Update On TNM Staging of Penile Cancer

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- **pTis**: Carcinoma in-situ (PeIN)
- **pTa**: Non-invasive localized squamous cell carcinoma
- **pT1**: Invades lamina propria
  - **pT1a**: no lymphovascular or perineural invasion, and/or G3 tumor
  - **pT1b**: with lymphovascular and/or perineural invasion, and/or G3 tumor
- **pT2**: Invades corpus spongiosum with/without urethra invasion
- **pT3**: Invades corpora cavernosa (including tunica albuginea) with/without urethra invasion
- **pT4**: Invades into adjacent structures (scrotum, prostate, bone)
History Of TNM Staging For Penile Cancer

1st and 2nd editions of TNM Cancer Staging Manual
- No mention of Penile Cancer
- "Second most important midline organ in GU pathology": Colleague who must not be named

- Penile Cancer finally has a staging system

3rd through 6th editions of Cancer Staging Manuals
- No change for 22 years (1988 to 2010)

3rd Through 6th Edition

pTis: Carcinoma in-situ
pTa: Non-invasive verrucous carcinoma
pT1: Tumor invades subepithelial connective tissue
pT2: Tumor invades corpus spongiosum or cavernosum
pT3: Tumor invades urethra or prostate
pT4: Tumor invades other adjacent structures

3rd to 6th Edition

pN1: Metastasis in single superficial inguinal lymph node
pN2: Metastasis in multiple or bilateral superficial inguinal lymph nodes
pN3: Metastasis in deep inguinal or pelvic lymph node(s), unilateral or bilateral

7th Edition

pT1: Lamina propria invasion
pT1a: No lymphovascular invasion, or grade 3 carcinoma component
pT1b: With lymphovascular invasion and/or grade 3 carcinoma component

pT3: Tumor invades urethra or prostate
pT4: Involves other adjacent structures (includes prostate gland)


3rd to 6th Edition

pTa
- Non-invasive verrucous carcinoma

7th Edition

pTa
- Non-invasive verrucous carcinoma
- Broad pushing penetration/invasion permitted
- Destructive invasion is pT1

3rd to 6th Edition
- pN1
  - Single superficial inguinal lymph node
- pN2
  - Multiple or bilateral superficial inguinal lymph nodes
- pN3
  - Deep inguinal or pelvic lymph node(s), unilateral or bilateral

7th Edition
- pN1
  - Single inguinal lymph node (both superficial and deep)
- pN2
  - Multiple or bilateral inguinal lymph nodes (both superficial and deep)
- pN3
  - Extra-nodal extension, or pelvic lymph node(s), unilateral or bilateral

Updates To 8th Edition From 7th Edition
- Most significant updates
  - pT2; pT3
- Less significant updates
  - pTa, pT1a, pT1b
  - pN1, pN2
- Change in wording
  - pTis, pT4

Practical Anatomy & Gross Examination
- Diagnosis is easy, but, staging is hard
  - "Diagnosing squamous cell carcinoma is so easy even a surgeon could do it"
- Accurate staging requires:
  - Understanding anatomy of the different penile components
  - Grossing appropriately according to specimen type
- Stage Dependent on penile component

pTx to pTis 7th Edition Compared To 8th Edition

7th Edition
- pTx:
  - Primary tumor cannot be assessed
- pT0:
  - No evidence of tumor
- pTis:
  - Carcinoma in-situ

8th Edition
- pTx:
  - Primary tumor cannot be assessed
- pT0:
  - No evidence of tumor
- pTis:
  - Carcinoma in-situ (Penile intraepithelial neoplasia [PeIN])
pTa 7th Edition Compared To 8th Edition

**7th Edition**

- Non-invasive verrucous carcinoma
- Broad pushing front

**8th Edition**

- Non-invasive localized Squamous cell carcinoma
- Verrucous Carcinoma, and, Non-invasive Squamous cell carcinoma

**What Parts Are Involved In Stage pTa**

- Foreskin
- Glans penis
- Skin of Penile Shaft
### pT1 7th Edition Compared To 8th Edition

<table>
<thead>
<tr>
<th><strong>7th Edition</strong></th>
<th><strong>8th Edition</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>pT1: Tumor invasive into lamina propria</td>
<td>pT1: Tumor invasive into lamina propria</td>
</tr>
<tr>
<td>pT1a • No lvi or grade 3 tumor</td>
<td>pT1a • No pni, lvi or grade 3 tumor</td>
</tr>
<tr>
<td>pT1b • With lvi and/or G3 tumor</td>
<td>pT1b • With pni, lvi and/or G3 tumor</td>
</tr>
</tbody>
</table>
**What Parts Are Involved In Stage pT1**

- **Foreskin**
  - Mucosal surface (more common), and, skin (less common)
  - Highest pT stage that can be assigned to foreskin tumors
- **Glans penis**
  - Mucosal surface: invasive into lamina propria
  - Coronal sulcus: invasive into lamina propria
- **Penile Shaft**
  - Tumors most common on dorsal aspect of penile skin
  - From skin invades into lamina propria, dartos, Buck’s fascia
Foreskin Anatomy & Gross Examination

- Foreskin
  - Reflection of skin of penile shaft, attached at coronal sulcus
- Squamous mucosa (innermost)
  - Non-keratinizing
  - Lamina propria
  - Loose connective tissue, blood vessels
- Dartos muscle
  - Irregular smooth muscle, loose connective tissue, blends with lamina propria
- Skin (outermost)
  - Dermis (no hair follicles)
  - Epidermis

Circumcision Specimen for foreskin tumors

- Rectangular fragment of skin and squamous mucosa
- Surgical margin along proximal long axis (resected at coronal sulcus)
- Opposite to the surgical margin, skin folds over to the squamous mucosal surface of the foreskin, and is not considered a margin
- Cut surface along the short axis is not a margin either
- Used to remove the foreskin after it is excised off the coronal sulcus and skin of the penile shaft

For gross exam

- Ink surgical margin
- Stretch and specimen and fix overnight in formalin
- Slice perpendicular to the long axis of surgical margin
- Each section demonstrates the skin, lamina propria, dartos muscle and the squamous mucosa
- Most invasive tumors arising from the foreskin are pT1; unless they extend along the surface of the glans penis and invade into the corpus spongiosum of the glans penis
Foreskin Stage

- **pT0**
  - No evidence of primary tumor
- **pTis**: Carcinoma in-situ (PeIN)
- **pTa**: Non-invasive localized squamous cell carcinoma
- **pT1**: Invades lamina propria
  - pT1a: no LVI or PNI, or, G3 tumor
  - pT1b: with LVI and/or PNI, and/or G3 tumor
- No pT2, pT3 or pT4 in tumors involving foreskin only

pT2 7th Edition Compared To 8th Edition

<table>
<thead>
<tr>
<th>7th Edition</th>
<th>8th Edition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pT2</strong></td>
<td><strong>pT2</strong></td>
</tr>
<tr>
<td>Corpus spongiosum invasion</td>
<td>Corpus spongiosum invasion ONLY. With or without urethral invasion</td>
</tr>
<tr>
<td>Corpus cavernosum/Corpora cavernosa invasion</td>
<td>Tunica albuginea, is thick and dense, enshathes C. cavernosa. Acts as barrier to tumor spread</td>
</tr>
</tbody>
</table>

What Parts Are Involved In Stage pT2

**Glans penis**
- Most common location for pT2 tumors
- Mucosal surface and coronal sulcus: invasive into corpus spongiosum

**Penile Shaft**
- Uncommon, but most arise on ventral aspect
- Dorsal tumors would have to grow along skin or Buck’s fascia to invade corpus spongiosum
Practical Anatomy & Gross Examination

Glans penis
- Distal most end of penis
- Squamous mucosa (keratinized in circumcised penis)
- Lamina propria
- Conical expansion of corpus spongiosum forms most of the glans
- Corpora cavernosa and tunica albuginea are variable
- Urethra on ventral aspect

Glans penis:
- Distal most end of penis
- Squamous mucosa (keratinized in circumcised penis)
- Lamina propria
- Conical expansion of corpus spongiosum forms most of the glans
- Corpora cavernosa and tunica albuginea are variable
- Urethra on ventral aspect
Specimen Types & Gross Examination

**Glans penis resection specimens**

- Surgical Goal
  - Maximal functional preservation
  - Local excision
- Small fragment of mucosa with underlying corpus spongiosum
- Glans sparing partial penectomy
  - Larger surface of glans along with some (not all) of the superficial corpus spongiosum is excised
  - Coronal sulcus and/or a short segment of urethra may also be excised

**Glans penis resection specimens (cont’d)**

- Partial penectomy without corpus cavernosum excision
  - Glans penis excised without opening tunica albuginea or excising corpora cavernosa
- Partial penectomy specimen includes the entire glans penis and a short segment of the penile shaft, including skin of penile shaft
Intra-op margin evaluation is urologist dependent
- Local excision
  - Ink deep margin, section perpendicular to mucosa
- Glans sparing partial penectomy
  - Ink deep margin, and other margins indicated by Urologist
  - Section perpendicular to mucosa (dependant on orientation)
  - Submit urethra margin en face if present
  - Coronal sulcus inked similar to glans penis

Glands penis resection margins Intra-op
- Partial penectomy without corpus cavernosum
  - Margins: Urethra, Corpus spongiosum of glans, Coronal sulcus
- Partial penectomy with corpus cavernosum
  - Margins: Urethra, Corpus spongiosum of glans, Penile skin, Corpus cavernosa
  - Freeze separately: Urethra, Corpus spongiosum, Corpus cavernosum, Penile skin

Glands penis gross examination
- Fix overnight in formalin
- Slice through sagittal plane (mid-line), dividing the urethra and glands penis into two halves (right and left)
- Subsequent sections are taken parallel to the first cut (para-sagittal sections)
- Lateral most ends are sliced as coronal sections
- This easily allows evaluation of tumor and invasion of penile structures important for pT stage
**Gross Examination & Block Selection**

Glans penis gross examination (cont’d)
- Submit sagittal sections entirely to visualize tumor with glans penis and urethra
- Can be in two cassettes (mention dorsal and ventral sections)
- Submit entire parasagittal sections with tumor
  - Can be in multiple blocks (mention dorsal and ventral sections)
- Gross photos to show each section submitted
  - Easier to reconstruct tumor on slides to allow evaluation of tumor and invasion of penile structures important for pT stage

**7th Edition Compared To 8th Edition**

<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
<td>pT3</td>
<td>pT3</td>
</tr>
<tr>
<td>Tumor invades urethra</td>
<td>Tumor invades corpus cavernosum (including tunica albuginea), with or without urethral invasion</td>
</tr>
</tbody>
</table>
Practical Anatomy & Gross Examination

Penile Shaft
- Skin (epidermis and dermis)
- Dartos muscle
- Buck’s fascia
- Paired corpora cavernosa (dorsal aspect)
- Urethra surrounded by corpus spongiosum (ventral aspect)

Tunica Albuginea
Corpus Cavernosum
Corpus Spongiosum Urethrae
Corpus Cavernosum
Tunica Albuginea
Urethrae
Urethral Mucosa
Peri-urethral Glands
Corpus Spongiosum
Urethra
Corpus Spongiosum
Tunica Albuginea
Buck's Fascia
Corpus Cavernosum
Tunica Albuginea
Corpus Cavernosum
Tunica Albuginea
Corpus Cavernosum
Corpus Spongiosum
TNM Update on Penile Cancer

- Corpus Cavernosum
- Corpus Spongiosum
- Tunica Albuginea
- Buck's Fascia
Specimen Types & Gross Examination

Penile shaft resection specimens
- Partial penectomy: With a short segment of the penile shaft, including skin of penile shaft
- Total penectomy: Entire penis removed, except for penile root (attached to pubic bones)
  - Variable length of urethra (for perineal urethrostomy)
  - Variable length of skin (for reconstruction)

Total Penectomy resection margins Intra-op
- Similar to partial penectomy with penile shaft excision
  - Margins: Urethra with surrounding corpus spongiosum, Penile skin, Corpora cavernosa
  - Freeze separately: Urethra, Corpus spongiosum, Corpus cavernosum, Penile skin

Total penectomy gross examination
- Fix overnight in formalin as layers fix at different rates (skin vs corpus spongiosum vs corpus cavernosum)
- Penile shaft is amputated a few centimeters proximal to the glans penis
  - Penile shaft is serially cross-sectioned from distal to proximal, so each cross section shows all the structures of the shaft (skin, Buck’s fascia, corpus spongiosum and corpora cavernosa)
  - Glans penis grossed same as in partial penectomies

Gross Examination & Margin Evaluation

Total Penectomy resection margins Intra-op
- Similar to partial penectomy with penile shaft excision
  - Margins: Urethra with surrounding corpus spongiosum, Penile skin, Corpora cavernosa
  - Freeze separately: Urethra, Corpus spongiosum, Corpus cavernosum, Penile skin

Gross Examination & Block Selection

Total penectomy gross examination
- Fix overnight in formalin as layers fix at different rates (skin vs corpus spongiosum vs corpus cavernosum)
- Penile shaft is amputated a few centimeters proximal to the glans penis
  - Penile shaft is serially cross-sectioned from distal to proximal, so each cross section shows all the structures of the shaft (skin, Buck’s fascia, corpus spongiosum and corpora cavernosa)
  - Glans penis grossed same as in partial penectomies
Gross Examination & Block Selection

Total penectomy gross examination (cont’d)
- Submit sagittal/parasagittal sections entirely to visualize tumor with urethra, glans penis, coronal sulcus and shaft
  - Submitted in multiple blocks
  - Map sections (easier to figure out block location)
  - Gross photos to show each section submitted
- Easier to reconstruct tumor on slides to allow evaluation of tumor and invasion of penile structures important for pT stage
**7th Edition Compared To 8th Edition**

**7th Edition**
- pT4
  - Tumor invades other adjacent structures

**8th Edition**
- pT4
  - Tumor invades into adjacent structures (i.e., scrotum, prostate, pubic bone)

**7th Edition**
- pN0
  - No regional lymph node metastasis
- pN1
  - Metastasis in a single inguinal lymph node

**8th Edition**
- pN0
  - No lymph node metastasis
- pN1
  - <2 unilateral inguinal metastases, no extra-nodal extension

**7th Edition**
- pN2
  - Metastasis in multiple or bilateral inguinal lymph nodes
- pN3
  - Extra-nodal extension of lymph node metastases or pelvic lymph node metastases

**8th Edition**
- pN2
  - >3 unilateral metastases or bilateral metastases
- pN3
  - Extra-nodal extension of lymph node metastases or pelvic lymph node metastases

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