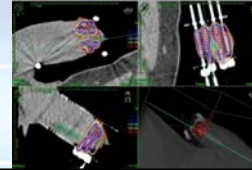




## Penile Carcinoma — Organ Preservation With Brachytherapy

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Erlangen, Germany



## Disclosure

Vratislav Strnad, MD, PhD, Prof., has received consulting fees from Elekta.



## Penile Carcinoma — Organ Preservation With Brachytherapy

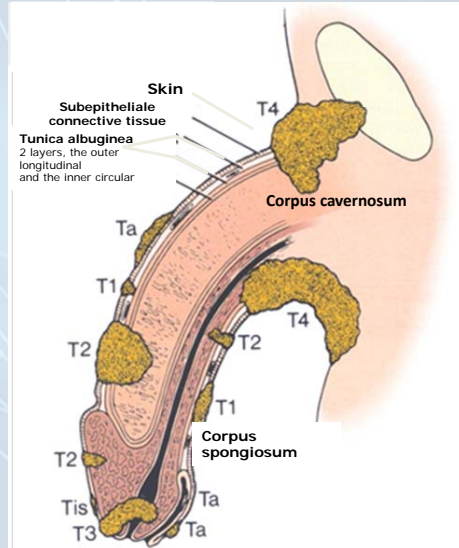


Table 3: 2009 TNM clinical classification of penile cancer.

T- Primary tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
Ta	Non-invasive verrucous carcinoma, not associated with destructive invasion
T1	Tumour invades subepithelial connective tissue
T1a	Tumour invades subepithelial connective tissue without lymphovascular invasion and is not poorly differentiated or undifferentiated (T1G1-2)
T1b	Tumour invades subepithelial connective tissue without with lymphovascular invasion or is poorly differentiated or undifferentiated (T1G3-4)
T2	Tumour invades corpus spongiosum/corpora cavernosa
T3	Tumour invades urethra
T4	Tumour invades other adjacent structures

## Penile Carcinoma — Organ Preservation With Brachytherapy

Table 6: Treatment strategies for penile cancer.

Primary tumour	Conservative treatment is to be considered whenever possible	LE	GR
Category Tis, Ta, T1a (G1, G2)	CO <sub>2</sub> or Nd:YAG laser surgery, wide local excision, glans resurfacing, or glans resection, depending on size and location of the tumour	2b	C
	Mohs' micrographic surgery or photodynamic therapy for well differentiated superficial lesions (Tis, G1 Ta)	3	C
Categories: T1b (G3) and T2 (glans only)	Glansectomy, with or without tips amputation or reconstruction	2b	B
Category T2 (invasion of the corpora)	Partial amputation	2b	B
Category T3 (invasion of urethra)	Total amputation with perineal urethrotomy	2b	B
Category T4 (other adj. structures)	Eligible patients: neoadjuvant chemotherapy followed by surgery in responders. Alternative: external radiation	3	C
Local disease recurrence after conservative therapy	Salvage surgery, consisting of penis-sparing treatment in small recurrences.	2b	B
	Larger recurrence: some form of amputation	2b	B
Radiotherapy	Organ-preserving treatment in selected patients with T1-2 of glans or coronal sulcus, lesions < 4 cm.	2b	B
Chemotherapy	Neoadjuvant, before surgery	3	C
	Palliation in advanced or metastatic disease	3	C

CO<sub>2</sub> = carbon dioxide; Nd:YAG = neodymium:yttrium-aluminum-garnet

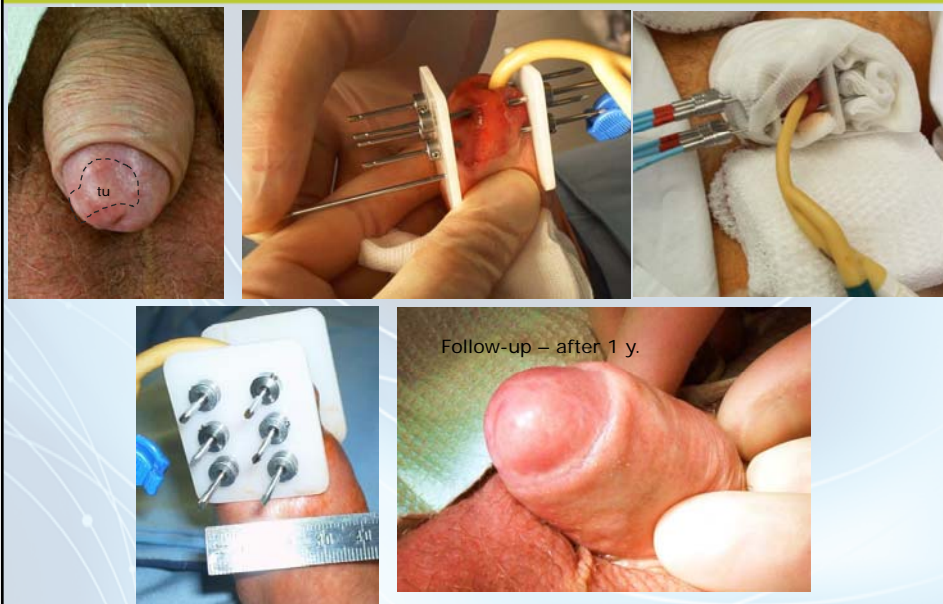


Guidelines on  
**Penile Cancer**

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## Interstitial Brachytherapy



### Penile Carcinoma — Organ Preservation With Brachytherapy

Reference	No. of Patients	Brachytherapy Technique	% 5-year Local Control	Side Effects	% Penis Preservation
Akimoto, 1997	15	LDR mould	80	27% necrosis	73
Chaudary, 1999	23	interstitial LDR	80	9% stenosis	78
Delannes, 1992	51	interstitial LDR	86	23% necrosis, 45% stenosis	75
Gerbaulet, 1994	109	interstitial LDR	82	13% necrosis, 15% stenosis	82
Guedea, 1991	16	interstitial LDR	87	25% necrosis or stenosis	87
Kanfir, 2000	145	interstitial LDR	84	14% necrosis, 24% stenosis	80
Kiltie, 2000	31	interstitial LDR	81	19% necrosis, 35% stenosis	81
Mazeron, 1984	50	interstitial LDR	78	6% necrosis, 16% stenosis	74
Rozan, 1995	184	interstitial LDR	85	21% necrosis, 45% stenosis	78
Suchaud, 1989	53	interstitial LDR	79	Necrosis or stenosis 28%	79
Soria, 1997	102	interstitial LDR	77	Not stated	72
Crook, 2009	67	interstitial LDR/PDR	87 (72%/10 y)	12% necrosis, 9% stenosis	88 (5 y), 67 (10 y)
de Crevoisier, 2009	144	interstitial LDR	80 (10 y)	26% necrosis, 29% stenosis	72 (10 y)



## Penile Carcinoma — Organ Preservation With Brachytherapy

Reference	No. of Patients	Brachytherapy Technique	% 5-year Local Control	Side Effects	% Penis Preservation
Akimoto, 1997	15	LDR mould	80	27% necrosis	73
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Mazeron, 1984	50	interstitial LDR	78	6% necrosis, 16% stenosis	74
Rozan, 1995	184	interstitial LDR	85	21% necrosis, 45% stenosis	78
Suchaud, 1989	53	interstitial LDR	79	Necrosis or stenosis 28%	79
Soria, 1997	102	interstitial LDR	77%	Not stated	72
<b>Crook, 2009</b>	<b>67</b>	<b>interstitial LDR/PDR</b>	<b>87 (72%/10 y)</b>	<b>12% necrosis, 9% stenosis</b>	<b>88 (5 y), 67 (10 y)</b>
<b>de Crevoisier, 2009</b>	<b>144</b>	<b>interstitial LDR</b>	<b>80 (10 y)</b>	<b>26% necrosis, 29% stenosis</b>	<b>72 (10 y)</b>

## Penile Carcinoma — Organ Preservation With Brachytherapy

Prescribed dose ranged from 55 to 65 Gy, with 45 of 49 patients receiving 60 Gy. The mean dose rate was 65 cGy/h (range, 33–160 cGy/h), corresponding to a mean implant duration of 98.8 h (range, 36–188 h).

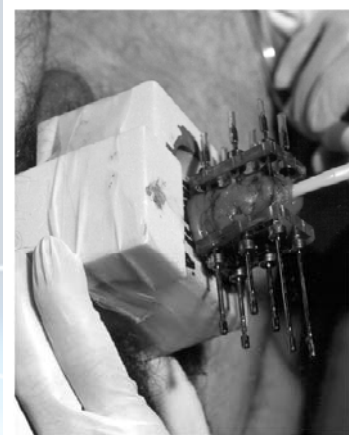


Fig. 1. Intraoperative photograph of two-plane, six-needle implant. Catheter *in situ*. Styrofoam collar around penis.



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doi:10.1016/j.ijrobp.2004.10.016

### CLINICAL INVESTIGATION

### Penis

#### PENILE BRACHYTHERAPY: RESULTS FOR 49 PATIENTS

JUANITA M. CROOK, M.D.,\* JOSE JEGORANSKI, M.MATH.,<sup>†</sup> LAVAL GERMARD, M.D.,<sup>‡</sup>  
BERND ESCHÉ, M.D.,<sup>§</sup> AND G. POND, M.Sc.<sup>‡</sup>

Departments of \*Radiation Oncology and †Radiation Physics, Princess Margaret Hospital, University Health Network, Toronto, Ontario, Canada; ‡Department of Biostatistics, University Health Network, Toronto, Ontario, Canada; §Department of Radiation Oncology, Ottawa Hospital Regional Cancer Centre, Ottawa, Ontario, Canada



## Penile Carcinoma — Organ Preservation With Brachytherapy

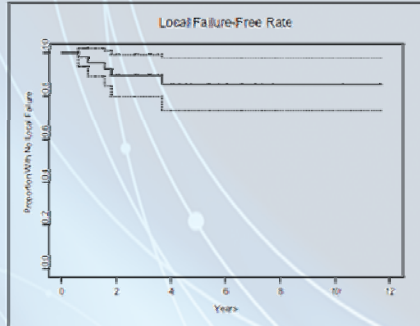


Fig. 2. Local failure-free rate. The probability of local failure was adjusted for the risk of death from other causes.  $n = 35$  at 1 year, 26 at 2 years, 11 at 5 years, and 2 at 10 years.

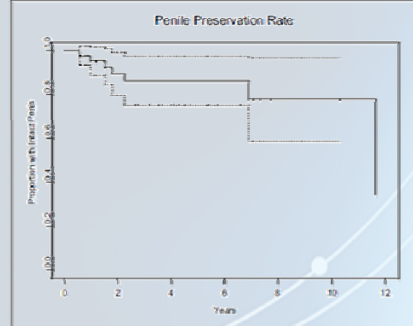


Fig. 6. Maintenance of intact penis.  $n = 35$  at 1 year, 26 at 2 years, 11 at 5 years, and 2 at 10 years.



Int J Radiat Oncol Biol Phys. Vol. 82, No. 2, pp. 204-210, 2011  
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doi:10.1016/j.ijrobp.2011.05.036

Clinical Investigation

Penis

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BENOËT ESCOFFIER, M.D.,<sup>4</sup> AND G. PONS, M.Sc.<sup>5</sup>

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## Penile Carcinoma — Organ Preservation With Brachytherapy

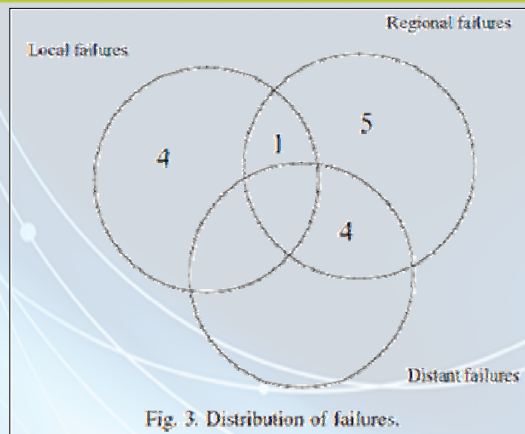


Fig. 3. Distribution of failures.



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Clinical Investigation

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## Penile Carcinoma — Organ Preservation With Brachytherapy

2 other men required penectomy for necrosis. The soft tissue necrosis rate was 16% and the urethral stenosis rate 12%.

Eight men (16%) have experienced a radiation ulcer or soft tissue necrosis at the implanted site. The risk of necrosis is not related to tumor size ( $p = 0.39$ ), number of planes ( $p = 0.21$ ), or use of PDR ( $p = 0.12$ ) but was significantly associated with the number of needles used in the implant ( $p = 0.044$ ) and tumor stage ( $p = 0.040$ ). The majority healed over time, but 2 men required partial penectomy for radiation necrosis. One patient (T3 tumor) responded well to a course of hyperbaric oxygen, with satisfactory healing of a deep ventral ulcer on the glans.



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CRITICAL INVESTIGATION

Penis

### PENILE BRACHYTHERAPY: RESULTS FOR 49 PATIENTS

JUANITA M. CROOK, M.D.,<sup>1\*</sup> JOHN JEZIORANSKI, M.MATH.,<sup>2</sup> LAVAL GRIMARD, M.D.,<sup>3</sup>  
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## Penile Carcinoma — Organ Preservation With Brachytherapy

### CONCLUSIONS

Our results support the use of interstitial brachytherapy as primary management of T1, T2, and selected T3 SCC of the penis. Five-year penile preservation is achieved in 86% of men without sacrifice of cancer control.



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CRITICAL INVESTIGATION

Penis

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## Penile Carcinoma — Organ Preservation With Brachytherapy

144 patients

Median follow-up: 5.7 y

Median treated volume was  $22 \text{ cm}^3$  (range, 5–110) and median reference isodose rate was  $0.4 \text{ Gy/h}$  (range, 0.2–1.2), and median dose was  $65 \text{ Gy}$  (range, 37–75).

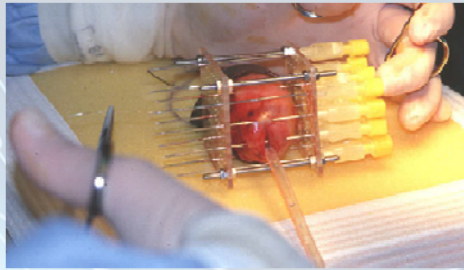


Fig. 1. The Gerbauer's glans applicator maintains the needles in a parallel and equidistant (15–18 mm) position. Needles are manually loaded with Ir-192 wires.



ESMO

doi:10.1093/jco/2008.08.055

CLINICAL INVESTIGATION

Penis

LONG-TERM RESULTS OF BRACHYTHERAPY FOR CARCINOMA OF THE PENIS (CONFINED TO THE GLANS) (N-0828)

RENATO DE CROMBIE, M.D., Ph.D.,<sup>1</sup> ANTONIO SERRANO, M.D.,<sup>2</sup> NICHOLAS SANFORD, M.D.,<sup>3</sup> ALBERTO BOVA, M.D.,<sup>4</sup> MALCOLM ARONSON,<sup>5</sup> LORENZO DENZA, Ph.D.,<sup>6</sup> PETER WINKLER, M.D.,<sup>7</sup> KARIM FICUS, M.D., Ph.D.,<sup>8</sup> ALAN GILBERT, M.D.,<sup>9</sup> and CHRISTINE HUN-MANN, M.D.<sup>9</sup>  
Departments of <sup>1</sup>Radiation Therapy and <sup>2</sup>Medical Oncology, Mount Sinai Hospital, <sup>3</sup>Virginia Francis, and <sup>4</sup>Department of Radiation Therapy, <sup>5</sup>Medical Oncology, Joralee Gustave Brown, <sup>6</sup>Nigilal Francis, and <sup>7</sup>Department of Radiation Therapy, <sup>8</sup>New York University School of Medicine, New York, NY

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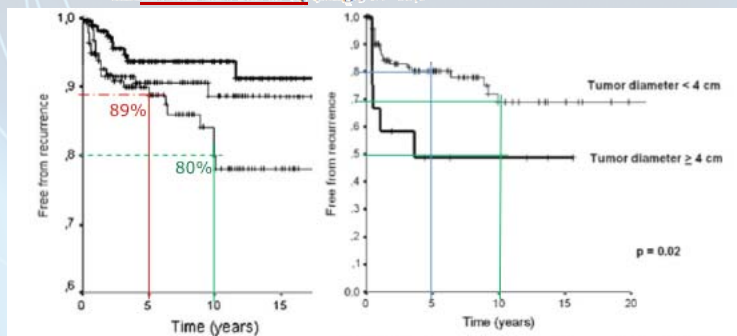


Fig. 6. Risk of penis recurrence, inguin and metastases by time (Kaplan-Meier).

Fig. 7. Risk of recurrence by tumor diameter (Kaplan-Meier).



ESMO

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Median treated volume was 22 cm<sup>3</sup> (range, 5–110) and median reference isodose rate was 0.4 Gy/h (range, 0.2–1.2), and median dose was 65 Gy (range, 37–78).

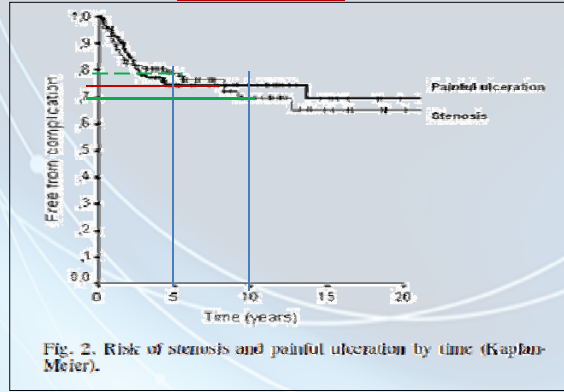


Fig. 2. Risk of stenosis and painful ulceration by time (Kaplan-Meier).

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**Clinical Investigation** **Penis**

**LONG-TERM RESULTS OF BRACHYTHERAPY FOR CARCINOMA OF THE PENIS (OWSPEN-01): A PHASE II TRIAL**

Ravi Prasad, M.D., Ph.D.,<sup>1</sup> Kishore Suresh, M.D.,<sup>2</sup> Nicolas Sorensen, M.D.,<sup>3</sup> Antonio Bion, M.D.,<sup>4</sup> Giovanni Salvetti, M.D.,<sup>5</sup> Thomas Wang, M.D.,<sup>6</sup> Kunal Shah, M.D.,<sup>7</sup> Anand Gopalakrishnan, M.D.,<sup>8</sup> and Christian Brix, M.D.,<sup>9</sup>

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## Penile Carcinoma — Organ Preservation With Brachytherapy

Table 1. Risk of complication (painful ulceration or stenosis) by brachytherapy parameters

Parameters (as continuous variables)	Univariate analysis		Multivariate analysis	
	RR (95% CI)	p value	RR	p value
Number of needles	1.13 (1.04–1.23)	0.005	NS	NS
Total radioactive length	1.03 (1.01–1.05)	0.03	NS	NS
Reference isodose rate	7.39 (1.48–36.91)	0.01	9.17 (1.80–46.6)	0.008
Treated volume	1.02 (1.01–1.03)	0.002	1.02 (1.01–1.03)	0.005

Abbreviations: RR = relative risk; NS = non-significant ( $p > 0.05$ ).

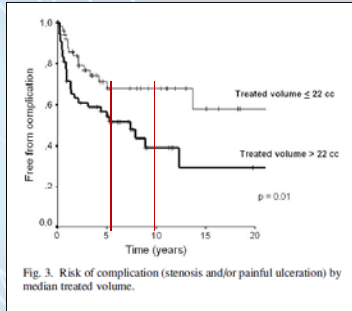


Fig. 3. Risk of complication (stenosis and/or painful ulceration) by median treated volume.

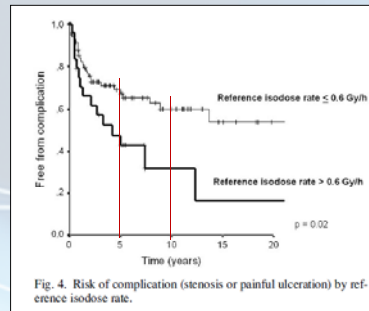


Fig. 4. Risk of complication (stenosis or painful ulceration) by reference isodose rate.

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**Clinical Investigation** **Penis**

**LONG-TERM RESULTS OF BRACHYTHERAPY FOR CARCINOMA OF THE PENIS (OWSPEN-01): A PHASE II TRIAL**

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Department of Radiation Oncology and <sup>2</sup>Department of Urology, University of Michigan, Ann Arbor, MI; <sup>3</sup>Department of Radiation Oncology, University of California, San Diego, CA; <sup>4</sup>Department of Radiation Oncology, University of Texas, Houston, TX; <sup>5</sup>Department of Radiation Oncology, University of Illinois, Chicago, IL; <sup>6</sup>Department of Radiation Oncology, University of Colorado, Denver, CO; <sup>7</sup>Department of Radiation Oncology, University of California, San Francisco, CA; <sup>8</sup>Department of Radiation Oncology, University of Texas, Houston, TX; <sup>9</sup>Department of Radiation Oncology, University of Michigan, Ann Arbor, MI





## Penile Carcinoma — Organ Preservation With Brachytherapy

### CONCLUSIONS

- 1 Our results support the use of Iridium-192 BT for SCC confined to the glans or the prepuce when tumor diameter is ≤4 cm. The 10-year local recurrence rate is 20%.
- 2 Careful, extended follow-up is recommended (10), because failure can occur several years after BT (up to 23 years in our experience). The 10-year risk of pain or necrosis is 25% to 30%. Toxicity can be decreased by employing
- 3 a low dose rate (<0.6 Gy/h).



Brachytherapy (2013) 24, 100–106  
doi:10.1016/j.brach.2012.09.004

#### CLINICAL INVESTIGATION

#### Penile

#### LONG-TERM RESULTS OF BRACHYTHERAPY FOR CARCINOMA OF THE PENIS (CONFINED TO THE GLANS (N=68))

RENÉE DE CROMBIE, M.D., Ph.D.,<sup>1</sup> KRISTINE SIMANS, M.D.,<sup>2</sup> NICHOLAS SANFORD, M.D.,<sup>3</sup> AUSTIN BROWN, M.D.,<sup>4</sup> MARCO ANTONIO LARREA, M.D.,<sup>5</sup> DANIEL WILSON, M.D.,<sup>6</sup> NARINE FIGUEROA, M.D.,<sup>7</sup> ALAN GILBERT, M.D.,<sup>8</sup> and CHRISTINE HUN-MANN, M.D.<sup>9</sup>  
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## Penile Carcinoma — Organ Preservation With Brachytherapy

### ...and HDR-brachytherapy??

*High-dose-rate brachytherapy. The literature on HDR <sup>192</sup>Ir brachytherapy for penile cancer is sparse.*



Brachytherapy (2013) 24, 100–106

#### BRACHYTHERAPY

#### American Brachytherapy Society—Groupe Européen de Curiothérapie—European Society of Therapeutic Radiation Oncology consensus guidelines for penile brachytherapy

Juanita M. Crook<sup>1,\*</sup>, Christine Haie-Meder<sup>2</sup>, B. Jeffrey Deane<sup>3</sup>, Jean-Jacques Mazeron<sup>4</sup>, Alvaro A. Martinez<sup>5</sup>, Mark J. Rivard<sup>6</sup>

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## Penile Carcinoma — Organ Preservation With Brachytherapy

10 pts, HDR-brachytherapy 18 x 3.0 Gy (54 Gy), twice daily

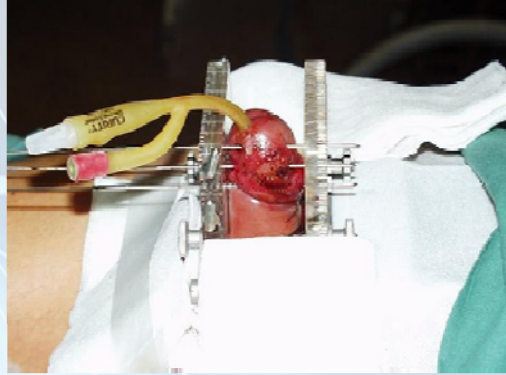


Fig. 1. The technique of application (Patient no. 6).



Brachytherapy 10 (2015) 40-46

BRACHYTHERAPY

High-dose rate brachytherapy in the treatment of penile carcinoma—First experience  
Iří Peterá<sup>1,\*</sup>, Ivo Srnák<sup>1</sup>, Linda Kasová<sup>1</sup>, Zuzana Macingová<sup>2</sup>, Petr Páluska<sup>2</sup>, Milan Zoubal<sup>2</sup>,  
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## Penile Carcinoma — Organ Preservation With Brachytherapy

10 pts, HDR-brachytherapy 18 x 3.0 Gy (54 Gy), twice daily

Median followup was **20 months** (3.4–90.6 months). We neither observed any postradiation necrosis nor urethral stenosis. The worst late side effects recorded were mild telangiectasias in the treatment region. At the last followup, all patients were without tumor recurrence and without signs of urethral toxicity.



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BRACHYTHERAPY

High-dose rate brachytherapy in the treatment of penile carcinoma—First experience  
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## Summary

1. The brachytherapy technique for penile carcinoma is a **simple, effective, organ- and function-saving therapy.**
2. For penile cancer stages I and II, brachytherapy is an **alternative for mutilating surgery.**

## Summary

3. Recommendation for dose schedule:
  - ✓ **LDR/PDR-Brachytherapy: 0.4–0.5 Gy/h ~ 60–65 Gy**
  - ✓ **HDR-Brachytherapy: twice daily 18 x 3.0 Gy ~ 54.0 Gy or 12 x 3.2 ~ 38.4 Gy(??)**  
*(only very few reports; currently it's not a standard)*



## Summary

4. Tumor control rate: 80–87%
5. Penis preservation rate: 87% (7 years), 70% (10 years)
6. Side effects:
  - ✓ **Soft tissue ulceration:** 6–26%
  - ✓ **Urethra stenosis:** 9–45%



## Conclusion

The worldwide experience confirms that **interstitial brachytherapy** for patients with cancer of the penis is an **effective organ- and function-sparing therapy** with minimal toxicity and therefore an excellent alternative to mutilating surgery.

