INTERNATIONAL SOCIETY OF UROLOGIC PATHOLOGY

PATHOLOGIC STAGING OF SELECT UROLOGIC MALIGNANCIES

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TOPICS FOR DISCUSSION

• Discuss changes in pathologic staging categories in urologic malignancies in the 7th edition (2011) AJCC Staging System, to be released later this year
• Select problematic areas:
  • Prostate – bladder neck involvement
  • Urinary bladder – determination of type of muscle invasion
  • Urothelial carcinoma of prostate – evaluation of prostatic stromal invasion

PROSTATE

SUMMARY OF CHANGES

• Extraprostatic invasion with microscopic bladder neck invasion (T4) is included with T3a
• Gleason Score now recognized as the preferred grading system
• Prognostic factors have been incorporated in the Anatomic Stage/Prognostic Groups
  • Gleason Score
  • Preoperative prostate specific antigen (PSA)
KIDNEY
SUMMARY OF CHANGES

- T2 lesions have been divided into T2a (greater than 7 cm but less than or equal to 10 cm) and T2b (greater than 10 cm)
- Ipsilateral adrenal involvement is reclassified as T4 if contiguous invasion and M1 if not contiguous
- Renal vein involvement is reclassified as T3a
- Nodal involvement is simplified to N0 vs. N1
### National Cancer Database
#### Renal Cell Carcinoma - Tumor size


<table>
<thead>
<tr>
<th>Size in cm</th>
<th>Dx</th>
<th>1 Year</th>
<th>2 Years</th>
<th>3 Years</th>
<th>4 Years</th>
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<tr>
<td>(\leq 4.0)</td>
<td>100</td>
<td>93.7</td>
<td>88.8</td>
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<td>4.1-7.0</td>
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<td>83.6</td>
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<td>7.1-10.9</td>
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<td>75.3</td>
<td>68.1</td>
<td>62.5</td>
<td>57.0</td>
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<tr>
<td>(\geq 10.0)</td>
<td>100</td>
<td>78.7</td>
<td>66.3</td>
<td>58.8</td>
<td>52.5</td>
<td>47.5</td>
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<table>
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<td>4.1-7.0</td>
<td>67.0-68.7</td>
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<tr>
<td>7.1-10.9</td>
<td>55.9-58.1</td>
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<tr>
<td>(\geq 10.0)</td>
<td>46.1-48.9</td>
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</table>

#### NCDB - 47,909 cases

### URINARY BLADDER

#### SUMMARY of CHANGES

- Subepithelial invasion of prostatic urethra is not pT4 disease.
  - pT4 defined as prostatic stromal invasion (seminal vesicles, uterus, vagina, pelvic wall, and abdominal wall also qualify)

- Grading: a low and high grade designation will replace previous 4 grade system to match current WHO/International Society of Urologic Pathology (ISUP) recommended grading system

- Nodal involvement is simplified to N1 (single positive) and N2 (multiple positive) - instead of N1, N2, and N3 which had size criteria within
Subepithelial invasion of prostatic urethra is not pT4 disease.

RENAL PELVIS AND URETER

SUMMARY OF CHANGES

Grading: a low and high grade designation will replace previous 4 grade system to match current WHO/International Society of Urologic Pathology (ISUP) recommended grading system.

URETHRA

SUMMARY OF CHANGES

Urothelial (Transitional Cell) Carcinoma Of The Prostate

- pT1: Tumor invades urethral subepithelial connective tissue (for tumors involving prostatic urethra only)
SUMMARY OF CHANGES

• T1 has been subdivided into T1a and T1b based on the presence or absence of lymphovascular invasion or poorly differentiated cancers.

• T3 category is limited to urethral invasion and prostatic invasion is now considered T4.
SUMMARY OF CHANGES
The definition of TNM and the Stage Grouping for this chapter has not changed from the Sixth Edition.

Staging of Bladder Cancer:
*Evaluation of Muscularis Propria Invasion*

Pathologic Staging of Bladder Cancer

<table>
<thead>
<tr>
<th>pT_1</th>
<th>non-invasive neoplasm</th>
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<tbody>
<tr>
<td>pT_{cis}</td>
<td>carcinoma in situ (flat)</td>
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<tr>
<td>pT_{1}</td>
<td>invasive into lamina propria</td>
</tr>
<tr>
<td>pT_{2}</td>
<td>invasive into muscularis propria</td>
</tr>
<tr>
<td>pT_{3}</td>
<td>invasive into perivesical fat</td>
</tr>
<tr>
<td>pT_{4}</td>
<td>invasive into adjacent organs</td>
</tr>
</tbody>
</table>

No change in Seventh edition of AJCC.
LAMINA PROPRIA-MUSCULARIS MUCOSAE

- Thin wispy muscle bundles
- 94-100% bladders
- Associated with large caliber blood vessels
- Awareness important so as not to overstage T1 as T2

Wispy or thin muscle bundles, 71/150 (47%)
M. mucosae muscle pattern

Hypertrophic – Haphazard (33%)

M. mucosae muscle pattern

Hypertrophic – M. propria-like (45%)

Typical
Typical pattern:
• Arranged in groups
• Distinct compact bundles
• Smooth outline of bundles
• Several layers both horizontally and vertically

Muscularis propria

2 types of muscle - awareness important for pT staging

LP inv. (M. mucosae)- pT1
M. propria inv. - pT2

Muscularis mucosae vs. Muscularis propria

- Inflammatory & desmoplastic response of invasion
- Prior biopsy
- Lack of parallel orientation
- Hypertrophy of m. mucosae
- Difficult cases - conservative stance
- Express inability to be certain
Muscularis mucosa or muscularis propria?
**Muscle Markers**

- Smooth muscle actin (SMA)
- Desmin
- H-caldesmon
- Smooth muscle myosin heavy chain
- Smoothelin
  - Contractile protein
  - Fully differentiated muscle cells
  - Hyperplastic muscularis mucosa negative to weak
  - Diffuse positivity in muscularis propria
  - 100% specificity with diffuse staining

Hypertrophic muscularis mucosa
SMA

**SMOOTHELIN at USCAP 2009**

- **GP Paner, Poster Monday 9.30**
  - Confirms value of smoothelin in TURBT specimens.
  - IR retained in the background of thermal tissue injury & involvement by carcinoma

- **Dvorakova et al, Poster Tuesday 9.30 am**
  - Smoothelin proved to be a reliable marker

- **S Khayyata et al, Poster Monday 1pm**
  - Intensity and extent of smoothelin staining accurately distinguishes MP from MM in the intact bladder
  - Documentation of patterns of smoothelin expression is warranted - variable positivity in GU tract smooth muscle may help define functional status (ureter, bladder neck) &/or impact cancer staging (bladder, urachus)

**Smoothelin: Negative – Suggestive of M. Mucosa**
Staging Issues in “Urothelial Carcinoma of the Prostate”

UROTHELIAL CARCINOMA INVOLVING THE PROSTATE GLAND

- The prostate is involved in approximately 30% of patients with invasive bladder carcinoma
- Occasionally, urothelial carcinoma involving the prostate may be first documented on prostate biopsy
- Staging issues are problematic and not well covered in traditional text books

INVolVEMENT OF PROSTATE GLAND

- Direct invasion of prostate gland: pT4a of bladder cancer – poor prognosis
- Urothelial CIS of urethra: if margin status (+), urethrectomy
- Involvement of prostatic glands without stromal invasion (pTCIS*): not adverse
- Involvement of seminal vesicle without stromal invasion: no ↑ risk of progression
- Involvement of prostate or seminal vesicle stroma (pT2*): poor prognosis, ↑ metastasis

*Staging for urothelial carcinoma of prostate
Direct extension of a urothelial carcinoma into prostatic stroma equates to pT4 disease—"urinary bladder cancer staging" system.

Extension of prostatic urethral urothelial carcinoma into prostatic stroma is not pT4 disease—pT2 by "urothelial carcinoma of the prostate staging" system.

PT4 Bladder Carcinoma
Bladder neck invasion- pT3a disease in AJCC, 7th Edition
Bladder neck

**Histo-anatomy**

- Most distal portion of bladder
- It merges with prostate gland in males
- It is formed by trigonal, detrusor, and urethral musculature; internal sphincter present in this region
- Devoid of glandular tissue- occasionally may have prostatic ducts/acini
**Bladder neck**

- Invasion of bladder neck interpreted as extension beyond prostate- pT4 PCa (AJCC, 6th Edition)
- SEER Site specific coding guidelines- ICD 67.5 for bladder neck (Bladder: 67, Prostate: 61)
- Multiple recent studies have documented that microscopic bladder neck involvement has outcome different from PCa involving rectum or striated sphincter
- Microscopic bladder neck invasion defined as pT3 disease in AJCC, 7th Edition

**Microscopic Bladder Neck Invasion (pT3 disease)**

- Microscopic involvement of muscular wall of bladder neck by PCa
- Absence of prostatic glands in corresponding slide or prostate glands in stroma distinct from bladder neck muscle

**Handling of radical prostatectomy**

- Prostate base (bladder neck) margin-inked and handled as a cone
- Microscopic sections- bladder neck tissue may or may not be present-depends on
  - Bladder neck sparing surgery
  - Age of the patient
  - Other surgical factors influencing dissection
Microscopic Bladder Neck Invasion (pT3 disease)

- Outcome of patients with bladder neck involvement is different from pT4 disease and similar to extraprostatic extension at other sites
- Prostate base (bladder neck) margin - positive if tumor inked in coned prostate base and not if tumor in bladder neck muscle
- Prostate base (bladder neck) margin - important adverse parameter - worse than other positive surgical margins