PERGAMON

European Journal of Cancer 37 (2001) 198–203

European Journal of Cancer

www.ejconline.com

Radiation therapy alone or combined surgery and radiation therapy in squamous-cell carcinoma of the penis?☆

A. Zouhair [a], P.A. Coucke [a], W. Jeanneret [a], P. Douglas [a], H.P. Do [a], P. Jichlinski [b], R.O. Mirimanoff [a], M. Ozsahin [a,*]

[a] *Department of Radiation Oncology, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland*
[b] *Department of Urology, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland*

Received 14 April 2000; received in revised form 10 August 2000; accepted 26 September 2000

Abstract

To assess the prognostic factors and the outcome in patients with squamous-cell carcinoma of the penis, a retrospective review of 41 consecutive patients with non-metastatic invasive carcinoma of the penis, treated between 1962 and 1994, was performed. The median age was 59 years (range: 35–76 years). According to the International Union Against Cancer (UICC) 1997 classification, there were 12 (29%) T1, 24 (59%) T2, 4 (10%) T3 and 1 TX (2%) tumours. The N-classification was distributed as follows: 29 (71%) patients with N0, 8 (20%) with N1, 3 (7%) with N2 and 1 (2%) with N3. Forty-four per cent ($n=18$) of the patients underwent surgery: partial penectomy with ($n=4$) or without ($n=12$) lymph node dissection, or total penectomy with ($n=1$) or without ($n=1$) lymph node dissection. 23 patients were treated with radiation therapy alone, and all but 4 of the patients who were operated upon received postoperative radiation therapy ($n=14$). The median follow-up period was 70 months (range 20–331 months). In a median period of 12 months (range 5–139 months), 63% ($n=26$) of the patients relapsed (local in 18, locoregional in 2, regional in 3 and distant in 3). Local failure (stump in the operated patients, and the tumour bed in those treated with primary radiation therapy) was observed in 4 out of 16 (25%) patients treated with partial penectomy ±postoperative radiotherapy versus 14 out of 23 (61%) treated with primary radiotherapy ($P=0.06$). 15 (83%) out of 18 local failures were successfully salvaged with surgery. In all patients, 5- and 10-year survival rates were 57% (95% confidence interval (CI), 41–73%) and 38% (95% CI, 21–55%), respectively. The 5-year local and locoregional rates were 57% (95% CI, 41–73%) and 48% (95% CI, 32–64%), respectively. In patients treated with primary radiotherapy, 5- and 10-year probabilities of surviving with penis preservation were 36% (95% CI, 22–50%) and 18% (95% CI, 2–34%), respectively. In multivariate analyses, survival was significantly influenced by the N-classification, and surgery was the only independent factor predicting the locoregional control. We conclude that, in patients with squamous-cell carcinoma of the penis, local control is better in patients treated with surgery. However, there seems to be no difference in terms of survival between patients treated by surgery and those treated by primary radiotherapy ±salvage surgery, with 39% having organ preservation.

Keywords: Penile cancer; Radiotherapy; Surgery; Organ preservation

1. Introduction

Squamous-cell carcinoma of the penis is a rare disease, and its incidence is estimated at 1/100 000 in the male population of the North American and European countries [1]. The mean age at presentation is 60 years. Many epidemiological studies have suggested that penile carcinoma is more frequent in uncircumcised men, poor genital hygiene and human papilloma virus infection [2–7].

The treatment is traditionally curative surgery [8–12]. However, more conservative modalities, such as external radiation and/or interstitial brachytherapy, can also result in good local control with the advantage of preserving a functional organ in early-stage penile cancers [13–20]. If this latter option is chosen, surgery can be reserved for salvage. To our knowledge, there are no randomised studies comparing different treatment options. Thus, we wanted to assess the prognostic factors and the outcome in patients with squamous-cell carcinoma of the penis treated in our department.

* Corresponding author. Tel. +41-21-314-4604; fax: +41-21-314-4601.
E-mail address: eozsahin@hola.hospvd.ch (M. Ozsahin).

☆ Presented at the 39th Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Orlando, Florida, 19–23 October 1997.

0959-8049/01/$ - see front matter
PII: S0959-8049(00)00368-3

2. Patients and methods

A retrospective study of 41 consecutive patients with non-metastatic invasive squamous-cell carcinoma of the penis, treated between 1962 and 1994, was performed. The median age was 59 years (range: 35–76 years). 8 (20%) patients were circumcised, and only 2 (5%) had a history of venereal disease. Existence of a penile mass was the first symptom in 32 (78%) patients. The anatomical site was distributed as follows: glans in 17 (41%), prepuce in 9 (22%), shaft in 8 (20%), coronary localisation in 4 (10%), prepuce and glans in 2 (5%) and shaft and prepuce in 1 (2%). All of the patients were classified according to the International Union Against Cancer (UICC) 1997 classification. Operated patients were staged pathologically, and those treated with radiation therapy alone were staged clinically. There were 12 (29%) T1, 24 (59%) T2, 4 (10%) T3 and 1 TX (2%) tumours [21]. The N-classification was distributed as follows: 29 (71%) patients with N0, 8 (20%) with N1, 3 (7%) with N2 and 1 (2%) with N3. 13 (32%) patients had grade 1, 7 (17%) grade 2 and 9 (22%) grade 3 tumours (grade was not determined in 12 (29%)).

Forty-four per cent ($n=18$) of the patients underwent surgery: partial penectomy with ($n=4$) or without ($n=12$) lymph node dissection, or total penectomy with ($n=1$) or without ($n=1$) lymph node dissection. All but 4 of the patients who underwent surgery had primary ($n=23$) or postoperative ($n=14$) radiotherapy (RT) to the penis and inguinal lymph nodes ($n=20$), penis alone ($n=9$), or inguinal lymph nodes alone ($n=8$). The details of the different treatment modalities are given in Table 1. Indications for postoperative radiotherapy were positive surgical margins and/or lymph node involvement.

In patients receiving primary RT ($n=23$), the treatment volume included the penis in all patients (22 external RT including a brachytherapy boost in 4 patients, and 1 patient treated with brachytherapy alone) and locoregional nodes in 22 patients. The dose to the penis ranged from 45–74 Gy given in 1.8–2 gray (Gy)/fractions. The most commonly used radiation dose was 60 Gy in 30 fractions over 6 weeks. The only patient treated with low dose rate brachytherapy alone (50–100 cGy/h; Paris system) received 65 Gy using Ir192 wires guided with Plexiglass templates to maintain the geometry of the implant. 4 patients boosted by low dose rate interstitial implants (50–100 cGy/h; Paris system), received a dose ranging from 15–25 Gy. The dose to the nodal areas ranged from 36 to 66 Gy given in 1.8–2 Gy/fractions.

Table 1
Characteristics of the patients according to different treatment modalities

	n	%
Surgery		
Total penectomy and lymph node dissection	1	2
Total penectomy	1	2
Partial penectomy and lymph node dissection	4	10
Partial penectomy	12	29
Radiotherapy		
Primary radiotherapy	23	56
Postoperative radiotherapy	14	34
No postoperative radiotherapy	4	10

Parallel opposed lateral (Co60 or 6 MV photons) fields were used to encompass the entire length of the penis. The physical set-up consisted of a rectangular wax block placed around the shaft of the penis to achieve a uniform dose distribution according to the Toronto technique [20].

Locoregional lymph nodes were treated using parallel opposed anterior posterior/posterior anterior (AP/PA) fields or the 'box' technique using high energy photons (18 MV). Booster doses to the positive nodes were delivered using suitable energy electrons.

The median and mean follow-up period was 70 and 96 months, respectively (range: 20–331 months).

Means were compared by Student's *t*-test. Proportions were compared using the Chi-square test for values greater than 5, and Fisher's exact test for those less than or equal to 5. Kaplan–Meier product-limit estimates were used to evaluate the survival, local control and locoregional control [22]. Time to any event was measured from the date of pathological diagnosis. The events were death (all causes of death included) for overall survival, and local or locoregional relapse for local and locoregional control (patients who died without local or locoregional relapse were censored at time of death), respectively. Information pertaining to the cause of death was always obtained from the clinical records and/or death certificates. No autopsies were carried out. 95% Confidence intervals (CI) were calculated from standard errors. Differences between groups were assessed using the logrank test [23]. The Bonferroni method was used to adjust the individual *P*-values in order to obtain overall significance levels depending on the number of parameters tested (*P*-adjusted equals individual *P*-value times the number of parameters tested) [24]. Multivariate analyses were carried out using the Cox stepwise regression analysis to determine the independent contribution of each prognostic factor [25].

3. Results

In a median period of 12 months (range: 5–139 months), 63% ($n=26$) of the patients relapsed (local in 18, locoregional in 2, regional in 3 and distant in 3). Local failure was observed in 4 out of 16 (25%) patients treated with partial penectomy ±postoperative radiotherapy compared with 14 out of 23 (61%) treated with

Table 2
Distribution of the relapses according to different treatment modalities

	n	%	*P* value*
Total	26	63	
Local	18	44	
Partial penectomy[a] ± postoperative radiotherapy	4 (out of 16)		0.06
Primary radiotherapy[b]	14 (out of 23)		
Locoregional[c]	2	5	
Regional[d]	3	7	
Distant	3	7	

*Fisher's exact test (two-sided).
[a] Relapse on the surgical stump.
[b] Relapse on the tumour bed.
[c] Local and inguinal relapse.
[d] Inguinal relapse alone.

primary radiotherapy ($P = 0.06$). Among the 12 patients with clinically positive lymph nodes, 5 underwent inguinal lymphadenectomy and postoperative radiotherapy and 7 radiotherapy alone. We observed 3 regional failures: 2 in the surgery and 1 in the radiotherapy group. The details are given in Table 2. 15 (83%) out of 18 local failures were successfully salvaged with surgery. At the time of analysis, among the 23 patients treated with primary radiotherapy, local control was obtained with organ preservation in 9 (39%) patients, and without organ preservation in 13 (57%) patients. One patient (4%) could not be salvaged.

In all patients, 5- and 10-year survival (Kaplan–Meier product-limit estimates) rates were 57% (95% CI, 41–73%) and 38% (95% CI, 21–55%), respectively. The 5- and 10-year local and locoregional control rates were 57% (95% CI, 41–73%) and 39% (95% CI, 21–59%) and 48% (95% CI, 32–64%) and 33% (95% CI, 16–40%), respectively.

Table 3
Univariate analyses (logrank test)

	n	5-year survival (%)	95% CI (%)	*P* value	Adjusted *P* value*
All patients	41	57	41–73		
Clinical T-classification					
T1	12	81	58–100	0.33	NS
T2	24	48	28–68		
T3	4	0	–		
TX	1	–	–		
Clinical N-classification					
N0	29	68	50–86	0.0002	0.001
N1	8	43	6–80		
N2	3	25	0–66		
N3	1	–	–		
Histological grade					
1	13	54	25–83	0.19	NS
2	7	33	0–70		
3	9	39	6–72		
?	12	83	62–100		
Circumcision					
No	33	55	38–72	0.61	NS
Yes	8	69	32–100		
Type of treatment					
Primary RT	23	62	41–83	0.82	NS
Surgery ±RT	18	55	30–80		

*Bonferroni correction.
NS, non significant; RT, radiotherapy; 95% CI, 95% confidence interval.

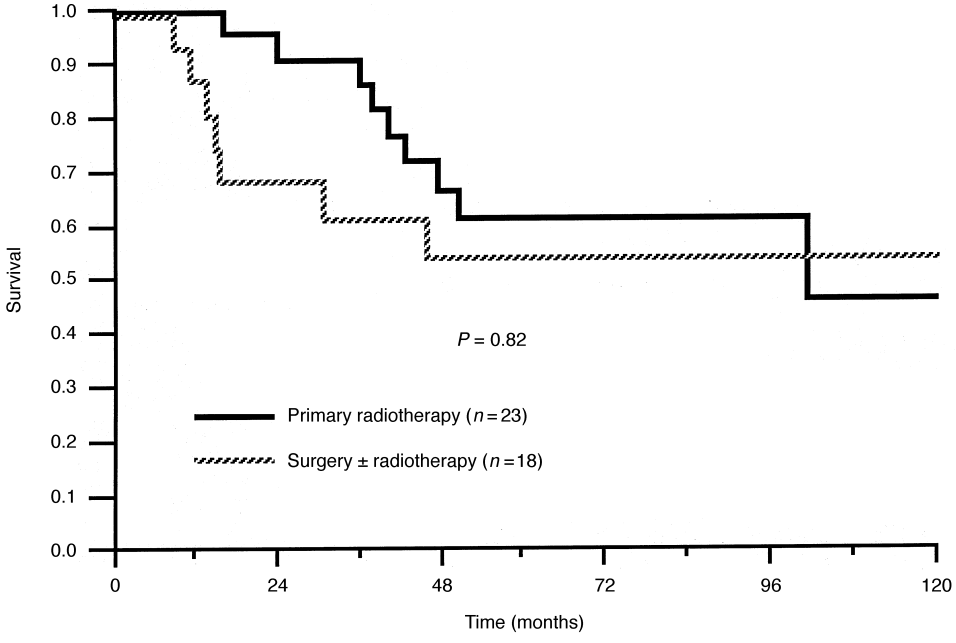

Fig. 1. Overall survival at 10 years according to the primary treatment modality.

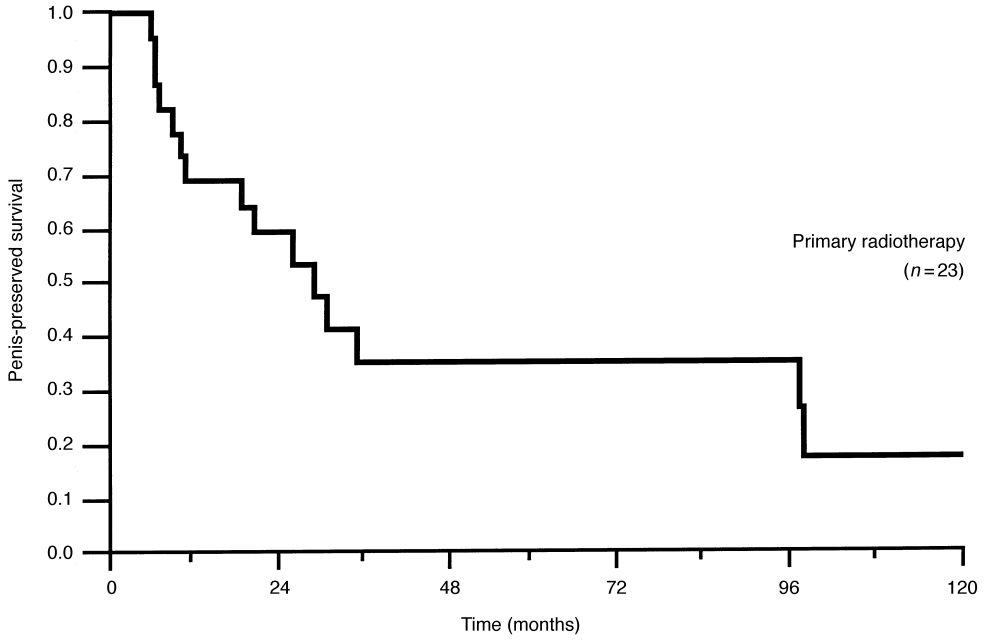

Fig. 2. Estimated survival with penis preservation at 10 years in 23 patients treated with primary radiotherapy ± salvage surgery.

In univariate analyses, among the various factors studied (clinical T- and N-classification, histological grade and the existence of a circumcision), only the clinical N-classification was a statistically significant prognostic factor for survival (Table 3). Local and locoregional control were significantly influenced only by the type of primary treatment (surgery ±radiotherapy versus primary radiotherapy; 81% (95% CI, 44–100%) versus 41% (95% CI, 25–57%) for local control, P = 0.009; 75% (95% CI, 54–96%) versus 31% (95% CI, 11–51%) for locoregional control, $P = 0.008$). The type of primary treatment did not influence survival (Fig. 1). In patients treated with primary radiotherapy, the 5- and 10-year probabilities of surviving with penis preservation was 36% (95% CI, 22–50%) and 18% (95% CI, 2–34%), respectively (Fig. 2). Salvage treatment consisted of excision alone ($n = 1$), partial ($n = 6$) or total penectomy ($n = 7$) in the 14 local failures in the primary radiotherapy group ($n = 23$). 4 patients relapsing in the surgery group ($n = 18$) were salvaged with a total penectomy.

In multivariate analyses (Cox model), statistically significant factors influencing the local and locoregional control were the type of primary treatment (surgery ±radiotherapy versus primary radiotherapy; $P = 0.02$ and 0.01, respectively) (Table 4). In contrast, survival was influenced only by the clinical N-stage (N0, 1 versus N2, 3; $P = 0.03$).

2 patients (9%) out of 23 patients treated with primary radiation therapy developed urethral stenosis following treatment, which were reversible after successful dilatation.

Table 4
Multivariate analyses (Cox model)

Factor	Relative risk	*P* value
Local control[a]		
Treatment (surgery ±RT[c] versus primary RT)	6.25*	0.02
Locoregional control[a]		
Treatment (surgery ±RT[c] versus primary RT)	5.65*	0.01
Survival[b]		
Clinical N-classification (N0, N1[c] versus N2, N3)	6.05**	0.03

*Surgery ±RT better than primary RT; **N0, N1 better than N2, N3. RT, radiotherapy; NS, statistically not significant.

[a] Analysis also includes clinical N-classification (N0, N1 versus N2, N3; NS), clinical T-classification (TX, T1, T2 versus T3; NS), histological grade (G?, G1 versus G2, G3; NS), tumour fixation (yes versus no; NS), and elective lymph node irradiation (yes versus no; NS).

[b] Analysis also includes clinical T-classification (TX, T1, T2 versus T3; NS), and histological grade (G?, G1 versus G2, G3; NS).

[c] Reference group.

4. Discussion

Penile carcinoma is an uncommon disease in developed countries while its incidence is higher in the developing ones. Several risk factors have been reported in the literature, such as poor genital hygiene, phimosis, venereal disease, smoking and association with human papilloma virus infection [2–7]. An important factor playing a protective role in the genesis of penis carcinoma is neonatal circumcision as encountered in Moslems and Jews [6,7]. Some authors do not agree with

Table 5
Conservative management of penile cancer: data from the literature

Author [Ref.]	Number of patients	Treatment	Total dose (Gy)	5-year local control (%)	Salvage surgery (*n*)	Organ preservation (%)	Late complications
Rozan [13]	184	BT alone	59	85	41	78	11 (penis necrosis)
	75	BT + XRT	59 + 40.5	88 (3-year)	27	64	5 (penis necrosis)
Delannes [17]	51	BT alone	60	67	7	86	20 (17 urethral stenosis, 3 skin sclerosis)
McLean [20]	26	XRT alone	35–60	61.5	5	85	7 (urethral stenosis or phimosis)
Modig [27]	25	XRT + bleomycin	56–58	75	5	75	1 (urethral stenosis)
Sarin [28]	72	XRT±BT	70	66	26	61	7 (urethral stenosis and/or stricture)
Neave [32]	24	BT	55.6	?	9/20	55	3 (urethral stricture)
	20	XRT	50–55	?	4/10	60	2 (urethral stricture)
Soria [33]	72	BT±XRT	60–70	?	18	72	5 (1 penis necrosis, 1 urethral stenosis, 1 orchitis, and 2 treatment-related deaths)
Present series	23	XRT±BT	45–74	41[a]	14	39	2 (urethral stenosis)

BT, brachytherapy; XRT, external radiotherapy.
[a] 95% CI, 25–57%.

that [26]. In our study, the majority of patients (33/41; 80%) were not circumcised.

Narayana and colleagues [9] reported a retrospective study of 107 patients with penile mass, while a study of 24 patients were also reported in Sweden by Modig and colleagues [27] and 43 patients by Sarin and colleagues [28]. In our series, the first symptom was penile mass in 32 patients (78%), and glans and prepuce were the predominant sites in 28 patients (68%). Rozan and colleagues [13] reported in their large survey of 259 patients with penile carcinoma, 130 with tumour involving the glans, 44 the prepuce, 83 in both sites and 2 patients with shaft infiltration alone.

Radical or partial penectomy is traditionally the standard management of invasive squamous-cell carcinoma of the penis [8–11,29,30]. It is obvious that local failure is very low after total penectomy or partial penectomy (2–6%), however, psychosexual morbidity is important, and rarely reported in surgical series [31]. Non-mutilating conservative therapies, such as laser resection, brachytherapy and/or external radiation therapy are alternative modalities offering good local control with functional organ preservation [13–20,32,33] (Table 5). In our series, local failure in patients undergoing partial penectomy ±postoperative radiotherapy was 4 out of 16 (25%). There were no relapses either in the 2 patients who underwent total penectomy or in the 2 patients with positive surgical margins and who underwent partial penectomy and postoperative radiotherapy. In our group of 23 patients treated with radiotherapy as a first curative intent, we observed 14 local relapses (61%), which is much higher than has been reported in other conservative treatment series (Table 5). Among the 14 local failures, only 5 patients received a total dose $\geqslant$64 Gy, whereas 9 had lower doses.

The management of regional nodes in penile cancer is controversial. Approximately 20% of the patients with clinical negative nodes have occult metastases. Inguinal lymphadenectomy remains questionable for clinically negative lymph nodes because 80% of the patients with pathologically uninvolved nodes would receive no benefit from surgery and yet be exposed to significant morbidity [12,34]. It has been suggested that patients with T2 grade 3, T3, and operable T4 tumours are suitable candidates for prophylactic inguinal lymphadenectomy [35]. In our series, we had only 1 clinically node-negative patient who became pN2 following surgery.

We conclude that, in patients with squamous-cell carcinoma of the penis, the local relapse rate is lower in patients treated with surgery. However, there seems to be no difference in terms of survival between patients treated by surgery and those treated by primary radiotherapy ±salvage surgery, with 39% having organ preservation. For small tumours, primary radiotherapy seems to be a reasonable treatment option if close follow-up is implemented, so that an important proportion of patients can have organ preservation. Nevertheless, with the introduction of better conformal techniques and/or the introduction of concomitant chemotherapy in future collaborative multicentric studies, better organ preservation can be obtained with less morbidity in this relatively rare malignancy.

References

1. Crawford ED, Dawkins CA. Cancer of the penis. In Skinner DG, Lieskowsky G, eds. *Diagnosis and Management of Genitourinary Cancer*. Philadelphia, WB Saunders, 1988, 549–563.
2. Maden C, Sherman KJ, Beckmann AM, *et al*. History of circumcision, medical conditions and sexual activity and risk of penile cancer. *J Natl Cancer Inst* 1993, **85**, 19–24.
3. Iversen T, Tretli S, Johansen A, Holte T. Squamous cell carcinoma of the penis and the cervix, vulva and vagina in spouses: is there any relationship? An epidemiological study from Norway, 1960–92. *Br J Cancer* 1997, **76**, 658–660.
4. Cupp MR, Malek RS, Goellner JR, Smith TF, Espy MJ. The detection of human papilloma virus deoxyribonucleic acid in

intra-epithelial, *in situ*, verrucous and invasive carcinoma of the penis. *J Urol* 1995, **154**, 1024–1029.
5. Favre M, Kremsdorf D, Jablonska S, *et al*. Two new human papillomavirus types (HPV 54 and 55) characterized from genital tumors illustrate the plurality of genital HPVs. *Int J Cancer* 1990, **45**, 40–46.
6. Schoen EJ. Neonatal circumcision and penile cancer. Evidence that circumcision is protective is overwhelming. *Br Med J* 1996, **46**, 313.
7. Pratt-Thomas HR, Heins HC, Latham E, Dennis EJ, McIver FA. Carcinogenic effect of human smegma: an experimental study. *Cancer* 1956, **9**, 671–680.
8. Fraley EE, Zhang G, Sazama R, Lange PH. Cancer of the penis: prognosis and treatment plans. *Cancer* 1985, **55**, 1618–1624.
9. Narayana AS, Olney LE, Loening SA, Weimar GW, Culp DA. Carcinoma of the penis: analysis of 219 cases. *Cancer* 1982, **49**, 2185–2191.
10. Ornellas AA, Correia-Seixas AL, 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**, 1244–1249.
11. Persky L, De Kernion J. Carcinoma of the penis. *CA: a Cancer Journal for Clinicians* 1986, **36**, 258–273.
12. Srinivas V, Choudary R, Ravikumar R, Metha H, Kundargi P, Phadke AG. Penile cancer: is lymphadenectomy necessary in all cases? *Urology* 1995, **46**, 710–712.
13. Rozan R, Albuisson E, Giraud B, *et al*. Interstitial brachytherapy for penile carcinoma: a multicentric survey (259 patients). *Radiother Oncol* 1995, **36**, 83–93.
14. Bissada NK. Conservative extirpative treatment of cancer of the penis. *Urol Clin North Am* 1992, **19**, 283–290.
15. Whindahl T, Hellsten S. Laser treatment for localized squamous cell carcinoma of the penis. *J Urol* 1995, **154**, 1020–1023.
16. Ardiet JM, Gérard JP, Romestaing P, *et al*. Traitement par curiethérapie à l'iridium 192 des épithéliomas de la verge. *J Urol* 1984, **90**, 557–561.
17. Delannes M, Malavaud B, Douchez J, Bonnet J, Daly NJ. Iridium-192 interstitial therapy for squamous cell carcinoma of the penis. *Int J Radiat Oncol Biol Phys* 1992, **24**, 479–483.
18. Gerbaulet A, Lambin P. Radiation therapy of cancer of the penis: indications, advantages and pitfalls. *Urol Clin North Am* 1992, **19**, 325–332.
19. Haile K, Delclos L. The place of radiation therapy in the treatment of carcinoma of the distal end of the penis. *Cancer* 1980, **45**, 1980–1984.
20. 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.
21. Sobin LH, Wittekind C. *TNM Classification of Malignant Tumours*. New York, Wiley-Liss, 1997, 167–169.
22. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958, **53**, 457–481.
23. Peto P, Pike MC, Armitage P, *et al*. Design and analysis of randomised clinical trials requiring prolonged observation of each patient: Part II. *Br J Cancer* 1977, **35**, 1–39.
24. Beck-Bornholdt HP, Dubben HH. Potential pitfalls in the use of p-values and in interpretation of significance levels. *Radiother Oncol* 1994, **33**, 171–176.
25. Cox DR. Regression models and life tables. *J Roy Stat Soc* 1972, **34**, 187–220.
26. Fleiss PM, Hodges F. Neonatal circumcision does not protect against penile cancer. *Br Med J* 1996, **312**, 779–780.
27. Modig H, Duchek M, Sjödin JG. Carcinoma of the penis: treatment by surgery or combined bleomycin and radiation therapy. *Acta Oncol* 1993, **32**, 653–655.
28. Sarin R, Norman AR, Steel GG, Horwich A. Treatment results and prognostic factors in 101 men treated for squamous carcinoma of the penis. *Int J Radiat Oncol Biol Phys* 1997, **38**, 713–722.
29. Das S. Penile amputations for the management of primary carcinoma of the penis. *Urol Clin North Am* 1992, **19**, 277–282.
30. Jones WG, Fosså SD, Hamers H, Van Den Bogaert W. Penis cancer: a review by the Joint Radiotherapy Committee of the European Organisation for Research and Treatment of Cancer (EORTC) Genito-Urinary and Radiotherapy Groups. *J Surg Oncol* 1989, **40**, 227–231.
31. Opjordsmoen S, Waehre H, Aass N, Fosså SD. Sexuality in patients treated for penile cancer: patient's experience and doctor's judgement. *Br J Urol* 1994, **73**, 554–560.
32. Neave F, Neal AJ, Hoskin PJ, Hope-Stone HF. Carcinoma of the penis: a retrospective review of treatment with iridium mould and external beam irradiation. *Clin Oncol* 1993, **5**, 207–210.
33. Soria JC, Fizazi K, Piron D, *et al*. Squamous cell carcinoma of the penis: multivariate analysis of prognostic factors and natural history in a monocentric study with a conservative policy. *Ann Oncol* 1997, **8**, 1089–1098.
34. Colberg JW, Andriole GL, Catalona WJ. Long-term follow-up of men undergoing modified inguinal lymphadenectomy for carcinoma of the penis. *Br J Urol* 1997, **79**, 54–57.
35. Horenblas S, van Tinteren H. Squamous cell carcinoma of the penis. IV. Prognostic factors of survival: analysis of tumor, nodes and metastasis classification. *J Urol* 1994, **151**, 1239–1243.