STAGING IN HNC- TNM AND BEYOND

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• Purpose of staging

• Principles of staging in HNC

• Moving ahead within the TNM and beyond the TNM
Purpose of staging

- Predicting **prognosis**
- Guiding **treatment decisions** (outcomes of previous patients with similar stage)
- Key component of inclusion, exclusion, and stratification criteria for **clinical trials**
- Basis of clinical and translational cancer research (exchange and comparison of info among different centers and registries)
TNM staging

AJCC-UICC

T
N
M
Principles of staging

- Clinical staging
- Pathological staging
Principles of staging

- **Clinical staging** -
  - using best possible estimate of the extent of disease (cTNM)
  - before initiation of first treatment.

- Clinical examination,
- CT, MRI, PET, USG (NPC, PNS, Nodes)
- Endoscopy, EUA
Principles of staging

• **Additional and important** staging, but cannot replace clinical staging.

• Based on clinical stage information supplemented/modified by operative findings and pathological evaluation of the resected specimens (primary and/or nodes)

• **pT** - actual measurement of unfixed tumor in surgical specimen

• **pN** - If SND- > 10 LN, If RND, MRND >15 nodes But examination of fewer negative nodes will be assigned N0 category.

• When biopsy proven mets- **pM1**
TNM staging

AJCC-UICC

T
N
M
Why revise and move ahead and beyond TNM??

Advancement in what we know - clinical and pathological data, diagnostic/ imaging modalities, treatment modalities

Prognostic significance of staging systems change

Evaluate for suitability of staging systems

Further exploration
Part II  Head and Neck

5. Staging Head and Neck Cancers ....
6. Cervical Lymph Nodes and Unknown Primary Tumors of the Head and Neck .............
7. Lip and Oral Cavity ....
8. Major Salivary Glands ..........
9. Nasopharynx ..............
10. HPV-Mediated (p16+)
    Oropharyngeal Cancer ........
11. Oropharynx (p16−) and Hypopharynx ..........
12. Nasal Cavity and Paranasal Sinuses ..........
13. Larynx ..............
14. Mucosal Melanoma of the Head and Neck ..........
15. Cutaneous Squamous Cell Carcinoma of the Head and Neck ..........
LIP AND ORAL CAVITY - STAGING
Mucosal Lip

Depth of Invasion

Extranodal extension
**Mucosal Lip**—vermilion surface or that portion of the lip that comes into contact with the opposed lip

Depth of invasion

SCIENTIFIC PAPERS

Predictive Value of Tumor Thickness in Squamous Carcinoma Confined to the Tongue and Floor of the Mouth

Ronald H. Spiro MD, Andrew G. Huvos, MD, George Y. Wang, PhD, Jeffrey D. Spiro, MD, Clare A. Gnecco, MS, and Elliot W. Strong, MD, New York, New York

From the Head and Neck Service, Departments of Surgery and Pathology, and the Division of Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York.

Requests for reprints should be addressed to Ronald H. Spiro, MD, 425 East 67th Street, New York, New York 10021.


Volume 152, October 1986

International Consortium for Outcomes Research in Head and Neck Cancer

- Retrospective analysis
- 3149, 11 centres, oral SCC
- Median followup 40 months

DOI was a significantly associated with disease-specific survival ($P < .001$)

Proposed an improved oral cancer T staging system based on incorporation of DOI
Depth of invasion

- Deepest level of Invasion beneath the plane defined by surrounding normal mucosa
- Not the same as tumor thickness (exophytic portion)

https://www.researchgate.net/profile/Lester-Thompson-3
Can we predict DOI before pathological examination??

History - dysphagia (sufficient invasion of oral structures)
- drooling, swallowing with difficulty
- trismus (not caused by pain)

Clinically – (by bidigital*, bimanual* palpation)
- crude measure
Even experienced clinicians may have difficulty in differentiating:

- Superficial and less invasive lesion (< 5mm)
- Moderate depth (>5, < 10mm)
- Deeply invasive lesion (>10mm)

If there are doubts, select the lesser depth to avoid stage migration.

DOI increases T category by 1 for each 5 mm of tumor depth (until ≥ 10 mm)
- The horizon is established at the level of the basement membrane relative to the closest intact squamous mucosa.

- dropping a “plumb line” perpendicular from the horizon to determine the greatest DOI.

- recorded in mm.

- Increases T category by 1 for each 5 mm of tumor depth (until ≥ 10 mm)
Extranodal extension

Influence of extracapsular nodal spread extent on prognosis of oral squamous cell carcinoma

Vukerić, V. Weisemann, MD, PhD, 1 Nora Katabi, MD, 2 Frank L. Palmer, BA, 1 Pablo H. Montero, MD, 1 Jocelyn C. Migliacci, MA, 1 Mithat Gökmen, PhD, 3 Diane Carlson, MD, 4 Ian Ganly, MD, PhD, 5 Jatin P. Shah, MD, 1 Ronald Ghossein, MD, 3 Snehal G. Patel, MD, 1

1 Head and Neck Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, New York, 2 Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, New York, 3 Department of Epidemiology–Biostatistics, Memorial Sloan Kettering Cancer Center, New York, New York, 4 Department of Pathology, Cleveland Clinic, Weston, Florida.

Accepted 3 July 2015
Published online 30 October 2015 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/hed.24190

- Pathological review of 245 pathologically +ve neck dissection specimens of oral SCC
- 73 months follow-up
- DSS was significantly better for patients without ECS than patients with ECS (p<0.01)
Extranodal extension
ENE for cN

- Assignment of ENE should be based almost entirely on **physical examination**, rather than imaging.
- **Unambiguous Gross ENE** on clinical exam supported by strong radiological evidence.

- multiple matted nodes
- fixed nodes
- skin invasion
- muscle invasion
- infiltration of cranial nerve, brachial plexus, sympathetic trunk, phrenic nerve
- **Irregular enhancement** of the nodal capsule (amorphous spiculated margins)
- **Infiltration into adjacent fat/muscle** (involvement of internodal fat resulting in loss of normal oval to round nodal shape)

ENE for pN

- ENEmi – microscopic ENE ≤ 2mm
- ENEma - Macroscopic ENE-
  - ENE apparent to naked eye at the time of dissection
  OR  - microscopic ENE >2mm beyond the LN capsule

ENE HAS BEEN INCORPORATED IN ALL HEAD AND NECK CANCER SITES EXCEPT NASOPHARYNGEAL CANCER AND HPV ASSOCIATED P16+ OPC
Tumor ≤ 2 cm, DOI > 5 mm and ≤ 10 mm
or
tumor > 2 cm but ≤ 4 cm, and ≤ 10 mm DOI

Tumor > 4 cm
or any tumor > 10 mm DOI
T4a- moderately advanced local disease

Adjacent structures only- eg- through cortical bones of mandible, maxilla into the maxillary sinus or skin of the face. A superficial erosion of bone/tooth socket (alone) by a primary in the gingiva is not T4a

lip- cortical bone, skin of the face, inferior alveolar nerve, floor of mouth
T4b - very advanced local disease- pterygoid plates, masticator space, skull base, encases ICA
cN categories

Diagram showing different categories of lymph node involvement (N0, N1, N2A, N2B, N2C, N3A, N3B) with color-coded regions indicating the extent of extranodal extension (ENE).
pN categories

N2a

OR

N3b

OR

Deepika Malik
Survival data

Fig. 5.2 Overall Survival based on 8th edition T category criteria. Kaplan-Meier methods were used to perform cancer-specific analyses predicting overall survival as the endpoint on a population of oral cavity cancer patients from MSKCC and PMH.

Fig. 5.4 Overall Survival based on 8th edition N category criteria that incorporate ENE as a prognostic factor. Kaplan-Meier methods were used to perform cancer-specific analyses predicting overall survival as the endpoint on a population of oral cavity cancer patients from MSKCC and PMH.

Fig. 5.6 Overall Survival based on Kaplan-Meier methods were used to perform cancer-specific analyses predicting overall survival as the endpoint on a population of oral cavity cancer patients from MSKCC and PMH.
ALL HEAD AND NECK CANCER SITES EXCEPT
NASOPHARYNGEAL CANCER AND HPV ASSOCIATED
P16+ OPC
HPV MEDIATED (P16+) OROPHARYNGEAL CANCER*
Why a separate staging system?

• Epidemic of HPV mediated OPC over the last 2 decades (↑ of 5%/year)
• Significantly different behaviour and natural history of disease

➢ YOUNGER
➢ HEALTHIER
➢ LITTLE OR NO TOBACCO EXPOSURE
Particularly over the last 15 years, since the official recognition of viral cause of OPC by WHO in 2007, evidence emerged that the previous staging system was unsuited to this particular group.
IHC for p 16 overexpression has emerged as a robust surrogate biomarker for HPV-mediated carcinogenesis

(Overexpression of tumor suppressor protein p16 (cyclin-dependent kinase 2 A))

- Lower cost
- Widespread availability
- Ease of interpretation
- Independent positive prognosticator
Development and validation of a staging system for HPV-related oropharyngeal cancer by the International Collaboration on Oropharyngeal cancer Network for Staging (ICON-S): a multicentre cohort study

Brian O’Sullivan, Shao Hui Huang, Jie Su, Adam S Garden, Erich M Sturgis, Kristina Dahlstrom, Nancy Lee, Nadeem Riaz, Xin Fei, Shlomo A Koyfman, David Adelstein, Brian B Burkey, Jeppe Friiborg, Claus A Kristensen, Anita B Goldblatt, Frank Hoegers, Bernd Kremer, Ernst-Jan Speel, Daniel W Bowles, David Rabon, Sana D Karam, Eugene Yu, Wei Xu

2600 patients, 1907 HPV +

5 year OS

<table>
<thead>
<tr>
<th>Stage</th>
<th>HPV +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>76%</td>
</tr>
<tr>
<td>Stage II</td>
<td>68%</td>
</tr>
<tr>
<td>Stage III</td>
<td>53%</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>45%</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>34%</td>
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HPV +ve

<table>
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<tr>
<th>Stage</th>
<th>HPV +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>88%</td>
</tr>
<tr>
<td>Stage II</td>
<td>82%</td>
</tr>
<tr>
<td>Stage III</td>
<td>84%</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>81%</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>60%</td>
</tr>
</tbody>
</table>
The 7th edition

- lost the ability to differentiate between stages
- Hazard discrimination
- lost hazard consistency
- Loss of predictive ability

AJCC cancer staging 8th edition
48% of seventh edition TNM stage III-IV would migrate to eight edition TNM stage I
T4

Tumor invades the
• larynx,
• extrinsic muscle of tongue,
• medial pterygoid,
• hard palate
• mandible or beyond
Nodal

Previous N1, N2a, N2b combined to N1 (ie I/L nodes ≤6 cm)

Previous N2c is N2 (B/L or C/L nodes ≤6 cm)

N3 any LN >6 cm

Role of ENE is less obvious in p16+ OPC, therefore not a factor in staging
Pathological p16+ OPC

Nx- regional LN cannot be assessed
pN0- no regional LN mets
pN1- mets in ≤ 4 LNs
pN2- mets in > 4 LNs
### AJCC Prognostic Stage Groups

#### Clinical

<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, T1 or T2</td>
<td>N0 or N1</td>
<td>M0</td>
<td>I</td>
</tr>
<tr>
<td>T0, T1 or T2</td>
<td>N2</td>
<td>M0</td>
<td>II</td>
</tr>
<tr>
<td>T3</td>
<td>N0, N1 or N2</td>
<td>M0</td>
<td>II</td>
</tr>
<tr>
<td>T0, T1, T2, T3 or T4</td>
<td>N3</td>
<td>M0</td>
<td>III</td>
</tr>
<tr>
<td>T4</td>
<td>N0, N1, N2 or N3</td>
<td>M0</td>
<td>III</td>
</tr>
<tr>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td>IV</td>
</tr>
</tbody>
</table>

#### Pathological

<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>
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<td>M0</td>
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<td>N2</td>
<td>M0</td>
<td>II</td>
</tr>
<tr>
<td>T3 or T4</td>
<td>N0, N1</td>
<td>M0</td>
<td>II</td>
</tr>
<tr>
<td>T3 or T4</td>
<td>N2</td>
<td>M0</td>
<td>III</td>
</tr>
<tr>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td>IV</td>
</tr>
</tbody>
</table>
Important considerations*

✔ Only radiological imaging may not help in distinguishing whether the BOT tumor is extending along mucosa of lingual surface of epiglottis (T3) or it is only abutting against it.

    NEED Direct Clinical observation

✔ When skull base involved, important to carefully evaluate for PNI and intracranial spread of disease. Important for radiation planning

✔ RPN to be carefully evaluated for OPC especially for PPW tumor

    Unless cystic or necrotic, RPN appear isodense to adj prevertebral muscles on CT, easily overlooked
NASOPHARYNGEAL CANCER STAGING

Deepika Malik
NPC - a unique HNC

- Natural behaviours
- Therapeutic considerations
- Staging

AJCC/UICC
Chinese systems
Ho’s staging from Hongkong

8th AJCC NPC staging
T0- no tumor identified, **but EBV +ve cervical nodal involvement**

Tm confined to the nasopharynx. Tumor that extends to the oropharynx &/or nasal cavity without parapharyngeal extension

Tm with parapharyngeal space extn and/or adjacent soft tissue involvement (medial pterygoid, LP, **Prevertebral muscles**)

---

*Tx*

Radiation Oncology: Imaging and Treatment 1st Edition by David K Gaffney, Dennis C. Shrieve (Christopher J Anker (Author), Mark K Buyyounouski Feng-ming (Spring) Kong)
Infiltration of bony structures at skull base, cervical vertebra, pterygoid structures, and/or paranasal sinuses

Intracranial, hypophx, cranial nerves, orbit, parotid gland and/or soft tissue inv beyond the lateral surface of LP muscle
In T4, the original “infratemporal fossa/masticator space” is replaced by specific description of soft tissue involvement BEYOND THE LATERAL SURFACE OF LP MUSCLE to avoid potential ambiguity.
• The previous N3b criterion of “supraclavicular fossa” is now changed to “below caudal border of cricoid cartilage”

• N3a and N3b are merged into a single N3

<table>
<thead>
<tr>
<th>Seventh edition</th>
<th>Eighth edition</th>
</tr>
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<tbody>
<tr>
<td>IVC</td>
<td>Any T, any N M1</td>
</tr>
</tbody>
</table>

**Summary of changes**

<table>
<thead>
<tr>
<th>T category</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0 is added for EBV-positive cervical node(s) involvement despite unidentified primary tumor</td>
</tr>
<tr>
<td>- Involvement of medial pterygoid, lateral pterygoid, and prevertebral muscles is now staged as T2</td>
</tr>
<tr>
<td>- In T4, the original “infratemporal fossa/masticator space” is replaced by specific description of soft tissue involvement to avoid potential ambiguity</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N category</th>
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<tr>
<td>- The previous N3b criterion of “supraclavicular fossa” is now changed to “below caudal border of cricoid cartilage”</td>
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<td>- N3a and N3b are merged into a single N3</td>
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</table>

**Stage group**

| The previous Stages IVA and IVB are merged into IVA |
| The previous IVC is now upstaged to IVB |
Changes to T0 category

➢ Elimination of the T0 category for all oral cavity, skin, larynx, salivary gland, HPV - oropharynx, hypopharynx, and sinus.

➢ For patients with a malignant cervical node, with no known primary- needs to be staged according to the staging for unknown primary with neck node

➢ T0 category is retained for 2 scenarios-

   Node is positive for p16 ➔ p16+ OPC staging

   Node is positive for EBV ➔ NPC staging
Cutaneous SCC of the Head and Neck

- A new staging classification in the 8th edition
- Cutaneous squamous cell carcinoma (CSCC) and other nonmelanoma skin carcinomas of the head and neck (except Merkel cell carcinoma [MCC]) (including the dry vermilion part of lip)*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be identified</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>TI</td>
<td>Tumor smaller than 2 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor 2 cm or larger, but smaller than 4 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor 4 cm or larger in maximum dimension or minor bone erosion or perineural invasion or deep invasion*</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor with gross cortical bone/marrow, skull base invasion and/or skull base foramen invasion</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor with gross cortical bone/marrow invasion</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor with skull base invasion and/or skull base foramen involvement</td>
</tr>
</tbody>
</table>
Why look further BEYOND traditional TNM??

Cancer cachexia update in head and neck cancer: Pathophysiology and treatment

Marion E. Couch, MD, PhD, MBA; 1 Kim Dittus, MD, PhD; 2 Michael J. Tobin, PhD; 3 Monte S. Willis, MD, PhD; 4 Dennis C. Guttridge, PhD; 5 Jonathan R. George, MD; 6 Eric Y. Chang; 7 Christine G. Gouin, MD; 8 Hink Der-Torossian, MD, MPH

1 Division of Otolaryngology–Head and Neck Surgery, Department of Surgery, Vermont Cancer Center, University of Vermont, College of Medicine, Burlington, Vermont, 2 Division of Hematology–Oncology, Department of Medicine, Vermont Cancer Center, University of Vermont, College of Medicine, Burlington, Vermont, 3 Department of Molecular Physiology and Biophysics, University of Vermont, College of Medicine, Burlington, Vermont, 4 Department of Pathology and Laboratory Medicine, McKeefer Heart Institute, University of North Carolina, Chapel Hill, North Carolina, 5 Department of Molecular Virology, Immunology, and Medical Genetics, Ohio State University, Columbus, Ohio, 6 Department of Otolaryngology–Head and Neck Surgery, University of California, San Francisco, California, 7 University of Vermont, College of Medicine, Burlington, Vermont, 8 Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins Hospital, Baltimore, Maryland.

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ASSOCIATION BETWEEN DEPRESSION AND SURVIVAL OR DISEASE RECURRENCE IN PATIENTS WITH HEAD AND NECK CANCER ENROLLED IN A DEPRESSION PREVENTION TRIAL

Kathryn E. Lazure, MPAS, 1 William M. Lydiatt, MD, 2,3 David Denman, MD, 3 William J. Burke, MD 4

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2 Department of Otolaryngology–Head and Neck Surgery, University of Nebraska Medical Center, Omaha, Nebraska. E-mail: wmlydiat@unmc.edu
3 Nebraska Methodist Hospital, Omaha, Nebraska
4 Department of Psychiatry, University of Nebraska Medical Center, Omaha, Nebraska

Accepted 3 October 2008
Published online 23 March 2009 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/hed.21046
Future of HN cancer staging- moving further beyond TNM

**Limitations** of Current system

- Unable to easily adapt to advances in understanding of cancer biology and incorporate new prognostic variables as they become available
- Static system- unable to use subsequent events in the course of disease
- Still a population based approach, not personalised
- Main end point is OS

**Precisión Medicine Core (PMC) of the AJCC**

- Risk Models for Individualized Prognosis in the Practice of Precisión Oncology
- Work on prognostication models rather than prognostic classifiers with the belief than individualized predictions are more accurate and more useful for clinical decision making.
- Prognostication tools were identified in the form of equations, equations and risk scores, equations and calculators, nomograms, risk scores, and other presentations.
TAKE HOME MESSAGE

Oral cavity cancers have inclusion of DOI

OPC’s are distinguished by p16 IHC

Inclusion of ENE for all sites (except NPC and p16+ OPC)

Further reading-
-Risk Models for Individualized Prognosis in the Practice of Precision Oncology, chapter 4, AJCC 8th edition

Deepika Malik
Acknowledgement

ICRO and AROI
Organisers
Dept. of Radiation Oncology, MMIMSR, Ambala
My teachers and patients

Thank-you