Summary of Changes

- Restructured pharynx into
  - New HPV-Mediated (p16+) Oropharyngeal
  - Nasopharynx
  - Oropharynx (p16-) and Oropharynx
- New criteria for extranodal extension (ENE)
  - Both for clinical and pathological staging
- New staging for unknown primaries with nodal involvement
- New cutaneous squamous cell carcinoma of head and neck
- Addition of Depth of Invasion in Oral Cavity T category

AJCC Cancer Staging Manual, 7th Ed.
Head and Neck Chapters

- Lip and Oral Cavity
- Pharynx (oro, naso and hypo)
- Larynx (supraglottic, glottic and subglottic)
- Nasal Cavity and Paranasal Sinuses
- Salivary Gland
- Mucosal Melanoma (new to the 7th Ed)
Head and Neck Chapters in 8th Edition

- Staging Head and Neck Cancers
- Cervical Lymph Nodes and Unknown Primary Tumors
- Lip and Oral Cavity
- Major Salivary Glands
- Nasopharynx
- HPV-Mediated (p16+) Oropharyngeal
- Oropharynx (p16-) and Hypopharynx
- Nasal Cavity and Paranasal Sinuses
- Larynx
- Mucosal Melanoma of Head and Neck
- Cutaneous Squamous Cell Ca of Head and Neck

HPV-Mediated (p16+)
Oropharyngeal Cancer

High-Risk HPV

- HR-HPV associated cancer
  - Younger, healthier individuals
  - Little or no tobacco exposure
  - Increasing at 5% per year
  - Much better survival than traditional tobacco-associated CA
  - Definition of disease
Definition

• High Risk-HPV
  – Defines what we think of as the disease entity
  – More expensive to run
  – Less universally available
  – Technically more variability with interpretation

• p16
  – Easily standardized interpretation
  – Inexpensive to use
  – Near universal availability
  – Surrogate for disease
  – p16 expression of weak intensity, or limited (<75% of cells)
  – Staged with p16- oropharynx and hypopharynx chapter
Clinical TNM Stage Grouping 8th Ed. p16+ Oropharyngeal Cancer

<table>
<thead>
<tr>
<th></th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>I</td>
<td>I</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>T1</td>
<td>I</td>
<td>I</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>T2</td>
<td>I</td>
<td>I</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>T3</td>
<td>II</td>
<td>II</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>T4</td>
<td>III</td>
<td>III</td>
<td>III</td>
<td>III</td>
</tr>
</tbody>
</table>

Pathological TNM Stage Grouping 8th Ed. p16+ Oropharyngeal Cancer

<table>
<thead>
<tr>
<th></th>
<th>N0</th>
<th>N1</th>
<th>N2</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>I</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>T1</td>
<td>I</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>T2</td>
<td>I</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>T3</td>
<td>II</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>T4</td>
<td>II</td>
<td>II</td>
<td>II</td>
</tr>
</tbody>
</table>

Cervical Lymph Nodes – Extranodal Extension (ENE)
### Extramodal Extension (ENE)

- ENE has profound effect on prognosis in head & neck
  - Evidence supports ENE as adverse prognostic factor
  - Most evidence from pathologic analysis of nodes
  - Pathology includes distinction between microscopic & macroscopic

- Inclusion of ENE in N category
  - p16- Oropharynx and Unknown Primary and Hypopharynx
  - Oral Cavity
  - Larynx
  - Skin
  - Salivary Gland
  - Nasal Cavity and Paranasal Sinus

- Terminology for extension outside lymph nodes
  - ENE is the preferred wording
  - Not extracapsular spread/extension or extranodal involvement

### Clinical Staging

- Stringent criteria *required* to permit ENE(+) diagnosis

- Unambiguous evidence of gross ENE on clinical exam
  - Invasion of skin
  - Infiltration of musculature or dense tethering to adjacent structures
  - Nerve invasion with dysfunction
    - Cranial nerve
    - Brachial plexus
    - Sympathetic trunk
    - Phrenic nerve
  - Supported by strong radiographic evidence

- Radiographic evidence *alone* is insufficient

- If any doubt or ambiguity, assign ENE(-)

### Pathological Staging

- Clearly defined pathological ENE(+) based on
  - Tumor present within confines of node and
  - Extending through the node capsule
  - Into surrounding connective tissue
  - With or without associated stromal reaction

- ENE(+) may be classified as
  - ENE<sub>m</sub> for microscopic ENE <2 mm
  - ENE<sub>ma</sub> for major ENE >2 mm

- If any doubt or ambiguity, assign ENE(-)
**ENE - N Characteristic 8th Edition**

- **Clinical**
  - Any ENE is N3b

- **Pathological**
  - ENE either Minor (≤2mm) or Major (>2mm) increases N by 1 step

---

**Unknown Primary Tumors of Head and Neck**

- **Unknown Primary Tumor – T0**
  - Unique to head & neck
    - Due to anatomic site staging differences
    - Impossible to choose between multiple head and neck chapters
    - Metastatic cervical node with no primary found
  - p16 and EBER are required for staging
    - p16+ will be staged as T0 N-appropriate in HPV-Mediated p16+ Oropharynx chapter
    - EBER + will be staged T0 N-appropriate in Nasopharynx Chapter
    - EBER-, p16- SCC will be staged in the Cervical Node Chapter as T0 N-appropriate and will need ENE designation
  - T0 eliminated from all other chapters except
    - EBV-related nasopharynx
    - HPV-related oropharynx
    - Salivary gland based on histology of lymph node
Prognostic Stage Groups

- Metastatic cervical adenopathy & unknown primary tumor
  - Except for EBV-related and HPV-related tumors

<table>
<thead>
<tr>
<th>When T is...</th>
<th>And N is...</th>
<th>And M is...</th>
<th>Then the stage group is...</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>N1</td>
<td>M0</td>
<td>III</td>
</tr>
<tr>
<td>T0</td>
<td>N2</td>
<td>M0</td>
<td>IVA</td>
</tr>
<tr>
<td>T0</td>
<td>N3</td>
<td>M0</td>
<td>IVB</td>
</tr>
<tr>
<td>T0</td>
<td>Any N</td>
<td>M1</td>
<td>IVC</td>
</tr>
</tbody>
</table>

p16 Expression Staging Differences

- T category differences based on p16 expression
  - p16+
    - No T1a
    - No T4b
  - p16-
    - No T0

- pN category observations for p16+
  - pN3 behaves as Stage I
  - pN2 behaves as Stage II
  - Findings are unprecedented
### Cutaneous Carcinoma

- Chapter title reflects mostly data from squamous cell ca
- Histologic types include
  - All non-melanoma skin carcinomas, except Merkel cell ca
- Primary sites
  - Skin of lip, external ear, face, scalp, and neck
  - Vermilion lip is included (and excluded from Oral Cavity Ca)
  - Etiology is primarily based on ultraviolet (UV) exposure

### Revised Cutaneous Carcinoma Staging System

- **T** category based on
  - Greatest dimension
  - Invasion >6mm or into subcutaneous tissue
  - Perineural invasion
  - Invasion of underlying bone
- **N** category mimics head & neck nodal staging and incorporates ENE

### Other Chapter Changes
Additional Changes

• Oral Cavity
  – Depth of invasion (DOI) added to T category
  – Extrinsic muscle infiltration eliminated for T4

Oral Cavity

• Depth of Invasion now increases T by 1 step for every 5 mm*
  • T1 =
    – Tumor ≤ 2 cm, ≤ 5 mm depth of invasion (DOI)
  • T2 =
    – Tumor ≤ 2 cm, DOI > 5 mm and ≤ 10 mm
    – or tumor > 2 cm but ≤ 4 cm, and ≤ 10 mm DOI
  • T3 =
    – Tumor > 4 cm
    – or any tumor > 10 mm DOI
  *DOI is depth of invasion and not tumor thickness

Depth is not Thickness
(Courtesy Margie Brandwein)
Additional Changes

- Nasopharynx
  - T2 includes adjacent muscle involvement including medial and lateral pterygoid and prevertebral muscles
  - T4 includes specific description of soft tissue involvement
  - N3a and N3b are now one category N3

Key Patient and Tumor Factors

- Comorbidity
  - Reporting of all major illnesses
- Performance Status
  - Zubrod/ECOG
- Lifestyle factors
  - Smoking: never, ≤10 years, >10 ≤20 years, >20 years
  - Alcohol abuse
- Nutrition
  - Weight loss of >10% over 3 months
- Depression diagnosis
  - Impacts quality of life and survival

Summary
Summary

- New HPV-Mediated (p16+) Oropharyngeal
- New criteria for extranodal extension (ENE)
- New staging for unknown primaries with nodal involvement
- New cutaneous squamous cell carcinoma of head and neck
- New T category addition of Depth of Invasion

Thank you