European Association of Urology

GUIDELINES ON PENILE CANCER*

F. Algaba, S. Horenblas, G. Pizzocaro, E. Solsona, T. Windahl

TABLE OF CONTENTS PAGE

1. BACKGROUND

Penile carcinoma is an uncommon malignant disease with an incidence ranging from 0.1 to 7.9 per 100,000 males. In Europe, the incidence is 0.1–0.9 and in the US, 0.7–0.9 per 100,000 (1). In some areas, such as Asia, Africa and South America, penile carcinoma accounts for as many as 10–20% of male cancers. Phimosis and chronic irritation processes related to poor hygiene are commonly associated with this tumour, whereas neonatal circumcision gives protection against the disease. There is strong evidence that human papilloma virus types 16 and 18 are associated with penile carcinoma in as many as 50% of cases, as well as with penile carcinoma in situ (2).

Penile carcinoma essentially metastasizes via the lymphatics and develops mainly through the embolization mechanism instead of lymphatic permeation. Distant metastases are very rare and are a result of vascular dissemination (3). Spreading essentially develops in a stepwise fashion: first there is inguinal lymphatic spread, followed by pelvic and lastly distant metastases. As a consequence, it is extremely rare to observe patients with positive pelvic nodes or distant metastasis without inguinal lymph node involvement. The localization of the primary tumour appears in the glans in 48% of cases, prepuce in 21%, both glans and prepuce in 9%, coronal sulcus in 6% and less than 2% in the shaft (4). Palpable inguinal nodes are present at diagnosis in 58% of patients (range 20–96%) (4). Of these patients, 17–45% actually have nodal metastases and the remaining patients have inflammatory disease secondary to infection of the primary tumour. The likelihood of bilateral involvement is considerable due to the large number of penile lymphatics in the subcutaneous tissue. Approximately 20% of patients with metastases to two or more nodes also have pelvic nodal involvement (5). Among patients with non-palpable nodes, around 20% harbour nodal micrometastases. Depth of invasion, tumour grade, vascular and lymphatic involvement and growth patterns, and their associations are related to the occurrence of nodal metastases (6–10).

An overall 5-year survival rate of 52% has been reported: 66% in patients with negative lymph nodes and 27% in patients with positive nodes (4,5,7,11,12). Most patients are elderly and the neoplasm has a slow growth rate. Death from cancer is usually a consequence of local complications, such as infection, haemorrhage of the ulcerated tumour or ulcerated inguinal metastases.

There are still many controversies regarding the management of penile cancer. Treatment of the primary tumour tends to be organ preserving in order to maintain sexual function (13). Another point of debate relates to the need and extent of lymphadenectomy in clinically node-negative patients. Also, social and cultural habits seem to be important factors related to penile cancer, exemplified by the fact that 44–90% of patients suffer from phimosis at presentation (3) and that there is a documented association between human papilloma virus and penile carcinoma (2).

All these factors, together with the low incidence of penile cancer in countries with good socio-economic conditions and the absence of large or randomized trials, have an important influence in the management of the disease.

2. CLASSIFICATION

2.1 Pathology

Squamous cell carcinoma is by far the most common malignant disease of the penis, accounting for more than 95% of cases. Malignant melanomas and basal cell carcinoma are less common. The extent to which squamous cell carcinoma is preceded by pre-malignant lesions is unknown.

Pre-malignant lesions

Pre-malignant lesions of squamous cell carcinoma of the penis include the following:

1. Lesions sporadically associated with squamous cell carcinoma of the penis (14):
   - Balanitis xerotica obliterans
   - Cutaneous horn of the penis
   - Bowenoid papulosis of the penis

2. Lesions at low risk of developing into squamous cell carcinoma of the penis [transformation to invasive squamous cell carcinoma has been reported in up to one-third of lesions (15)]:
   - Penile intraepithelial neoplasia (erythroplasia of Queyrat, Bowen's disease)

Penile neoplasias

Although squamous cell carcinoma is the most common form of penile cancer, various types of this entity and different growth patterns can be observed:

1. Squamous cell carcinoma types:
   - Classic
   - Basaloid
   - Verrucous
   - Sarcomatoid
   - Adenosquamous

2. Squamous cell carcinoma growth patterns:
   - Superficial spread
   - Nodular or vertical-phase growth
   - Verrucous

3. Differentiation grades: the Broders system (16) has been traditionally used as a grading system, but currently the Maiche score system (17) seems to be the most suitable

Mesenchymal tumours

Mesenchymal tumours are very uncommon, with an incidence of less than 3% (Kaposi's sarcoma, angiosarcoma, epithelioid haemangio-endothelioma, etc.).

Metastatic disease

The penis is a very rare metastatic site, but bladder, prostate and rectal tumours are reported as primary tumours in cases of metastatic disease.

Tumour, node, metastasis (TNM) classification

The 1997 TNM classification for penile cancer is shown in Table 1.

Table 1: 1997 TNM classification of penile cancer

Primary tumour	
Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma *in situ*
Ta	Non invasive verrucous carcinoma
T1	Tumour invades subepithelial connective tissue
T2	Tumour invades corpus spongiosum or cavernosum
T3	Tumour invades urethra or prostate
T4	Tumour invades other adjacent structures
Regional lymph nodes	
Nx	Regional lymph nodes cannot be assessed
N0	No evidence of lymph node metastasis
N1	Metastasis in a single inguinal lymph node
N2	Metastasis in multiple or bilateral superficial lymph nodes
N3	Metastasis in deep inguinal or pelvic lymph nodes (unilateral or bilateral)
Distant metastasis	
Mx	Distant metastases cannot be assessed
M0	No evidence of distant metastases
M1	Distant metastases

2.2 REFERENCES

1. Persky L.
Epidemiology of cancer of the penis. Recent Results Cancer Res 1977; 60: 97.

2. McCance DJ, Kalache A, Ashdown K, Andrade L, Menezes F, Smith P, Doll R.
Human papilloma virus types 16 and 18 in carcinomas of the penis from Brazil. Int J Cancer 1986; 37: 55–59.

3. Burgers JK, Badalament RA, Drago JR.
Penile cancer. Clinical presentation, diagnosis and staging. Urol Clin North Am 1992; 19: 247.

4. **Sufrin G, Huben R.**
Benign and malignant lesions of the penis. In: Adult and Pediatric Urology, 2nd ed. Gillenwater JY (ed.). Year Book Medical Publisher: Chicago, 1991; 1643.
5. **Horenblas S, van Tinteren H, Delemarre JF, Moonen LM, Lustig V, van Waardenburg EW.**
Squamous cell carcinoma of the penis. III. Treatment of regional lymph nodes. J Urol 1993; 149: 492–497.
6. **Horenblas S, Tinteren HV.**
Squamous cell carcinoma of the penis. IV. Prognostic factors of survival: analysis of tumor, nodes and metastasis classification system. J Urol 1994; 151: 1239.
7. **Lopes A, Hidalgo GS, Kowallski LP, Torloni H, Rossi BM, Fonseca FP.**
Prognostic factors in carcinoma of the penis: multivariate analysis of 145 patients treated with amputation and lymphadenectomy. J Urol 1996; 156: 1637.
8. **Solsona E, Iborra I, Ricós JV, Monrós JL, Dumont R, Casanova J, Calabuig C.**
Corpus cavernosum invasion and tumor grade in the prediction of lymph node condition in penile carcinoma. Eur Urol 1992; 22: 115–118.
9. **Morgenstern NJ, Slaton JW, Levy DA, Ayala AG, Santos MW, Pettaway CA.**
Vascular invasion and tumor stage are independent prognosticators of lymph node (LN) metastasis in squamous penile cancer (SPC). J Urol 1999; 161: 158 (abstract 608).
10. **Villavicencio H, Rubio J, Regalado R, Chéchile G, Algaba F, Palou J.**
Grade, local stage and growth pattern as prognostic factors in carcinoma of the penis. Eur Urol 1997; 32: 442.
11. **Fraley EE, Zhang G, Manivel C, Niehans GA.**
The role of ilioinguinal lymphadenectomy and significance of histological differentiation in treatment of carcinoma of the penis. J Urol 1989; 142: 1478.
12. **Ornellas AA, Seixas ALC, Marota A, Wisnescky A, Campos F, de Moraes JR.**
Surgical treatment of invasive squamous cell carcinoma of the penis: retrospective analysis of 350 cases. J Urol 1994; 151: 1244.
13. **Opjordsmoen S, Fossà SD.**
Quality of life in patients treated for penile cancer. A follow-up study. Br J Urol 1994; 74: 652.
14. **Lucia MS, Miller GJ.**
Histopathology of malignant lesions of the penis. Urol Clin North Am 1992; 19: 227.
15. **Mikhail GR.**
Cancers, precancers, and pseudocancers on the male genitalia: a review of clinical appearances histopathology, and management. J Dermatol Surg Oncol 1980; 6: 1027.
16. **Broders AC.**
Squamous cell epithelioma of the skin. Ann Surg 1921; 73: 141.
17. **Maiche AG, Pyrhonen S, Karkinen M.**
Histological grading of squamous cell carcinoma of the penis: a new score system. Br J Urol 1991; 67: 522.

3. RISK FACTORS

The best prognostic factors related to survival from penile cancer are the presence of positive lymph nodes, the number of positive nodes and the presence of extracapsular nodal involvement (1,2). Therefore, these are important factors to consider when applying complementary therapies after pathological examination. Predictive factors for the presence of lymph node metastasis have been assessed thoroughly. Parameters from the primary tumour, i.e. location, size, depth of infiltration, tumour grade (3–7) and associations (7), have shown an important predictive value. According to these factors, high, intermediate and low risk groups of patients have been defined (4,7,8). Vascular invasion, lymphatic invasion and the growth pattern of the primary tumour (9,10) are other important predictive factors with particular relevance in the intermediate risk group. All these factors have been taken into account when therapy recommendations have been outlined.

Molecular markers are currently under investigation as prognostic factors, but they currently have no use in clinical practice.

3.1 REFERENCES

1. **Ricós JV, Casanova JL, Iborra I, Monrós JL, Dumont R, Solsona E.**
El tratamiento locorregional del carcinoma de pene. Arch Esp Urol 1991; 44: 667.
2. **Srinivas V, Morse M, Herr E, Sogani P, Whitmore W.**
Penile cancer: relation of node extent of nodal metastasis to survival. J Urol 1987; 137: 880.
3. **Fraley EE, Zhang G, Manivel C, Niehans GA.**
The role of ilioinguinal lymphadenectomy and significance of histological differentiation in treatment of

carcinoma of the penis. J Urol 1989; 142: 1478.
4. **Horenblas S, Tinteren HV.**
Squamous cell carcinoma of the penis. IV. Prognostic factors of survival: analysis of tumor, nodes and metastasis classification system. J Urol 1994; 151: 1239.
5. **Maiche AG, Pyrhönen S.**
Clinical staging of cancer of the penis: by size? by localization? or by depth of infiltration? Eur Urol 1990; 18: 16–22
6. **Morgenstern NJ, Slaton JW, Levy DA, Ayala AG, Santos MW, Pettaway CA.**
Vascular invasion and tumor stage are independent prognosticators of lymph node (LN) metastasis in squamous penile cancer (SPC). J Urol 1999; 161: 158 (abstract 608).
7. **Solsona E, Iborra I, Ricós JV, Monrós JL, Dumont R, Casanova J, Calaburg C.**
Corpus cavernosum invasion and tumor grade in the prediction of lymph node condition in penile carcinoma. Eur Urol 1992; 22: 115–118.
8. **Pizzocaro G, Piva L, Bandieramonte G, Tana S.**
Up-to-date management of carcinoma of the penis. Eur Urol 1997; 32: 5.
9. **Lopes A, Hidalgo GS, Kowallski LP, Torloni H, Rossi BM, Fonseca FP.**
Prognostic factors in carcinoma of the penis: multivariate analysis of 145 patients treated with amputation and lymphadenectomy. J Urol 1996; 156: 1637.
10. **Villavicencio H, Rubio J, Regalado R, Chéchile G, Algaba F, Palou J.**
Grade, local stage and growth pattern as prognostic factors in carcinoma of the penis. Eur Urol 1997; 32: 442.

4. DIAGNOSIS

In order to establish a rational diagnostic approach to penile cancer, the primary lesion, regional lymph nodes and distant metastases, should be taken into account initially and during follow-up.

4.1 Primary lesion

Patients with a suspicious penile lesion should undergo very careful physical examination. This is often sufficient to determine the diagnosis and staging, as well as aiding therapeutic decision making. It is important to record the:

- Diameter of the penile lesion or suspicious areas
- Location(s) on the penis
- Number of lesions
- Morphology: papillary, nodular, ulcerous or flat
- Relationship with other structures (e.g. submucosa, corpora spongiosa and/or cavernosa, urethra)
- Colour and boundaries

Cytological or histological diagnosis is absolutely necessary before making treatment decisions. The aim is not only to confirm the pathological diagnosis, but also to determine the tumour grade. This will assist in therapeutic decisions concerning the primary tumour, as well as in establishing risk groups for regional therapeutic strategies (1). The preference of the pathologist should be taken into account when choosing the most suitable histological diagnostic method. The pathological diagnosis can be made by incisional biopsy, tissue core biopsy, fine-needle aspiration or brush biopsy (like cervical cancer). Excisional biopsy can also be used as a conservative approach if a small lesion is located in the prepuce or in another area in which this is feasible.

Diagnostic imaging can assist in identifying the depth of tumour invasion, particularly with regard to corpora cavernosa infiltration. However, penile ultrasound imaging is sometimes difficult to interpret and is an unreliable method with microscopic infiltration (2). Magnetic resonance imaging (MRI) is an optional method if ultrasound is inconclusive; however, there is limited experience with this method (3).

4.2 Regional nodes

A careful inguinal physical examination is necessary, taking into account the following aspects.

Non-palpable nodes

There is no indication for imaging or histological examination if the nodes are non-palpable. If poor prognostic factors were observed on the primary tumour, pathological surgical inguinal nodal staging is advised (see later). Nevertheless, biopsy of the sentinel node, as described by Cabañas (4), is not recommended because false-negative rates as high as 25% (range 9–50 %) have been reported (5). More recently, dynamic sentinel lymph node biopsy with isosulphan blue and/or 99m Tc-colloid sulphur has been shown to be a promising procedure under investigation (6,7).

Palpable nodes

The following parameters should be recorded if palpable nodes are present:

- Diameter of node(s) or mass(es)
- Uni- or bilateral localization
- Number of nodes identified in each inguinal area
- Mobile or fixed nodes or mass
- Relationship to other structures (skin, Cooper ligament, etc.) with respect to infiltration, perforation, etc.
- Presence of oedema on the leg and/or scrotum

The histological diagnosis involves fine needle aspiration biopsy, tissue core biopsy or open biopsy according to the preference of the pathologist. In the case of a negative biopsy and clinically suspicious nodes, a repeat biopsy or excisional biopsy should be performed.

4.3 Distant metastases

An assessment of distant metastases should only be performed in patients with proven positive nodes (8,9). Pelvic/abdominal computed tomography (CT) scanning is used in the identification of pelvic and/or retroperitoneal nodes in patients with inguinal metastases. Although this is not a reliable diagnostic method (10), the detection of pelvic masses has a considerable impact on therapy and prognosis (11,12). A chest X-ray should be performed on patients with positive lymph nodes. Routine blood determinations should be carried out only in patients with bulky inguinal masses and pelvic nodes, and in those with metastases (13,14). A bone scan is recommended only in symptomatic cases (8). A diagnostic schedule is summarized in Table 2.

Table 2: Diagnosis schedule for penile cancer

Lesion level	**Procedures**		
	Mandatory	**Advisable**	**Optional**
Primary tumour	Physical examination Cytological or histological diagnosis	Ultrasound (if invasion suspected)	MRI (if ultrasound inconclusive)
Regional disease Non-palpable nodes Palpable nodes	Physical examination Cytological or histological diagnosis		Sentinel node biopsy (investigational)[1]
Distant metastases		Pelvic CT (if nodes positive) Abdominal CT (if pelvic nodes positive) Chest X-ray (if nodes positive)	Bone scan (in symptomatic patients)

MRI = magnetic resonance imaging; CT = computed tomography.

[1] Cabañas technique (4) is no longer advisable. Isosulphan blue or 99m Tc-colloid sulphur are promising new investigational procedures.

4.4 GUIDELINES ON THE DIAGNOSIS OF PENILE CANCER

Primary tumour

1. Physical examination is mandatory, recording the morphology and characteristics of the physical lesion.
2. Cytological or histological diagnosis is also mandatory.
3. Imaging: penile ultrasound is advisable, demonstrate corpora cavernosa invasion. In cases of inconclusive results, MRI is an optional method.

Regional lymph nodes

1. Physical examination is mandatory:
   - If nodes are non-palpable there is no indication for imaging or histological examination. A new investigational technique, sentinel node biopsy, is available for use in high-risk patients.
   - If nodes are palpable it is mandatory to record nodal morphological and physical characteristics and to perform a histological diagnosis.

Distant metastasis (only in patients with metastatic inguinal nodes)

1. A pelvic/abdominal CT scan (positive pelvic nodes) is advisable.
2. A chest X-ray is also advisable.
3. Routine laboratory determinations are optional for specific conditions.
4. A bone scan is only recommended in symptomatic cases.

4.5 REFERENCES

1. **Solsona E, Iborra I, Ricós JV, Monrós JL, Dumont R, Casanova J, Calabuig C.**
   Corpus cavernosum invasion and tumor grade in the prediction of lymph node condition in penile carcinoma. Eur Urol 1992; 22: 115–118.
2. **Horenblas S.**
   The accuracy of ultrasound in squamous cell carcinoma. In: The Management of Penile Squamous Cell Carcinoma. A Retrospective and Prospective Study. Thesis. Amsterdam Zoetermeer: BV Export drukkerij, 1993; 71–83.
3. **Vapnek JM, Hricak H, Carroll PR.**
   Recent advances imaging studies for staging of penile and urethral carcinoma.
   Urol Clin North Am 1992; 19: 257.
4. **Cabañas RM.**
   An approach for the treatment of penile carcinoma. Cancer 1977; 39: 456.
5. **Pettaway CA, Pisters LL, Dinney CPN, Jularbal F, Swanson DA, von Eschenbach AC, Ayala A.**
   Sentinel lymph node dissection for penile carcinoma: the MD Anderson Cancer Center Experience.
   J Urol 1995; 154: 1999–2003.
6. **Horenblas S.**
   Surgical management of carcinoma of the penis and scrotum. In: Medical Radiology. Diagnostic Imaging and Radiation Oncology. Carcinoma of the Kidney and Testis, and Rare Urologic Malignancies. Petrovich Z, Baert L, Brady LW (eds). Springer Verlag: Berlin, 1999; 341–354.
7. **Pettaway CA, Jularbal FA, Babaian RJ, Dinney CPN, Pisters LL.**
   Intraoperative lymphatic mapping to detect inguinal metastases in penile carcinoma: results of a pilot study. J Urol 1999; 161: 612.
8. **Burgers JK, Badalament RA, Drago JR.**
   Penile cancer: clinical presentation, diagnosis and staging. Urol Clin North Am 1992; 19: 247.
9. **Horenblas S, van Tinteren H, Delemarre JFM, Moonen LM, Lustig V, van Waardenburg EW.**
   Squamous cell carcinoma of the penis. III. Treatment of regional lymph nodes. J Urol 1993; 149: 492–497.
10. **Horenblas S, van Tinteren H, Delemarre JFM, Moonen LM, Lustig V, Kröger R.**
    Squamous cell carcinoma of the penis. Accuracy of tumor nodes and metastasis classification system, and role of lymphangiography, computerized tomography scan and fine needle aspiration cytology.
    J Urol 1991; 146: 1279–1283.
11. **Ricós JV, Casanova JL, Iborra I, Monrós JL, Dumont R, Solsona E.**
    El tratamiento locorregional del carcinoma de pene. Arch Esp Urol 1991; 44: 667.
12. **Srinivas V, Morse M, Herr E, Sogani P, Whitmore W.**
    Penile cancer: relation of node extent of nodal metastasis to survival. J Urol 1987; 137: 880.
13. **Dexeus FH, Logothetis CJ, Sella A, Amato R, Kilbourn R, Fitz K, Striegel A.**
    Combination chemotherapy with methotrexate, bleomycin and cisplatin for advanced squamous cell carcinoma of the male genital tract. J Urol 1991; 146: 1284–1287.
14. **Montie JE.**
    Follow-up after penectomy for penile carcinoma. Urol Clin North Am 1994; 21: 725.

5. TREATMENT

5.1 Primary lesion

Penile intraepithelial neoplasia

In cases of penile intraepithelial neoplasia, a penis-preserving strategy is strongly recommended. The following therapies have been used successfully: laser therapy (CO_2-laser or Nd-YAG), cryotherapy, local excision and Mohs' surgery. The therapeutic approach should be chosen according to the preference of the surgeon and the available technology.

Category Ta–1 G1–2

For patients who can guarantee regular follow-up, a penis-preserving strategy (laser therapy, local excision plus reconstructive surgery, brachytherapy) is strongly recommended. A pathological assessment of surgical margins is essential when applying these procedures (1). Local recurrence rates range between 12% and 17% (1–4). Meticulous follow-up is essential so that local disease recurrences can be treated as soon as possible. In patients who do not comply with regular follow-up procedures, partial amputation is an optional recommendation.

Category T1 G3, T ≥ 2

Partial or total amputation or emasculation according to tumour extent can be considered as standard therapies (5–7). A conservative strategy is an alternative in very carefully selected patients with tumours encompassing less than half of the glans in whom close follow-up can be carried out (8). Chemotherapy induction courses within the context of a clinical trial, followed by conservative procedures in cases of complete or partial response, can be considered as investigational recommendations. Promising results have been reported with the latter procedure, even in cases of corpora cavernosa infiltration (9).

Local disease recurrence

For local disease recurrence after conservative therapy, a second conservative procedure is strongly advised if no corpora cavernosa invasion is present (10). However, if there is a large or deep infiltrating recurrence, partial or total amputation is strongly recommended.

Radiotherapy

External beam irradiation or brachytherapy can ensure excellent results in infiltrating tumours less than 4 cm in diameter. Late sequelae (meatal stenosis, skin necrosis, etc) are not uncommon. A single technique gives better results than combined external irradiation and brachytherapy.

5.2 Regional nodes

In penile carcinoma, the success of therapy is related to lymph node status and treatment. Lymphadenectomy has been shown to be an effective therapy for patients with positive lymph nodes (11–13). However, this procedure is associated with a high morbidity rate of 30–50% (14), even with modern technical modifications (15,16). This morbidity precludes its prophylactic use, although some controversy still surrounds this aspect (17,18). The rational use of lymphadenectomy requires careful groin assessment and awareness of predictive factors for positive lymph nodes (11,19–21).

Non-palpable nodes

In patients at low risk of developing nodal micrometastases (pTis, pTa G1–2 or pT1 G1), a surveillance programme is strongly advised, as the probability of occult micrometastases occurring in inguinal lymph nodes is less than 16.5% (19,22,23). If patients are considered unfit for surveillance, 'modified' inguinal lymphadenectomy is suggested as an optional recommendation.

In cases of intermediate risk (T1 G2), vascular or lymphatic invasion and growth pattern should be taken into account before therapeutic decision-making (19–24). In patients with no vascular or lymphatic invasion, or a superficial growth pattern on the primary tumour, a surveillance programme is mandatory. However, modified lymphadenectomy is strongly recommended in cases of vascular or lymphatic involvement or of infiltrating growth pattern unless patients can reliably receive regular follow-up.

In patients at high risk of nodal involvement (T ≥ 2 or G3), modified or radical inguinal lymphadenectomy can be strongly recommended. In these patients, the incidence of occult metastases ranges between 68% and 73% (19,22–24).

A modified lymphadenectomy can be extended to a radical lymphadenectomy if positive nodes are present on frozen sections. A sentinel lymph node biopsy with isosulphan blue and/or 99m Tc-colloid sulphur should be considered before undertaking lymphadenectomy as an investigational procedure (25,26).

Palpable nodes with positive histopathology

Bilateral radical inguinal lymphadenectomy is strongly recommended as treatment for positive palpable nodes. Great controversy exists concerning when to perform pelvic lymphadenectomy as only a few patients with positive pelvic nodes have been rescued with this approach (27,28). Immediate or delayed pelvic lymphadenectomy could be performed in cases where two or more positive inguinal lymph nodes or extracapsular invasion are found on frozen section biopsies or standard pathology examination. In these cases, the incidence of positive pelvic nodes increases up to 30% (27) and only microscopic metastases offer a chance for cure. On contralateral inguinal areas with no palpable nodes modified lymphadenectomy can initially be considered, and this may be extended if positive nodes are present in frozen section biopsies.

For patients with fixed inguinal masses or clinically positive pelvic nodes (CT scan or MRI), induction courses of chemotherapy followed by radical ilio-inguinal lymphadenectomy when a complete or partial response is achieved is strongly recommended (29). With systemic chemotherapy, a partial or complete clinical response can be achieved in 21–60% of cases (30–34). It is suggested that this strategy be adopted within the context of clinical trials. Another strategy is to use pre-operative radiotherapy (35), but the increased morbidity of lymphadenectomy after radiotherapy should be taken into account. Nevertheless, this approach is known to be beneficial with other types of cancer, e.g. rectal and squamous cell carcinoma of head and neck regions. When inguinal palpable nodes appear after a surveillance programme, two strong recommendations for treatment are made:

- Bilateral radical inguinal lymphadenectomy following similar criteria to those discussed above
- Inguinal lymphadenectomy, performed at the site of positive nodes in the case of a long disease-free interval. The development of positive nodes in both inguinal areas after surveillance should appear synchronously or within a very short interval. Thus, the probability of developing subsequent late lymph node metastases in the contralateral inguinal area after initial unilateral inguinal lymph node recurrence is around 10% (36). Therefore, unilateral lymphadenectomy could be warranted in these cases, but a follow-up programme is advised.

Adjuvant therapy is advised when there are two or more positive nodes or extracapsular nodal involvement on pathological examination as the prognosis of these patients is poorer than that of those with a single positive lymph node (22,37). Even though the results of randomized trials are not available, those of phase II trials suggest that adjuvant chemotherapy is beneficial for these patients (38). These adjuvant programmes should be performed within the context of controlled clinical trials. Fewer data are available on adjuvant radiotherapy (35).

5.3 GUIDELINES ON THE TREATMENT OF PENILE CARCINOMA

Recommendations for therapy of the primary lesion

1. Penile intraepithelial neoplasia: a penis-preserving strategy is strongly recommended.
2. Category Ta–1 G1–2: a penis-conserving strategy is strongly recommended. In patients who do not comply with regular follow-up procedures, partial amputation is an optional alternative.
3. Category T1 G3, T ≥ 2: partial or total amputation or emasculation according to tumour extent can be considered as standard therapies. Conservative therapies may be applied in very carefully selected patients. Chemotherapy followed by conservative procedures is an investigational option.
4. If local disease recurrence develops after conservative therapy, a second conservative procedure is strongly advised if there is no corpora cavernosa invasion. If there is a large or infiltrating recurrence, partial or total amputation is also strongly recommended.

Recommendations for regional node therapy if non-palpable nodes are present

1. In patients at low risk of developing occult metastases (pTis, pTa G1–2 or pT1 G1), a surveillance programme is strongly advised. For patients considered unfit for surveillance, modified lymphadenectomy is an optional recommendation.
2. In patients at high risk (pT ≥ 2 or G3), modified or radical lymphadenectomy is strongly recommended.
3. In cases of intermediate risk (pT1 G2), vascular or lymphatic invasion and growth pattern can be considered to aid the therapeutic decision. Strict surveillance could be an option in patients suitable for reliable regular follow-up.
4. Modified lymphadenectomy can be extended to radical lymphadenectomy if positive nodes are present.
5. A sentinel lymph node biopsy with isosulphan blue or/and 99m Tc-colloid sulphur should be considered as an investigational procedure before deciding inguinal Lymphadenectomy.

Recommendations for regional node therapy if palpable pathological positive nodes are present

1. Bilateral radical inguinal lymphadenectomy is the standard recommendation. Pelvic lymphadenectomy could be performed in cases where there are at least two positive inguinal nodes or extracapsular invasion. Modified lymphadenectomy can initially be considered on contralateral inguinal areas with no palpable nodes.
2. Patients with fixed inguinal masses or clinically positive pelvic nodes (on CT scan or MRI) are good candidates for induction chemotherapy followed by radical ilio-inguinal lymphadenectomy. Another strategy is to use pre-operative radiotherapy, but this has possibly harmful complications.
3. When inguinal palpable nodes appear after a surveillance programme, there are two possible recommendations: (a) bilateral radical inguinal lymphadenectomy; or (b) inguinal lymphadenectomy at the site of positive nodes according to the disease-free interval.
4. Adjuvant chemotherapy is advisable when there are at least two positive nodes or extracapsular nodal involvement. Another option is adjuvant radiotherapy.

5.4 Integrated therapy

In patients presenting with a primary tumour together with positive nodes, both problems should be managed simultaneously. In patients presenting initially with positive pelvic nodes, induction chemotherapy could be administered first and radical or palliative surgery or radiotherapy then indicated according to the tumour response.

5.5 Distant metastases

Chemotherapy courses or palliative therapy can be tried according to the patient's age, performance status and preference. Because of the poor efficacy of chemotherapy in metastatic disease, this approach is only recommended as an option in selected cases where prolonging survival may be important or in symptomatic patients with good performance status, in combination with palliative procedures.

5.6 Quality of life

With regard to quality of life, the patient's age, performance status, socio-economic status, sexual function and motivation, and the morbidity of different procedures should be considered as part of the decision-making process. Other important factors to take into account in therapeutic decision-making are the patient's psychological condition, economic status and geographical location, and tumour biology, since penile carcinoma is a malignant disease with a high probability of cure but a high degree of therapeutic morbidity.

5.7 Technical aspects

- With the primary lesion, the simplicity and morbidity of the procedures, and the surgeon's experience play a more important role in the choice of conservative strategy than anything else. Formal circumcision is mandatory before brachytherapy.
- Partial amputation traditionally required removal of 2 cm free margins. Although this is probably more than is necessary, it is essential to achieve free tumour margins with pathological confirmation.
- Radical inguinal lymphadenectomy should include the following anatomical landmarks: inguinal ligament, adductor muscle, sartorius muscle with the femoral vein and artery as the floor of dissection.
- Modified inguinal lymphadenectomy implies preservation of the saphenous vein and 1–2 cm reduction of the lateral and inferior boundaries. With these modifications, complications and morbidity rates are lower than with radical ilio-inguinal lymphadenectomy.
- Pelvic lymphadenectomy includes the external iliac lymphatic chain and the ilio-obturator chain (proximal boundary, iliac bifurcation, lateral boundary, ilio-inguinal nerve).

5.8 Chemotherapy

The chemotherapy regimen should be discussed with the medical oncologist. However, the following can be used as guidelines:

- Induction chemotherapy comprised of three to four courses of cisplatin and 5-fluorouracil in appropriate doses and sequence.
- Adjuvant chemotherapy with two courses of cisplatin and 5-fluorouracil may be sufficient, or vincristine, methotrexate and bleomycin may be administered once a week for 12 weeks on an outpatient basis (38).

A therapeutic schedule for the treatment of penile cancer is shown in Table 3.

Table 3: Therapeutic schedule for penile cancer

Lesion level	Therapy	Recommendations		
		Strong	**Optional**	**Investigational**
Primary tumour	Conservative therapy	Primary/recurrent Tis, Ta–1 G1–2	T1 G3, T ≥ 2 (fit patients for surveil-lance) with < 50% of glans affected	After chemotherapy according to tumour respons
	Total/partial amputation	Primary/recurrent T1 G3, T ≥ 2	Primary or recurrent Ta–1 G1–2 (conserva-tive therapy not feasible)	
	Radiotherapy	Infiltrating tumours < 4 cm	Primary T1-2 < 4cm Amputation refusal	In combination with chemotherapy
Regional (non-palpable nodes)	Surveillance	Tis, Ta G1–2, T1 G1, T1 G2 superficial growth vascular (-)	T2 G2–3 (preference and fit patients for follow-up)	Negative dynamic sentinel node
	Modified LND[1]	T1 G2 nodular growth or vascular (+), T1 G3 or any T2	T1 G2 vascular (-) flat growth (unfit patients for follow-up)	Positive dynamic sentinel node
Regional (palpable nodes)	Radical LND[2]	Positive nodes at presentation Positive nodes after surveillance	Plus adjuvant chemotherapy[3] or radiotherapy[4] (> one positive node) Unilateral LND on nodal site (disease-free interval > 3–6 months)	
	Chemotherapy +/- LND[3]	Fixed inguinal masses, pelvic nodes > 2 cm (fit patients for chemotherapy)		
	Radiotherapy[4] +/- LND		Fixed masses (unfit patients for chemotherapy)	
Distant metastases			Chemotherapy[3] or palliative therapy (according to performance status, age, etc)	

LND = lymphadenectomy.

[1] Modified LND can be extended to radical in cases where there are positive nodes.

[2] If unilateral non-palpable nodes on the opposite side, modified LND can be carried out. Pelvic LND for more than one positive inguinal node only.

[3] Chemotherapy should be discussed with the medical oncologist and preferably carried out in the context of clinical trials.

[4] Radiotherapy has inconsistent results and high morbidity associated with surgery.

5.9 REFERENCES

1. **Hoffman MA, Renshaw AA, Loughlin KR.**
Squamous cell carcinoma of the penis and microscopic margins: how much margin is needed for local cure? Cancer 1999; 85: 1565.
2. **Bandieramonte G, Santoro O, Boracchi P, Pival L, Pizzocaro G, De-Palo G.**
Total resection of glans penis surface by CO_2 laser microsurgery. Acta Oncol 1988; 27: 575.
3. **Tietjen DN, Malek RS.**
Laser therapy of squamous cell dysplasia and carcinoma of the penis. Urology 1998; 52: 559.
4. **Windahl T, Hellsten S.**
Laser treatment of localised squamous cell carcinoma of the penis. J Urol 1995; 154: 1020.
5. **Fossa DS, Hall KS, Johannessen NR, Urnes T, Kaalhus O.**
Cancer of the penis: experience at the Norwegian Radium Hospital 1974–1985. Eur Urol 1997; 13: 372.
6. **Hoppmann HJ, Fraley EE.**
Squamous cell carcinoma of the penis. J Urol 1978; 120: 393.
7. **Horenblas S, van Tinteren H, Delemarre JFM, Boon TA, Moonen LMF, Lustig W.**
Squamous cell carcinoma of the penis. II. Treatment of the primary tumor. J Urol 1992; 147: 1533.
8. **Horenblas S.**
Surgical management of carcinoma of the penis and scrotum. In: Medical Radiology. Diagnostic Imaging and Radiation Oncology. Carcinoma of the Kidney and Testis, and Rare Urologic Malignancies. Petrovich Z, Baert L, Brady LW (eds). Springer Verlag: Berlin, 1999; 341–354.
9. **Bandieramonte G, Lepera P, Koronel R, Moglia D, Piva L, Pizzocaro G.**
Primary systemic chemotherapy and conservative surgery of exophytic T1 N0 carcinoma of the penis. Eur. Urol. Abstract Xth Congress of E.A.U. abstract 88. p. 166.
10. **Koch MO, Smith JA.**
Local recurrence of squamous cell carcinoma of the penis. Urol Clin North Am 1994; 21: 739.
11. **Lopes A, Hidalgo GS, Kowallski LP, Torloni H, Rossi BM, Fonseca FP.**
Prognostic factors in carcinoma of the penis: multivariate analysis of 145 patients treated with amputation and lymphadenectomy. J Urol 1996; 156: 1637.
12. **Fraley EE, Zhang G, Manivel C, Niehans GA.**
The role of ilioinguinal lymphadenectomy and significance of histological differentiation in treatment of carcinoma of the penis. J Urol 1989; 142: 1478.
13. **Ornellas AA, Seixas ALC, Marota A, Wisnescky A, Campos F, de Moraes JR.**
Surgical treatment of invasive squamous cell carcinoma of the penis: retrospective analysis of 350 cases. J Urol 1994; 151: 1244.
14. **Johnson DE, Lo RK.**
Complications of groin dissection in penile carcinoma. Experience of 101 lymphadenectomies. Urology 1984; 24: 312–314.
15. **Catalona WJ.**
Modified inguinal lymphadenectomy for carcinoma of the penis with preservation of saphenous veins: Technique and preliminary results. J Urol 1988; 140: 306.
16. **Solsona E, Iborra I, Ricós JV, Monrós JL, Dumont R, Casanova J.**
Safety and morbidity of modified inguinal lymphadenectomy in patients with penis cancer.
Eur Urol 1999; 35(Suppl 2): 490.
17. **Grabstald H.**
Controversies concerning lymph node dissection for cancer of the penis. Urol Clin North Am 1980; 7: 793.
18. **Puras A, Rivera-Herrera J, Miranda G, Gonzalez-Flores B, Fortuño R.**
Role of superficial inguinal lymphadenectomy in carcinoma of the penis.
J Urol 1995; 153: 246A (abstract 69).
19. **Solsona E, Iborra I, Ricós JV, Monrós, Dumont R, Casanova J, Calabuig C.**
Corpus cavernosum invasion and tumor grade in the prediction of lymph node condition in penile carcinoma. Eur Urol 1992; 22: 115–118.
20. **Morgensterm NJ, Slaton JW, Levy DA, Ayala AG, Santos MW, Pettaway CA.**
Vascular invasion and tumor stage are independent prognosticators of lymph node (LN) metastasis in squamous penile cancer (SPC). J Urol 1999; 161: 608.
21. **Villavicencio H, Rubio J, Regalado R, Chéchile G, Algaba F, Palou J.**
Grade, local stage and growth pattern as prognostic factors in carcinoma of the penis. Eur Urol 1997; 32: 442.
22. **Horenblas S, Tinteren HV.**
Squamous cell carcinoma of the penis. IV. Prognostic factors of survival: analysis of tumor, nodes and metastasis classification system. J Urol 1994; 151: 1239.
23. **Theodorescu D, Russo P, Zhang ZF, Morash C, Fair WF.**

Outcomes of initial surveillance of invasive squamous cell carcinoma of the penis and negative nodes. J Urol 1996; 155: 1626.

24. **Pizzocaro G, Piva L, Bandieramonte G, Tana S.**
Up-to-date management of carcinoma of the penis. Eur Urol 1997; 32: 5.

25. **Horenblas S.**
Surgical management of carcinoma of the penis and scrotum. In: Medical Radiology. Diagnostic Imaging and Radiation Oncology. Carcinoma of the Kidney and Testis, and Rare Urologic Malignancies. Petrovich Z, Baert L, Brady LW (eds). Springer Verlag: Berlin, 1999; 341–354.

26. **Pettaway CA, Jularbal FA, Babaian RJ, Dinney CPN, Pisters LL.**
Intraoperative lymphatic mapping to detect inguinal metastases in penile carcinoma: results of a pilot study. J Urol 1999; 161: 612.

27. **Horenblas S, van Tinteren H, Delemarre JFM, Moonen LM, Lustig V, van Waardenburg EW.**
Squamous cell carcinoma of the penis. III. Treatment of regional lymph nodes. J Urol 1993; 149: 492–497.

28. **Pow Sang JE, Benavente V, Pow Sang JM, Pow Sang M.**
Bilateral ilioinguinal lymph node dissection in the management of cancer of the penis. Semin Surg Oncol 1990; 6: 241.

29. **Fisher HA, Barada JH, Horton J.**
Neoadjuvant therapy with cisplatin and 5-fluorouracil for stage III squamous cell carcinoma of the penis. Acta Oncol 1990; 27: A-653 (abstract 352A).

30. **Dexeus FH, Logothetis CJ, Sella A, Amato R, Kilbourn R, Fitz K, Striegel A.**
Combination chemotherapy with methotrexate, bleomycin and cisplatin for advanced squamous cell carcinoma of the male genital tract. J Urol 1991; 146: 1284–1287.

31. **Corral DA, Sella A, Pettaway CA, Amato RJ, Logothetis CJ, Ellerhorst J.**
Combination chemotherapy for metastatic or locally advanced genitourinary squamous cell carcinoma: a phase II study of methotrexate, cisplatin and bleomycin (MPB). J Urol 1998; 159: 625.

32. **Haas GP, Blumesnstein BA, Gagliano RG, Russell CA, Rivkin SE, Culkin DJ, Wolf M, Crawford ED.**
Cisplatin, methotrexate and bleomycin for the treatment of carcinoma of the penis: a Southwest Oncology Group study. J Urol 1999; 161: 1823–1825.

33. **Husseim AM, Benedetto P, Sridhar KS.**
Chemotherapy with cisplatin and 5 fluorouracil for penile and urethral squamous cell carcinomas. Cancer 1990; 65: 433.

34. **Pizzocaro G, Piva L, Nicolai N.**
Improved management of nodal metastases of squamous cell carcinoma of the penis. J Urol 1995; 153: 246 (abstract 69).

35. **Gerbaulet A, Lambin P.**
Radiation therapy of cancer of the penis. Urol Clin North Am 1992; 19: 325.

36. **Fair WR, Pérez CA, Anderson T.**
Cancer of the urethra and penis. In: Cancer: Principles and Practice of Oncology. De Vita V, Hellman S, Rosemberg SA (eds). Lippincott Company: Philadelphia, 1989; 1063–1070.

37. **Srinivas V, Morse M, Herr E, Sogani P, Whitmore W.**
Penile cancer: Relation of node extent of nodal metastasis to survival. J Urol 1987; 137: 880.

38. **Pizzocaro G, Piva L.**
Adjuvant and neoadjuvant vincristine, bleomycin and methotrexate for inguinal metastases from squamous cell carcinoma of the penis. Acta Oncol 1988; 27: 823.

6. FOLLOW-UP

Penile carcinoma is one of the few solid tumours in which lymphadenectomy can provide a high cure rate even if lymph nodes are involved. This is related to its particular biology, as the disease essentially develops in a stepwise fashion. However, penectomy and inguinal node dissection are associated with important morbidity. Urologists are faced, therefore, with the dilemma of reaching an appropriate balance between decreasing the morbidity with conservative procedures and disease control. In this context, follow-up is crucial in order to achieve similar survival rates to those achieved with definitive surgery. Moreover, most relapses occur during the first 2 years and late recurrences, although uncommon, can be present. Penile carcinoma is associated with poor socio-economic conditions, thus close surveillance cannot always be performed.

6.1 Why follow up?

With respect to the primary lesion, the local disease recurrence rate is extremely variable according to the type

of therapy carried out. With partial or total penectomy, the incidence of local recurrence ranges from 0% to 7% (1,2); with conservative therapies, this might increase to 50% (2–5). Nevertheless, local disease recurrence does not have a negative impact on cause-specific survival provided an early diagnosis is made (6).

Controversy remains as to whether early or delayed lymphadenectomy should be carried out in patients with initial non-palpable inguinal lymph nodes. Some authors achieve similar survival rates with both approaches (5,7). However, a surveillance programme implies the use of close follow-up as late diagnosis seems to be a negative prognostic factor.

In summary, the potential development of local disease recurrence and inguinal lymph nodes in patients treated with conservative approaches and the possibility of curing patients after early detection justify the need for follow-up in patients with penile carcinoma.

6.2 How to follow up?

As penile and inguinal lymph nodes are externally situated areas, follow-up in patients with penile carcinoma is based essentially on inspection and physical evaluation. In patients with initially palpable inguinal nodes, the reliability of physical evaluation with respect to pathological examination ranges from 47–86% (8,9). Moreover, in patients with non-palpable lymph nodes initially, the development of palpable nodes during the follow-up means metastases in 100% of cases.

CT scans and chest X-rays can be carried out in addition in order to identify pelvic lymph nodes or distant metastases in specific circumstances as the tumour spreads mainly into these areas. Other diagnostic tests should be used in symptomatic patients.

6.3 When to follow up?

The follow-up interval and strategies for patients with penile cancer are directly related to the initial treatment of the primary lesion and regional lymph nodes.

Primary tumour

If the primary lesion was treated with conservative therapy (local resection, laser therapy, brachytherapy, Mohs' procedure, associated therapies), a follow-up interval of 2 months for 2 years and then every 3 months for a further year is recommended because most local disease recurrences occur in this period. Long-term follow-up is also recommended every 6 months because late local recurrences have been observed (10). Patient self-evaluation is also advisable and patients should be informed about the possible warning signals. This follow-up schedule is advised because the disease recurrence rate is high and follow-up increases the chance of improving the cure rate.

If patients were treated with partial or total penectomy, a follow-up appointment every 4 months for 2 years, then at 6-monthly intervals for 1 year and annually thereafter is recommended. For the latter period, no hard data are available to suggest a specific interval. This schedule is recommended because local disease recurrence, although infrequent, usually occurs very early and because an early diagnosis is necessary because of the aggressive behaviour of the tumour (6).

Regional areas

If a surveillance programme was implemented after the primary tumour was removed, a groin evaluation every 2 months for 2 years, then every 3 months for the next year and then every 6 months for a further 2 years is recommended. No CT scan and chest X-rays are necessary. The rationale for this scheme is based on the fact that most inguinal lymph node recurrences are detected during the first 2 years. Moreover, when recurrences develop their growth is very quick and the prognosis is related to the number, size and bilaterality of the lymph nodes (11,12). Very close follow-up is therefore advisable.

If inguinal lymphadenectomy was performed and no tumour was found on pathological examination of the specimen, a physical evaluation is recommended every 4 months for 2 years and then every 6 months for the next year; subsequently, it is not completely necessary to carry out follow-up. In these cases, a local or distant relapse is rare if a radical procedure and extensive pathological examination have been performed. The follow-up is focused essentially on the quality of life of these patients as inguinal lymphadenectomy has a high morbidity rate.

If inguinal lymphadenectomy was performed and positive lymph nodes were observed on pathological examination, specific follow-up cannot be recommended as many variables need to be taken into account, including:

- The number of positive lymph nodes (uni- or bilaterality)
- Whether pelvic lymphadenectomy performed, with or without positive lymph nodes
- The adjuvant therapy carried out and the scheme used.

In relation to these variables, the physical examination, CT scan, chest X-ray and the appropriate intervals between them should be defined by each institution.

Bone scans and other tests are only recommended in symptomatic patients. Quality of life assessment should essentially encompass sexual activity and lymphadenectomy morbidity (lymphoedema). The follow-up schedule is summarized in Table 4.

Table 4: Follow-up schedule for penile cancer

Lesion level	Therapy	Interval			Examinations	
		Years 1 and 2	Year 3	Years 4 and 5	Mandatory	Advisable
Primary tumour	Conservative therapy	2 months	3 months	6 months	Physical/self-examination/ QOL	
	Partial/total penectomy	4 months	6 months	Yearly	Physical/self-examination/ QOL	
Regional approach	Surveillance	2 months	3 months	6 months	Physical/self-examination/ QOL	Cytology or biopsy if unclear clinical findings
	LND (pN0)	4 months	6 months	Not necessary	Physical/self-examination/ QOL	
	LND (pN+)	Institutional protocol[1]	Institutional protocol[1]	Institutional protocol[1]	Physical/self-examination/ QOL/CT scan/ Chest X-ray	Bone scan (symptoms)

LND = lymphadenectomy; QOL = quality of life (physical and sexual); CT = computed tomography.

[1] Based on the therapeutic approach applied. It is advisable, however, to carry out follow-up every 2–3 months for 2 years, then every 4–6 months during the third year and every 6–12 months thereafter.

6.4 GUIDELINES FOR FOLLOW-UP IN PENILE CANCER

Primary tumour

1. Patients treated with conservative therapies: follow-up every 2 months for 2 years, then every 3 months for 1 more year; long-term follow-up is also recommended every 6 months. Physical self-examination should be performed regularly.
2. Patients treated with partial or total penectomy: follow-up every 4 months for 2 years, twice during the third year and then annually is recommended.

Regional nodes and distant metastasis

1. If a surveillance programme was implemented after the primary tumour was removed, a groin evaluation every 2 months for 2 years, then every 3 months for 1 more year and every 6 months for the next 2 years is recommended.
2. If inguinal lymphadenectomy was performed (pN0), physical evaluation is recommended every 4 months for 2 years, then every 6 months for 1 more year. After this, it is not absolutely necessary to carry out follow-up.
3. If inguinal lymphadenectomy was performed (pN1-3), specific follow-up cannot be recommended. Physical examination, CT scan, chest X-ray and the appropriate intervals between them should be defined by each institution.
4. Bone scans and other tests are only recommended in symptomatic patients.

6.5 REFERENCES

1. **Ricós JV, Casanova JL, Iborra I, Monrós JL, Dumont R, Solsona E.**
   El tratamiento locorregional del carcinoma de pene. Arch Esp Urol 1991; 44: 667.
2. **Horenblas S, van Tinteren H, Delemarre JFM, Boon TA, Moonen LMF, Lustig W.**
   Squamous cell carcinoma of the penis. II. Treatment of the primary tumor. J Urol 1992; 147: 1533.
3. **Bandieramonte G, Santoro O, Boracchi P, Pival L, Pizzocaro G, De-Palo G.**
   Total resection of glans penis surface by CO_2 laser microsurgery. Acta Oncol 1988; 27: 575.
4. **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 Rad Oncol Bios Phys 1993; 25: 623.
5. **Narayana AS, Olney LE, Loening SA, Weimar GW, Culp DA.**
   Carcinoma of the penis. Analysis of 219 cases. Cancer 1982; 49: 2185.
6. **Lerner SE, Jones JG, Fleischmann J.**
   Management of recurrent penile cancer following partial or total penectomy. Urol Clin North Am 1994; 21: 729.
7. **Young MJ, Reda DJ, Waters WB.**
   Penile carcinoma: a twenty-five-year experience. Urology 1991; 38: 528.
8. **Horenblas S, van Tinteren H, Delemarre JFM, Moonen LM, Lustig V, van Waardenburg EW.**
   Squamous cell carcinoma of the penis. III. Treatment of regional lymph nodes. J Urol 1993; 149: 492–497
9. **Solsona E, Iborra I, Ricós JV, Monrós JL, Dumont R, Casanova J, Calabuig C.**
   Corpus cavernosum invasion and tumor grade in the prediction of lymph node condition in penile carcinoma. Eur Urol 1992; 22: 115–118.
10. **Horenblas S, Newling DW.**
    Local recurrence tumour after penis-conserving therapy. A plea for long-term follow-up. Br J Urol 1993; 72: 976.
11. **Horenblas S, Tinteren HV.**
    Squamous cell carcinoma of the penis. IV. Prognostic factors of survival: analysis of tumor, nodes and metastasis classification system. J Urol 1994; 151: 1239.
12. **Srinivas V, Morse M, Herr E, Sogani P, Whitmore W.**
    Penile cancer: relation of node extent of nodal metastasis to survival. J Urol 1987; 137: 880.

7. ABBREVIATIONS USED IN THE TEXT

CT: computed tomography
MRI: magnetic resonance imaging
TNM: tumour, node, metastasis
QOL: quality of life

* These EAU Guidelines on Penile Cancer are endorsed by all members of the EAU Oncological Urology Group (Chairman: C. Abbou). Members of the Oncological Urology Group are the EAU Working parties on: Bladder Cancer, Renal Cancer, Prostate Cancer, Testis Cancer & Penile Cancer.