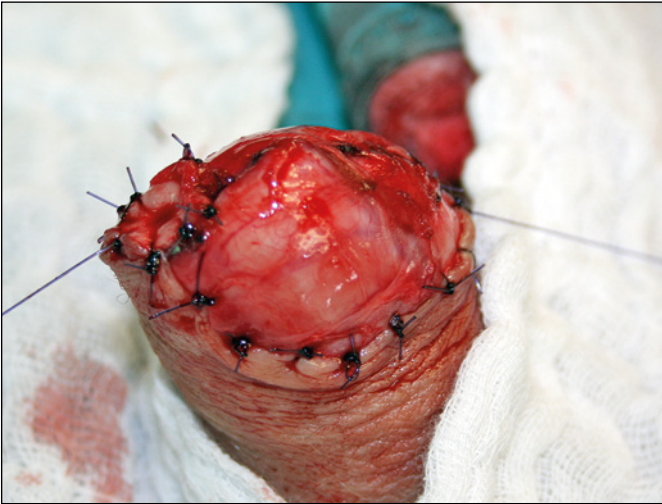
Figure 4. *Ventral spatulation of the urethra and formation of a new meatus by fixing it to the corpora cavernosa.*

Figure 5. *Split-skin graft is placed creating a neoglans covering the corporal tips.*

Figure 6. *Completed glansectomy with split-sking graft.*

it to the corpora cavernosa (Figure 4). Before the glans reconstruction, sections of tunica albuginea and distal urethral margin must be taken for intraoperative microscopic assessment. The neoglans is usually formed from SSG in a fashion similar to the one described for glans resurfacing, covering the corporal tips (Figures 5 and 6). The penis may be also reconstructed without grafting, as in a 'parachute technique', where corporal tips are covered with sectioned shaft [40]. Efforts have been made to further improve reconstructive surgery for better outcomes. Depasquale's technique of cavernous rotation in which the extremities of corpora are separated and rotated ventrally and then sutured under the urethra to imitate the appearance of the glans and coronal sulcus was used in one series with good cosmetic and functional results, yet with considerably high complications rate of 27% [34]. Since reduction of penile sensitivity seems to be a major functional problem after grafting, neoglans formation by everting the spatulated urethra was also tried to avoid this side effect [36, 41]. For smaller lesions located distally near the urethral meatus and up to stage T1a, partial glansectomy may be performed. Reconstruction with our without grafting is possible, the latter through penile shaft skin coverage or using a preputial flap [27, 42].

Local recurrence rate for glansectomy has been reported to be 8% in long-term follow-up, and 9% for inguinal nodes metastases [40]. Potential complications for this method are graft loss, meatal stenosis and urine spraying. As to functional outcomes, it is connected with decreased penile length and reduced sensibility and may therefore negatively affect sexual satisfaction [33].

Partial penectomy with glans reconstruction

If tunica albuginea or early corporal involvement occurs, traditionally it would be treated with partial penectomy for the best oncological outcomes [8]. Alternatively, in patients who are adamant about penile preservation, distal corporectomy with reconstruction of the corporal heads and grafting may be performed [43]. The corpora cavernosa are sutured and a neoglans is reconstructed. The neoglans gets covered by a split-skin graft.

Radiotherapy

Radiation therapy is an option in the management of penile cancer, stages CIS-T3 [8]. There is a need for two forms of radiation therapy in the treatment of penile carcinoma: external-beam radiotherapy (EBRT) or brachytherapy (BT). Indications for EBRT include superficial or exophytic lesions of <4 cm,

and tumour location on the glans or coronal sulcus. A tumor <4 cm on the glans penis with <1 cm of invasion may be treated with BT [44, 45]. Contraindications for EBRT or BT include any penile tumor >4 cm with concurrent inguinal lymphadenopathy [11]. Typically, ERBT is administered in 2 Gy fractions per day. The treatment schedule consists of five fractions per week for a duration of 6–7 weeks. A total provided dose is 66–70 Gy. Two differing BT techniques have been employed in the treatment of penile cancer. The first technique involves a radioactive mold placed over the penis. The second technique is the implantation of a radioactive seed (Ir 192) which delivers a predetermined dose to the penile tissue. In order to reduce radiation-induced complications, circumcision should be performed prior to radiotherapy [11]. Penile brachytherapy usually delivers a total dose of 55-60 Gy over 4–5 days. Local recurrence after radiotherapy occurs in 10–40% of cases [44, 46]. The 5-year rate of penile preservation after BT ranges from 70% to 88%, which is higher than the corresponding 36–66% rates for EBRT [47]. Complications after radiotherapy include urethral adhesions with a deviated stream; urethral strictures; meatal stenosis; fibrosis; pigmentation; and radiation-induced penile ulceration or necrosis [11, 48].

CONCLUSIONS

Penile sparing procedures are acceptable management options in the select risk-informed patient after establishing disease-risk variables. Candidates for penile-sparing procedures must undergo close surveillance and be adherent to follow-up requirements which allows early detection of local recurrences. Disease recurrence mandates prompt and effective salvage procedures.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

References

1. Pow-Sang MR, Ferreira U, Pow-Sang JM, Nardi AC, Destefano V. Epidemiology and natural history of penile cancer. Urology. 2010; 76 (2 Suppl 1): S2-6.

2. Martins FE, Rodrigues RN, Lopes TM. Organ-preserving surgery for penile carcinoma. Adv Urol. 2008: 634216.

3. Favorito LA, Nardi AC, Ronalsa M, Zequi SC, Sampaio FJ, Glina S. Epidemiologic study on penile cancer in Brazil. Int Braz J Urol. 2008; 34: 587-591.

4. Cubilla AL, Dillner J, Schellhammer PF, Horenblas S. Malignant epithelial tumors. Pathology and Genetics of Tumors of the Urinary System and Male Genital Organs. In: Eble JN, Sauter G, Eppstein J, Sesterhenn I, editors. Lyon: IARC Press; 2004. pp. 281-290

5. Dillner J, von Krogh G, Horenblas S, Meijer CJ. Etiology of squamous cell carcinoma of the penis. Scand J Urol Nephrol Suppl. 2000; 205: 189-193.

6. Stern RS. Genital tumors among men with psoriasis exposed to psoralens and ultraviolet A radiation (PUVA) and ultraviolet B radiation. The Photochemotherapy Follow-up Study. N Eng J Med. 1990; 322: 1093-1097.

7. Daling JR, Madeleine MM, Johnson LG, et al. Penile cancer: importance of circumcision, human papillomavirus and smoking in in situ and invasive disease. Int J Cancer. 2005; 116: 606-616.

8. Hakenberg OW, Compérat E, Minhas S, Necchi A, Protzel C, Watkin N. Penile Cancer. European Association of Urology; 2014; Available from: http://uroweb.org/guideline/penile-cancer/

9. Caso JR, Rodriguez AR, Correa J, Spies PE. Update in the management of penile cancer. Int Braz J Urol. 2009; 35: 406-415.

10. Leijte JA, Kirrander P, Antonini N, Windahl T, Horenblas S. Recurrence patterns of squamous cell carcinoma of the penis: recommendations for follow-up based on a two-centre analysis of 700 patients. Eur Urol. 2008; 54: 161-168.

11. Zukiwskyj M, Daly P, Chung E. Penile cancer and phallus preservation strategies: a review of current literature. BJU Int. 2013; 112 Suppl 2: 21-26.

12. Alnajjar HM, Lam W, Bolgeri M, Rees RW, Perry MJ, Watkin NA. Treatment of carcinoma in situ of the glans penis with topical chemotherapy agents. Eur Urol. 2012; 62: 923-928.

13. Porter WM, Francis N, Hawkins D, Dinneen M, Bunker CB. Penile intraepithelial neoplasia: clinical spectrum and treatment of 35 cases. Br N Dermatol. 2002; 147: 1159-1165.

14. Hegarty PK, Eardley I, Heidenreich A, et al. Penile cancer: organ-sparing techniques. BJU Int. 2014; 114: 799-805.

15. Hadway P, Corbishley CM, Watkin NA. Total glans resurfacing for premalignant lesions of the penis: initial outcome data. BJU Int. 2006; 98: 532-536.

16. Micali G, Nasca MR, Tedeschi A. Topical treatment of intraepithelial penile carcinoma with imiquimod. Clin Exp Dermatol. 2003; 28 Suppl 1: 4-6.

17. Goette DK, Carson TE. Erythroplasia of Queyrat: treatment with topical 5-fluorouracil. Cancer. 1976; 38: 1498-1502.

18. Schlenker B, Tilki D, Seitz M, et al. Organ-preserving neodymium-yttrium-aluminium-garnet laser therapy for penile carcinoma: a long-term follow-up. BJU Int. 2010; 106: 786-790.

19. Conejo-Mir JS, Muñoz MA, Linares M, Rodriguez L, Serrano A. Carbon dioxide laser treatment of erythroplasia of Queyrat: a revisited treatment to this condition. J Eur Acad Dermatol Venereol. 2005; 19: 643-644.

20. Tewari M, Kumar M, Shukla HS. Nd:YAG laser treatment of early stage carcinoma of the penis preserves form and function of penis. Asian J Surg. 2007; 30: 126-130.

21. Frimberger D, Hungerhuber E, Zaak D, Waidelich R, Hofstetter A, Schneede P. Penile carcinoma. Is Nd:YAG laser therapy radical enough? J Urol. 2002; 168: 2418-2421.

22. Bandieramonte G, Colecchia M, Mariani L, et al. Peniscopically controlled CO2 laser excision for conservative treatment of in situ and T1 penile carcinoma: report on 224 patients. Eur Urol. 2008; 54: 875-882.

23. Mohs FE, Snow SN, Larson PO. Mohs micrographic surgery for penile tumors. Urol Clin North Am. 1992; 19: 291-304.

24. Shindel AW, Mann MW, Lev RY, et al. Mohs micrographic surgery for penile cancer: management and long-term followup. J Urol. 2007; 178: 1980-1985.

25. Bissada NK. Conservative extirpative treatment of cancer of the penis. Urol Clin North Am. 1992; 19: 283-290.

26. Li J, Zhu Y, Zhang SL, et al. Organ-sparing surgery for penile cancer: complications and outcomes. Urology. 2011; 78: 1121-1124.

27. Spitzer WO, Dobson AJ, Hall J, et al. Measuring the quality of life of cancer patients: a concise QL-index for use by physicians. Chronic Dis. 1981; 34: 585-597.

28. Agrawal A, Pai D, Ananthakrishnan N, Smile SR, Ratnakar C. The histological extent of the local spread of carcinoma of the penis and its therapeutic implications. BJU Int. 2000; 85: 299-301.

29. Minhas S, Kayes O, Hegarty P, Kumar P, Freeman A, Ralph D. What surgical resection margins are required to achieve oncological control in men with primary penile cancer? BJU Int. 2005; 96: 1040-1043.

30. Philippou P, Shabbir M, Malone P, et al. Conservative surgery for squamous cell carcinoma of the penis: resection margins and long-term oncological control. J Urol. 2012; 188: 803-808.

31. Gunia S, Koch S, Jain A, May M. Does the width of the surgical margin of safety or premalignant dermatoses at the negative surgical margin affect outcome in surgically treated penile cancer? J Clin Pathol. 2014; 67: 268-271.

32. Lont AP, Gallee MP, Meinhardt W, van Tinteren H, Horenblas S. Penis conserving treatment for T1 and T2 penile carcinoma: clinical implications of a local recurrence. J Urol. 2006; 176: 575-580.

33. Sedigh O, Falcone M, Ceruti C, et al. Sexual function after surgical treatment for penile cancer: Which organ-sparing approach gives the best results? Can Urol Assoc J. 2015; 9: E423-427.

34. Depasquale I, Park AJ, Bracka A. The treatment of balanitis xerotica obliterans. BJU Int. 2000; 86: 459-465.

35. Shabbir M, Muneer A, Kalsi J, et al. Glans resurfacing for the treatment of carcinoma in situ of the penis: surgical technique and outcomes. Eur Urol. 2011; 59: 142-147.

36. Gulino G, Sasso F, Palermo G, et al. Sexual outcomes after organ potency-sparing surgery and glans reconstruction in patients with penile carcinoma. Indian J Uol. 2013; 29: 119-123.

37. Pietrzak P, Corbishley C, Watkin N. Organ-sparing surgery for invasive penile cancer: early follow-up data. BJU Int. 2004; 94: 1253-1257.

38. Corbishley CM, Tinwell B, Kaul A, Ayres B, Watkin NA. Glans resurfacing for precancerous and superficially invasive carcinomas of the glans penis: Pathological specimen handling and reporting. Semin Diagn Pathol. 2015; 32: 232-237.

39. McDougal WS. Phallic preserving surgery in patients with invasive squamous cell carcinoma of the penis. J Urol. 2005; 174: 2218-2220.

40. Austoni E, Fenice O, Kartalas Goumas Y, Colombo F, Mantovani F, Pisani E. New trends in the surgical treatment of penile carcinoma. Arch Ital Urol Androl. 1996; 68: 163-168.

41. Morelli G, Pagni R, Mariani C, et al. Glansectomy with split-thickness skin graft for the treatment of penile carcinoma. Int J Impotence Res. 2009; 21: 311-314.

42. Brown CT, Minhas S, Ralph DJ. Conservative surgery for penile cancer: subtotal glans excision without grafting. BJU Int. 2005; 96: 911-912.

43. Hegarty PK, Shabbir M, Hughes B, et al. Penile preserving surgery and surgical strategies to maximize penile form and function in penile cancer: recommendations from the United Kingdom experience. World J Urol. 2009; 27: 179-187.

44. Crook JM, Jezioranski J, Grimard L, Esche B, Pond G. Penile brachytherapy: results for 49 patients. Int J Radiat Oncol Biol Phys. 2005; 62: 460-467.

45. Crook J, Jezioranski J, Cygler JE. Penile brachytherapy: technical aspects and postimplant issues. Brachytherapy. 2010; 9: 151-158.

46. McLean M, Akl AM, Warde P, Bissett R, Panzarella T, Gospodarowicz M. The results of primary radiation therapy in the management of squamous cell carcinoma of the penis. Int J Radiat Oncol Biol Phys. 1993; 25: 623-628.

47. Crook J, Ma C, Grimard L. Radiation therapy in the management of the primary penile tumor: an update. World J Urol. 2009; 27: 189-196.

48. Smith Y, Hadway P, Biedrzycki O, Perry MJ, Corbishley C, Watkin NA. Reconstructive surgery for invasive squamous carcinoma of the glans penis. Eur Urol. 2007; 2: 1179-1185. ■