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### Original article

## Laser ablation as monotherapy for penile squamous cell carcinoma: A multi-center cohort analysis

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#### Abstract

**Introduction:** Although the trend towards penile sparing therapy is increasing for penile squamous cell carcinoma, outcomes for laser ablation therapy have not been widely reported. We assessed the clinical outcomes of penile cancer patients treated with only laser ablation.

**Materials and methods:** A retrospective review was performed on 161 patients across 5 multi-center tertiary referral centers from 1985 to 2015. All patients underwent penile sparing surgery with only laser ablation for squamous cell carcinoma of the penis. Laser ablation was performed with neodymium-doped yttrium aluminum garnet or carbon dioxide. Overall and recurrence-free survival was calculated using the Kaplan-Meier method and compared with the log rank test.

**Results:** A total of 161 patients underwent laser ablation for penile cancer. The median age was 62 (IQR: 52–71) years and median follow-up was 57.7 (IQR: 28–90) months. The majority of patients were pTa/Tis (59, 37%) or pT1a (62, 39%). Only 19 (12%) had a poorly differentiated grade. The 5-year recurrence-free survival was 46%. When stratified by stage, the 5-year local recurrence-free survival was pTa/Tis: 50%; pT1a: 41%; pT1b: 38%; and pT2: 52%. The inguinal/pelvic nodal recurrence was pTa/Tis: 2%; pT1a: 5%; pT1b: 18%; and pT2: 22%. There were no differences among stages with respect to recurrence-free survival (P = 0.98) or overall survival (P = 0.20).

**Conclusion:** Laser ablation therapy is safe for appropriately selected patients with penile squamous cell carcinoma. Due to the increased risk of nodal recurrence, laser ablation coupled with diagnostic nodal staging is indicated for patients with pT1b or higher. © 2017 Elsevier Inc. All rights reserved.

Keywords: Laser ablation; Recurrence; Penile sparing surgery; Penile squamous cell carcinoma

#### 1. Introduction

Penile squamous cell carcinoma is a rare malignancy that traditionally requires radical resection of the primary tumor as definitive treatment. However, radical procedures can significantly impact a person's quality of life and sexual function. With the development of safe and effective penile sparing strategies, recent guidelines have recommended the use of penile preservation for lower stage disease [1,2]. Consequently, there has been a movement towards penile sparing surgery as lower recurrence rates for penile amputation has not been shown to effect survival [3].

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Penile preservation strategies that have been described include laser ablation, local excision, glans resurfacing, and glansectomy. Commonly used types of laser energy sources include carbon dioxide (CO<sub>2</sub>) and neodymium-doped yttrium aluminum garnet (Nd:YAG) and is a recommended modality for penile lesions that are pT1 or lower [1,2]. However, there continues to be a paucity of literature for laser ablative therapies largely due to the rarity of disease as most reports include small, single center series [4–8]. As a result, we sought to use a large, multi-international cohort to analyze the clinical outcomes of penile carcinoma treated with only laser ablation.

#### 2. Material and methods

#### 2.1. Patient demographics

After international board review, we performed a retrospective review of 1,459 patients across 5 multi-center, multi-international tertiary referral centers. We identified 161 patients that underwent laser ablation as monotherapy treated between 1985 and 2015 for biopsy proven or clinically suspicious squamous cell carcinoma of the penis. All patients had nonpalpable inguinal lymph nodes and had no evidence of metastatic disease based on cross-sectional imaging. None of these patients underwent a diagnostic sentinel lymph node biopsy or inguinal lymph node dissection at time of diagnosis. Patients who underwent laser ablation in combination with other treatment modalities for the local tumor were excluded. Laser ablation was performed with either Nd:YAG or  $CO_2$ . Variables recorded included age, stage, grade, and tumor size.

Tumors were staged according to the 7th edition of the American Joint Committee on Cancer (AJCC) tumor-nodemetastasis (TMN) classification [9]. Tumors treated prior to 2010 were re-staged according to the 7th edition TMN classification. Follow-up for overall survival was defined as date of laser ablation to date of death or last date of follow-up.

#### 2.2. Recurrence

Recurrence was defined as local if there was evidence of disease in the primary resection bed at follow-up. All local recurrences (LRs) recorded were found at least 1 month after surgery. Patients defined as having LR did not have recurrences at any other sites. Follow-up for recurrence was defined as date of laser ablation to date of recurrence or last date of follow-up.

#### 2.3. Statistical analysis

Patient demographics and clinical characteristics were recorded as frequency and percentages. Continuous variables were recorded as median and interquartile ranges (IQR). The Kaplan-Meier method and log rank tests were used to calculate survival and LR-free survival. A multivariable Cox proportional hazards model for recurrence was calculated using pathologic stage, tumor size, treatment year, and tumor grade. All P values less than 0.05 were considered statistically significant. All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) software package version 24.0 (IBM corporation, Armonk, NY).

#### 3. Results

Table 1 describes demographic and tumor characteristics. A total of 161 patients underwent laser ablation as monotherapy. The median age was 62 years (IQR: 52–71) and the median follow-up was 57.7 months (IQR: 28–90). In total, 19 (20%) patients had a poorly differentiated grade. Patients who were pTa/Tis comprised of 59 (37%) patients. In total, 62 (39%) patients were pT1a. Seventeen (11%) and 18 (11%) had pT1b and pT2 disease, respectively. For 69 patients (43%), recurred locally while 11 (7%) recurred in the inguinal/pelvic region, and 1 (1%) had distant recurrence.

Table 2 describes demographic and tumor characteristics stratified by stage. Tumors that were pT1a and pT1b were larger with a median size of 2.0 cm (IQR: 1.3-2.2) and 2.0 cm (IQR: 1.3-2.2), respectively (P = 0.019). Pathologic T2 tumors selected for laser ablation tended to be

Table	1
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Demographics of patients undergoing laser ablation

n       161         Median age (IQR)       62 (52–71)         Median tumor size (IQR)       1.5 (1.0–2.2)         Grade $(n = 94)$ 32 (20)         2       43 (27)         3/4       19 (12)         Stage $pTa/Tis$ $pTa/Tis$ 59 (37) $pTla$ 62 (39) $pTlb$ 17 (11) $pTz$ 18 (11) $pTx$ 3 (2)         Recurrence       69 (43)         local       69 (43)         inguinal/pelvic       11 (7)         distant       1 (1)         Year of diagnosis       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	Variables	Total (%)
Median age (IQR) $62 (52-71)$ Median tumor size (IQR) $1.5 (1.0-2.2)$ Grade $(n = 94)$ $32 (20)$ 1 $32 (20)$ 2 $43 (27)$ $3/4$ $19 (12)$ Stage $pTa/Tis$ $pTa/Tis$ $59 (37)$ $pT1a$ $62 (39)$ $pT1b$ $17 (11)$ $pT2$ $18 (11)$ $pTx$ $3 (2)$ Recurrence $69 (43)$ local $69 (43)$ inguinal/pelvic $11 (7)$ distant $1 (1)$ Year of diagnosis $8 (5)$ $1990-1999$ $47 (29)$ $2000-2009$ $69 (43)$ $2010-2016$ $37 (23)$	n	161
Median tumor size (IQR) $1.5 (1.0-2.2)$ Grade $(n = 94)$ 32 (20)         2       43 (27) $3/4$ 19 (12)         Stage $pTa/Tis$ $pTa/Tis$ 59 (37) $pT1a$ 62 (39) $pT1b$ 17 (11) $pT2$ 18 (11) $pTx$ 3 (2)         Recurrence       69 (43)         local       69 (43)         inguinal/pelvic       11 (7)         distant       1 (1)         Year of diagnosis       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	Median age (IQR)	62 (52–71)
Grade $(n = 94)$ 32 (20)243 (27) $3/4$ 19 (12)Stage19 (12)pTa/Tis59 (37)pT1a62 (39)pT1b17 (11)pT218 (11)pTx3 (2)Recurrence69 (43)local69 (43)inguinal/pelvic11 (7)distant1 (1)Year of diagnosis8 (5)1990–199947 (29)2000–200969 (43)2010–201637 (23)	Median tumor size (IQR)	1.5 (1.0–2.2)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Grade $(n = 94)$	
$\begin{array}{cccccccc} 2 & 43 & (27) \\ 3/4 & 19 & (12) \end{array}$ Stage $\begin{array}{cccccccccccccccccccccccccccccccccccc$	1	32 (20)
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2	43 (27)
$\begin{array}{cccccc} Stage & & & & & \\ pTa/Tis & & 59 & (37) \\ pT1a & & 62 & (39) \\ pT1b & & 17 & (11) \\ pT2 & & 18 & (11) \\ pTx & & 3 & (2) \\ \hline \\ Recurrence & & & \\ local & & 69 & (43) \\ inguinal/pelvic & & 11 & (7) \\ distant & & 1 & (1) \\ \hline \\ Year of diagnosis & & & \\ 1985-1989 & & 8 & (5) \\ 1990-1999 & & 47 & (29) \\ 2000-2009 & & 69 & (43) \\ 2010-2016 & & 37 & (23) \\ \hline \end{array}$	3/4	19 (12)
pTa/Tis       59 (37)         pT1a       62 (39)         pT1b       17 (11)         pT2       18 (11)         pTx       3 (2)         Recurrence       69 (43)         local       69 (43)         inguinal/pelvic       11 (7)         distant       1 (1)         Year of diagnosis       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	Stage	
pT1a       62 (39)         pT1b       17 (11)         pT2       18 (11)         pTx       3 (2)         Recurrence       69 (43)         local       69 (43)         inguinal/pelvic       11 (7)         distant       1 (1)         Year of diagnosis       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	pTa/Tis	59 (37)
pT1b       17 (11)         pT2       18 (11)         pTx       3 (2)         Recurrence       69 (43)         local       69 (43)         inguinal/pelvic       11 (7)         distant       1 (1)         Year of diagnosis       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	pT1a	62 (39)
pT2       18 (11)         pTx       3 (2)         Recurrence       69 (43)         inguinal/pelvic       11 (7)         distant       1 (1)         Year of diagnosis       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	pT1b	17 (11)
pTx     3 (2)       Recurrence     69 (43)       inguinal/pelvic     11 (7)       distant     1 (1)       Year of diagnosis     8 (5)       1990–1999     47 (29)       2000–2009     69 (43)       2010–2016     37 (23)	pT2	18 (11)
Recurrence       69 (43)         local       69 (43)         inguinal/pelvic       11 (7)         distant       1 (1)         Year of diagnosis       8 (5)         1985–1989       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	рТх	3 (2)
local       69 (43)         inguinal/pelvic       11 (7)         distant       1 (1)         Year of diagnosis       8 (5)         1985–1989       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	Recurrence	
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distant     1 (1)       Year of diagnosis     8 (5)       1985–1989     8 (5)       1990–1999     47 (29)       2000–2009     69 (43)       2010–2016     37 (23)	inguinal/pelvic	11 (7)
Year of diagnosis8 (5)1985–19898 (5)1990–199947 (29)2000–200969 (43)2010–201637 (23)	distant	1 (1)
1985–1989       8 (5)         1990–1999       47 (29)         2000–2009       69 (43)         2010–2016       37 (23)	Year of diagnosis	
1990–199947 (29)2000–200969 (43)2010–201637 (23)	1985–1989	8 (5)
2000–2009         69 (43)           2010–2016         37 (23)	1990–1999	47 (29)
2010–2016 37 (23)	2000–2009	69 (43)
	2010–2016	37 (23)

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