

Brachytherapy for penile cancer: Efficacy and impact on sexual function

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ABSTRACT

PURPOSE: Penis brachytherapy (PB) remains an alternative in the cancer treatment. The objective of this study was to assess the oncologic outcomes, sexual function, and the sexual behavior of men treated by PB for a cancer of the penis.

METHODS AND MATERIALS: Between 1992 and 2009, 47 patients with a cancer of the penis were treated by PB (¹⁹²Ir), in the Toulouse, Montpellier, and Barcelona cancer centers. The investigation into their sexuality was obtained by means of questionnaire. A total of 21 French patients were approached, of whom 19 (mean age = 73.2 years) agreed to answer the questionnaire (participation rate = 90.5%).

RESULTS: Oncologic data: The specific survival and the disease-free survival at 5 years was 87.6% (95% confidence interval, 72.4–94.7%) and 84% (95% confidence interval, 57.6–94.7%), respectively. The rate of preservation of the penis was 66% ($n = 31$). Sexual data: Among the 17 patients sexually active before brachytherapy, 10 patients remained sexually active after treatment (58.8%). Of the 18 patients who had erections before PB, 17 still had them after treatment (94.4%). Age was the main predictive factor.

CONCLUSION: The PB seems to have a moderated impact on the sexual functions and the sexual behavior of the patients. © 2014 American Brachytherapy Society. Published by Elsevier Inc.

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Keywords:

Penile carcinoma; Brachytherapy; IIEF score; Oncological data

Introduction

Penile carcinoma accounts for 0.4–0.6% of all malignant neoplasms among men in Europe (1, 2). Its incidence may reach 20% in some Asian, African, and South American countries.

Penile cancer is a disease of elderly men in Europe and North America, with a peak incidence in the sixth decade of life (3), although it may affect a younger age group in

developing countries. Most tumors of the penis are squamous cell carcinomas and occur most commonly on the glans, prepuce, and the coronal sulcus.

For small lesions, treatment enabling the penis body to be preserved, notably penis brachytherapy (PB) (4), is recommended to improve the quality of life. Surprisingly, sexuality, which is nevertheless an important component of the quality of life in men with cancer, has not been well studied after conservative treatment of penile cancer. By analyzing a previous series of 51 patients treated between 1971 and 1989, we obtained information about the persistence of sexuality and penile erections of patients (5), but we did not have access to information on the impact of PB on all sexual functions and sexual behavior. To answer these questions, we established a database in the Catalan and Occitan Oncology Group, which includes two cancer centers each in France and Spain. We analyzed the

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Table 1
Characteristics of the tumors

Parameters	Classification	N (%)
Histology	T1	33 (70.2)
	T2	5 (10.6)
	Unknown	9 (19.2)
Grade	Well differentiated	28 (59.6)
	Moderate differentiation	3 (6.4)
	Low differentiation	3 (4.3)
	Unknown	14 (29.7)
Size (mm)	<20	18 (38.3)
	20–30	13 (27.7)
	>30	1 (2.1)
	Unknown	15 (31.9)
Pathology	Epidermoid carcinoma	43 (91.5)
	Spino-cellular carcinoma	3 (6.4)
	Cuniculatum carcinoma	1 (2.1)
Localization	Glans	43 (91.5)
	Body	4 (8.5)

oncologic outcome of penile cancer, and conducted a survey by questionnaire on the sexual functions and behavior after PB treatment, in the two French centers.

Methods and materials

Population and treatment modalities

Between 1992 and 2009, 47 patients were treated for cancer of the penis by interstitial PB in the centers of Toulouse (Institut Claudius Regaud, $n = 31$), Montpellier (Centre Val D'Aurelle, $n = 4$), and Barcelona (Catalan Institute of Oncology and Hospital de Sant Pau, $n = 12$). At the time of PB, the mean age of the patients was 64.7 years (range, 38–84 years). The tumor characteristics are summarized in Table 1. None of the patients had palpable lymph nodes on initial physical examination. The treatment consisted in all cases of exclusive PB, low dose rate, with manual implantation of ^{192}Ir . All uncircumcised patients had been circumcised before treatment. A Foley catheter was left in place until removal of the sources. The parameters of PB are summarized in Table 2.

Sexuality questionnaire

To evaluate not only the sexual function but also the sexual behavior of patients after treatment, we used the grid BASIC IDEA of Lazarus (6) and Cottraux *et al.* (7) that addresses nine areas, namely Behavior (B), Affect (A), Sensation (S), Imagery (I), Cognition (C), Interpersonal (I), Drugs (D), Expectation (E), and Attitude (A). A pretest was conducted among 5 patients who underwent surgery for phimosis after the age of 60 years. In common with

Table 2
Brachytherapy parameters

Parameters	Mean	Minimum	Maximum
Wires number	5	2	8
Dose (Gy)	60	42	70
Dose rate (cGy/h)	80	35	161
Active length (mm)	32.7	20	45

Gy = unit dose delivered by implantation.

the studied population, these patients were of the same age and had a similar history of disease of the terminal area of the penis (a history of inflammation). The final questionnaire includes 31 questions and takes about 20 min to be completed by the patient. The survey on sexuality also used the validated French version of the International Index of Erectile Function (IIEF) questionnaire that explores five domains (desire, erection, orgasm, satisfaction from sexual relations, and overall satisfaction).

In June 2010, we conducted a survey on sexuality among 21 French patients in remission from their disease. After sending a newsletter, it was proposed to the patients that they complete the questionnaire on sexuality. Patients were considered as accepting to participate in the survey if they filled out the questionnaire. The study was approved by our Institutional Research Board. Finally, we obtained the participation of 19 of the 21 patients (90.5%). The participation of the patients is detailed in Fig. 1.

Statistical analysis

The software used for the statistical data was Stata (Stata, Corp., College Station, TX). The χ^2 test or Fisher exact test (F) were used for comparison of qualitative variables. The Mann–Whitney, Wilcoxon, or Kruskal–Wallis tests were used for the comparison of the distributions of quantitative variables. The Spearman rank test was used to assess the correlation between quantitative variables. Survival tables were designed for each type of survival (overall, specific, and recurrence free), and were used to assess survival at different times of followup. Survival analysis was performed using the Kaplan–Meier method.

Results

Oncologic results ($n = 47$)

Approximately 80 months after PB (12.8–189.8), 28 patients (59.6%) showed no recurrence, 16 (34%) experienced a local recurrence that required a partial ($n = 15$) or total amputation ($n = 1$), and 8 (17%) had regional and/or distant recurrence. The rate of preservation of the penis was 66% ($n = 31$). At the time of our survey, 23 (48.9%) patients were cured without recurrence, 10 (21.3%) were cured after treatment of local recurrence, 8

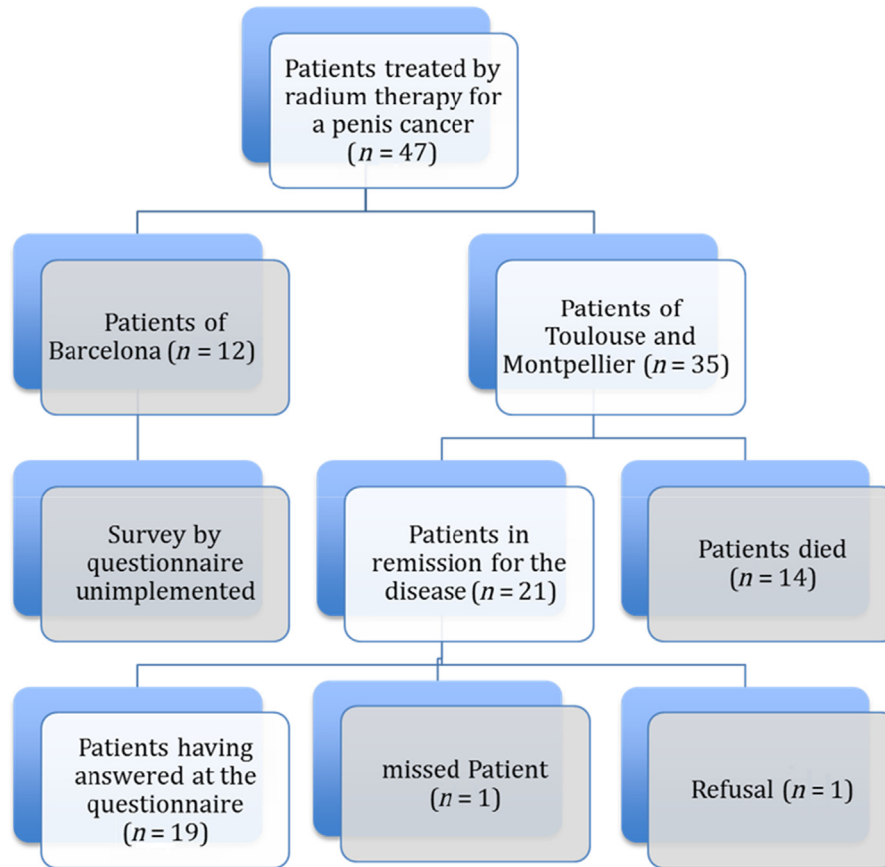


Fig. 1. Population participating in the survey on sexual functions and behaviors.

(17%) died of penile cancer, and 6 (12.8%) died of other causes (Fig. 2).

The overall survival at 2 and 5 years was 86.4% (95% confidence interval [CI], 72.1–93.6%) and 80.9% (95% CI, 65.2–90%), respectively (Fig. 3). The specific survival at 2 and 5 years was 90.7% (95% CI, 77.1–96.4%) and 87.6% (95% CI, 72.4–94.7%), respectively (Fig. 4). The disease-free survival at 2 and 5 years was 90.5% (95% CI, 67–97.5%) and 84% (95% CI, 57.6–94.7%), respectively (Fig. 5).

Patients with a tumor in the penis body had a significantly higher risk of recurrence (regional/distant) than those with glans tumors ($p = 0.013$; Mann–Whitney test and Fisher test). In contrast, lesion size, stage, histologic type, and grade do not emerge as prognostic factors of local, regional, and distant recurrence, despite a nonsignificant tendency for patients with squamous cell carcinoma ($p = 0.074$).

Survey on sexuality ($n = 19$)

The average age of the population was 73.2 years (range, 45–89 years). A total of 17 patients (89.5%) were sexually active before treatment (Table 3), with 78.9% reporting no erectile dysfunction.

Sexuality after treatment

A total of 10 (58.8%) of 17 patients remained sexually active before and after treatment (Table 4). Around 7 (36.8%) patients had no erectile dysfunction, 8 (42.1%) had frequent erections, 15 (78.9%) maintained nocturnal erections, and 10 (58.8%) rated their erections as “hard” or “almost hard.” None of the men in the study suggested a loss of manliness. Nine men (47.3%) felt that PB had not changed their sexuality, and three (15.8%) evoked mild changes. A total of 10 men (52.6%) observed modifications in the glans sensitivity.

Among the patients who continued to have sexual intercourse, 8 (80%) maintained orgasms. The average age of sexual partner was 66.6 years (median = 70 years; range, 37–85 years). The average duration of cohabitation was 38.2 years (median, 40 years; minimum, 4 years; maximum, 67 years). A total of 11 (57.9%) of the 19 men felt that sexuality was between “very important” to “moderately important” to their partner. A total of 12 men (63.1%) felt that they had between a “very good” ($n = 8$) or “good” ($n = 4$) communication about sexuality with their partners. Concerning the consequences of PB on the sexuality, six men (31.6%) noted that they were “well informed,” but six (31.6%) and seven declared to be “poorly informed” and

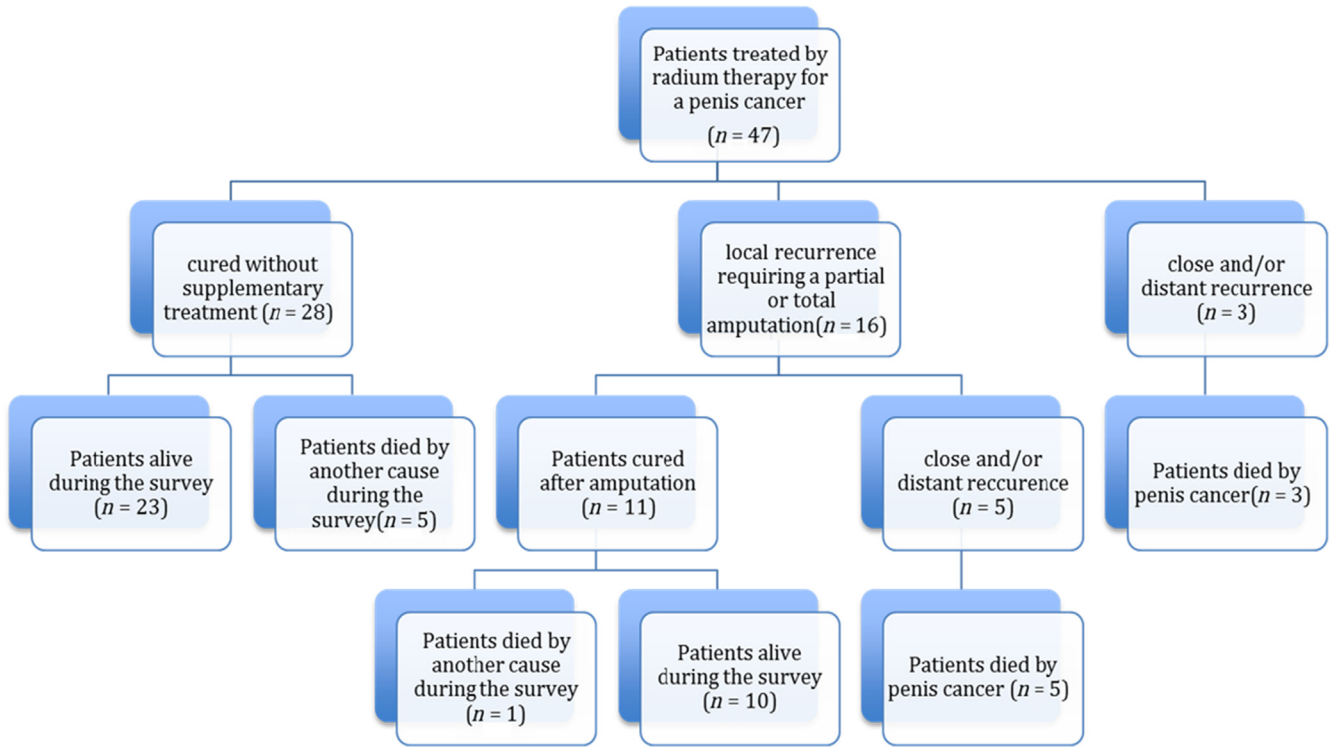


Fig. 2. Status of the overall population at the date of the survey.

“not informed,” respectively. The patient’s age and the age of their sexual partner were correlated with the frequency of sexual intercourse ($p = 0.032$ and 0.019 , respectively).

Patients who felt that PB had little or no changes in their sexuality had an IIEF-5 score ($p = 0.016$), IIEF-15 ($p = 0.003$), and a frequency of sexual intercourse ($p = 0.026$) significantly higher. We found no significant correlation among the sexuality items and the parameters of PB (dose, dose rate, number of needles, and active length), and the tumor size. The level of sexual desire was correlated with the frequency of sexual intercourse

before ($p = 0.0498$) and after treatment ($p = 0.0009$), and to the satisfaction of sexual intercourse ($p = 0.00001$). The age of the patient and their partner were correlated with the level of sexual desire ($p = 0.0093$ and 0.0113 , respectively). Changes in sensitivity of the glans, the discomfort or the appearance of the penis, pain, and ulceration were not significantly related to changes in sexuality. Nonsexual morbidity is described in Table 5. After PB, 73.7% of patients had “no” or “little” pain. One patient had “frequent” bleeding, and the rate of frequency of meatal stenosis was 21.1%.

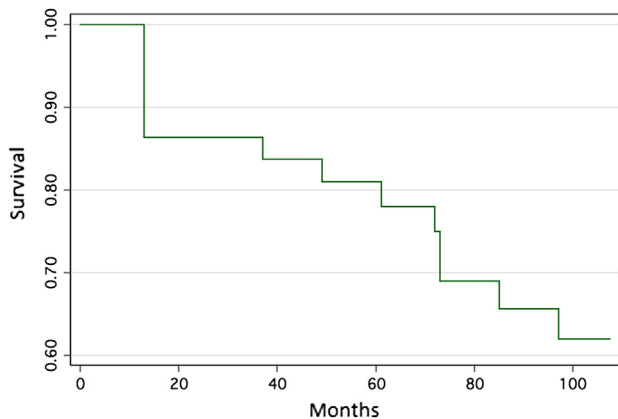


Fig. 3. Kaplan–Meier representation of the global survival.

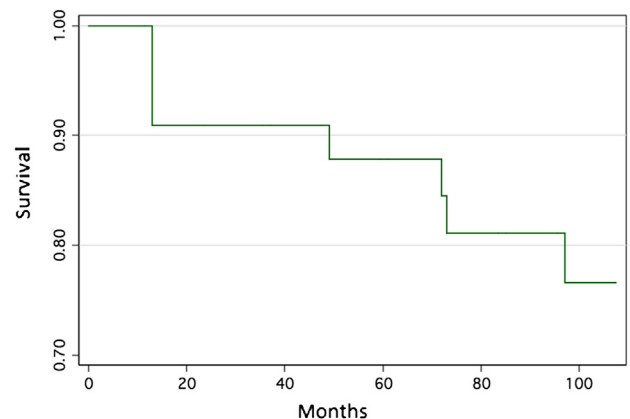


Fig. 4. Kaplan–Meier representation of the specific survival.

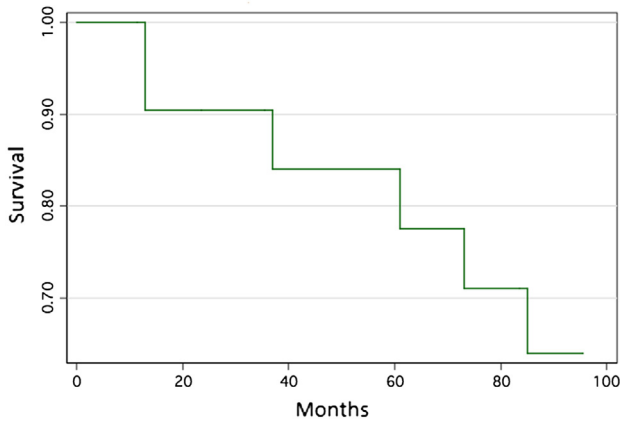


Fig. 5. Kaplan–Meier representation of the disease-free survival.

Discussion

By analyzing a previous series of 51 patients treated between 1971 and 1989, Delannes *et al.* (5) had concluded that apart from a patient who developed painful erections because of penile sclerosis, “sexual function did not appear to be altered by the implant.” Little information is provided in the literature on the effects of PB on sexual behavior. All the studies evoked the persistence of sexuality after PB (8, 9), but they did not provide an answer to the impact of PB on all sexual functions and the sexual behavior of treated men. This present study is the first detailed assessment of sexuality in this population. The men treated with PB are a potential target population for the sexual function and behavior study.

A total of 89.5% of patients in our series had sexual intercourse before treatment, although the median age at

diagnosis was 64.7 years. Approximately 78.9% reported never having presented with erectile dysfunction, and 73.7% had frequent orgasms before treatment of the cancer. Finally, 68.4% of the patients considered that they were misinformed about the impact of PB on sexuality. Through the grid BASIC IDEA of Lazarus (6) and Cottraux *et al.* (7), we observed that the overall satisfaction of sex was good, with 57.9% of patients declaring themselves satisfied by their current sexual life, and 47.4% optimistic concerning the future. A total of 17 (89.5%) patients were not concerned by the sexual performance. It is interesting to note that 89.5% of patients considered that PB did not result in any impairment of their sense of masculinity. The look and the appearance of their penis after PB were not a source of problems, confirming the observations of Crook *et al.* (8). Fantasy production was not interrupted by treatment because it is present in all patients and abundant in 47.4% of them. Desire is also maintained in the vast majority, although it is often less intense. These results explain rather well that more than 60% of the patients believe that the PB has little or no effect on their sexuality. Our investigation reveals that the decision to stop sexual intercourse was, according to the men, often a voluntary choice of the women. In 66.7% of the cases, the cause was the loss of the desire. During the conversations, some men gave reasons for the cessation of sexual intercourse such as age, cancer, and its treatment.

However, among men aged older than 70 years, 42.9% continued to be sexually active. This result reminds us that there is no a limitation to the maintenance of a sexual life (10). The problem of the lack of a partner, which is often reported in series of elderly and aging populations, was not observed here because all the patients were in a couple or married. In a recent study in Anderson Cancer Center in Houston, Huyghe *et al.* (11) had observed that the lack of a sexual partner was less frequent as a cause of cessation of sexuality in men than in women. The PB is not the only treatment modality of localized early penile cancer. Among the other treatments available for localized early disease, there are partial penectomy, reconstruction glansectomy, laser therapy, and glans resurfacing. All these treatments may be disfiguring and may have an impact on the patient’s sexual function, sexual intercourse, self-image, and self-esteem. In this study, there were no patients who were treated with partial amputation of the penis. It would be interesting to use the same questionnaire in a surgical population to assess the real impact of the partial amputation of the penis on sexuality. To date, most studies have focused on sexual function in men treated with amputation of the penis, but they have not explored the impact of treatment on male behavior. They have quickly concluded a low impact of partial amputations on sexual function. Romero *et al.* (12), questioning a population of 18 men, reported that 55.6% maintained erectile function during sexual intercourse, and 72% maintained ejaculation and orgasm during

Table 3
Pretreatment sexual functions

Parameters	Classification	N (%)
Sexual intercourse	Often	7 (36.9)
	Sometimes	5 (26.3)
	Rarely	5 (26.3)
	Never	2 (10.5)
Erectile dysfunction	Often	1 (5.3)
	Sometimes	1 (5.3)
	Rarely	2 (10.5)
	Never	15 (78.9)
Ejaculation	Always	13 (68.4)
	Often	3 (15.8)
	Rarely	2 (10.5)
	Never	1 (5.3)
Orgasm	Always	14 (73.7)
	Often	3 (15.7)
	Rarely	1 (5.3)
	Never	1 (5.3)

Table 4
Post-treatment sexual functions and behaviors

Parameters	Classification	N (%)
Sexual intercourse		
	Often	4 (21.1)
	Sometimes	2 (10.5)
	Rarely	4 (21.1)
	Never	9 (47.3)
Erection		
	Often	8 (42.1)
	Sometimes	5 (26.3)
	Rarely	4 (21.1)
	Never	2 (10.5)
Nocturnal/morning erection		
	Often	7 (36.7)
	Sometimes	4 (21.1)
	Rarely	4 (21.1)
	Never	4 (21.1)
Quality of erections		
	Hard	4 (23.5)
	Almost hard	6 (35.3)
	Moderately hard	3 (17.8)
	Soft	4 (23.5)
Masturbation		
	Very often	0 (0)
	Often	0 (0)
	Rarely	4 (21.1)
	Never	15 (78.9)
Worry about sexuality		
	Very often	0 (0)
	Often	0 (0)
	Rarely	2 (10.5)
	Never	17 (89.5)
Sensitivity of gland penis		
	No modification	10 (52.6)
	Increase in sensitivity	5 (26.3)
	Decrease in sensitivity	4 (21.1)
Size of penis		
	Suitable	16 (84.2)
	Moderately suitable	3 (15.8)
	Least inconvenient	0 (0)
	Inconvenient	0 (0)
Appearance of penis		
	Suitable	14 (73.7)
	Moderately suitable	3 (15.8)
	Least inconvenient	2 (10.5)
	Inconvenient	0 (0)
Fantasy		
	Very often	9 (47.4)
	Often	6 (31.6)
	Rarely	4 (21)
	Never	0 (0)
Drugs for erection		
	Very often	0 (0)
	Often	1 (5.2)
	Rarely	2 (10.5)
	Never	16 (84.2)
Satisfaction of future sexuality		
	Very satisfied	9 (47.4)
	Satisfied	3 (15.8)
	Moderately satisfied	5 (26.3)
	Not much satisfied	2 (10.5)
Frequency of desire		
	Almost always/always	4 (21.1)

(Continued)

Table 4 (continued)

Parameters	Classification	N (%)
	Most of the time	5 (26.2)
	Sometimes	4 (21.1)
	Rarely	4 (21.1)
	Almost never/never	2 (10.5)
Intensity of desire		
	Very strong	1 (5.9)
	Strong	2 (11.8)
	Moderate	8 (47.1)
	Mild	5 (29.3)
	Almost nothing/nothing	1 (5.9)
Satisfaction of sexual life		
	Very satisfied	11 (57.9)
	Satisfied	2 (10.5)
	Moderately satisfied	3 (15.8)
	Unsatisfied	3 (15.8)
	Very unsatisfied	0 (0)
IIEF erectile domain		
	No ED (26–30)	7 (36.8)
	Mild ED (22–25)	1 (5.3)
	Mild-to-moderate ED (17–21)	1 (5.3)
	Moderate ED (11–16)	0 (0)
	Severe ED (1–10)	10 (52.6)

IIEF = International index of erectile dysfunction; ED = erectile dysfunction.

each sexual intercourse. However, only 33.3% had frequent sexual intercourse before surgery. Among those with no more sexual activity, the main reasons were the small size of their penis and lack of glans. On a meta-analysis, Maddineni *et al.* (13) found a greater impact of the partial amputation of the penis, with an absence of sexual function (assessed by IIEF score-15) in 36–67% of the patients. It is interesting to compare the information provided by patients treated surgically and PB for the sense of manliness. In a series of 17 patients treated with partial ($n = 11$) or total amputation ($n = 4$) of the penis, Ficarra *et al.* (14) had found that emotional and mood disorders were common in this population, with 35% with “problems in society,” 29.5% pathologic anxiety, and 6% depression. The loss of masculinity and the inability to penetrate is likely to cause emotional stress, and it can therefore be expected that patients treated with total or partial amputation of the penis feel it to varying degrees. As in our study, 100% of the patients said that their virility had not been altered; PB is a treatment that probably has less psychological impact than penile surgery. A therapeutic alternative for small lesions of the penis is yttrium–aluminum–garnet laser ablation. In 2004, Windahl *et al.* (15) reported that of 10 of the 36 men treated by laser ablation who completed the IIEF-15, 6 were not sexually active, whereas 4 scored mild-to-moderate erectile dysfunction. However, using the Fugl–Meyer Life satisfaction Check List scores, 50% were shown to be satisfied with their sexual life. Taking the series of patients treated in the same institution between 1986 and 2000, Windahl *et al.* (16) concluded that most men treated with laser for localized cancer of the penis

Table 5
Nonsexual morbidity of treatment

Complications	Score	N (%)
Pain	Never	9 (47.4)
	Rarely	5 (26.3)
	Often	3 (15.8)
	Very often	2 (10.5)
Bleeding	Never	12 (63.2)
	Rarely	4 (21.1)
	Often	2 (10.5)
	Very often	1 (5.2)
Ulcerations	Never	11 (57.9)
	Rarely	3 (15.8)
	Often	1 (5.2)
	Very often	4 (21.1)
Stenosis	Never	11 (57.9)
	Rarely	3 (15.8)
	Often	1 (5.2)
	Very often	4 (21.1)

resume to be sexually active at a level equivalent to that before treatment, with good overall satisfaction concerning their sexual life. However, these data are single centered, and it seems premature to conclude the impact of laser ablation.

Limitations

The first detailed analysis of the impact of PB on the functions of the penis and sexual behavior has several limitations. First, sexuality is an area highly dependent on sociocultural elements. The findings on the impact of PB of the penis on sex were obtained only from the French men. Therefore, it may be difficult to extrapolate to other cultures, including the Spanish Catalanian population. In addition, because of the low incidence of this disease in Europe, the size of our study population was relatively small, which limits our ability to achieve a detailed analysis, including subgroups (young males, circumcised patients, gay, and so on). In the absence of a control group, it is impossible to compare the results of PB with other treatments of localized cancer of the penis, in particular, partial penectomy (17) and laser ablation and whether PB causes less sexual dysfunction than the latter. For the methodology, although we have chosen the form of self-administered questionnaire, followed by an interview so that the patients are not influenced in their responses or misunderstand the questions, we cannot rule out the subjectivity of responses. In addition, the use of the IIEF in this population is quite questionable because it is a poor score that applies to a population with few penetrating sexual reports. For this reason, we have completed a questionnaire specifically designed for the study. However, the conclusions drawn from it must be taken with caution; this

questionnaire has not been previously subject to a validation study. Therefore, these results should therefore be considered as preliminary data, which need to be confirmed with a larger scale study.

Recently, a consensus guideline was developed between the American Brachytherapy Society and Groupe Européen de Curiethérapie/European Society for Therapeutic Radiation and Oncology for the use of brachytherapy in the primary management of carcinoma of the penis. The good tumor control rates, acceptable morbidity, and functional organ preservation warrant recommendation of brachytherapy as the initial treatment for invasive T1, T2, and selected T3 penile cancers (18).

Conclusion

After treatment, most patients reported that PB has little or no effect on their sexuality. More than half of patients remained sexually active after treatment and almost all continued to have erections even if they were of lower quality. There was little damage to body image and sense of manliness. This information may play a key role in the choice of penis cancer treatment leading to the maintenance of a good sexual life. These results could also be the first step in the development of targeted interventions on sexuality in this population.

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