

AJCC Oropharynx HPV-Associated and Salivary Glands: Insights from the Expert Panel

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AJCC v9 Head and Neck Taskforce
CAP Cancer Committee – Head and Neck



NCRA ANNUAL EDUCATIONAL CONFERENCE
OFF TO THE RACES
ACCELERATING EXCELLENCE IN ONCOLOGY DATA

May 5-8, 2026 | Louisville, Kentucky



AJCC Core Group – Head and Neck

General

Guiding Principles



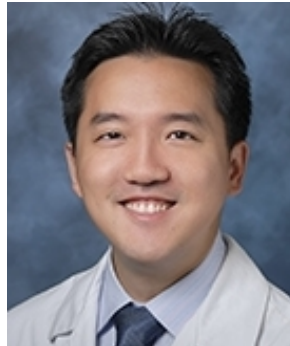
William B. Lydiatt
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Chair



Brian O'Sullivan
UICC Rep & Radiation Oncology



Allen Ho
Vice Chair

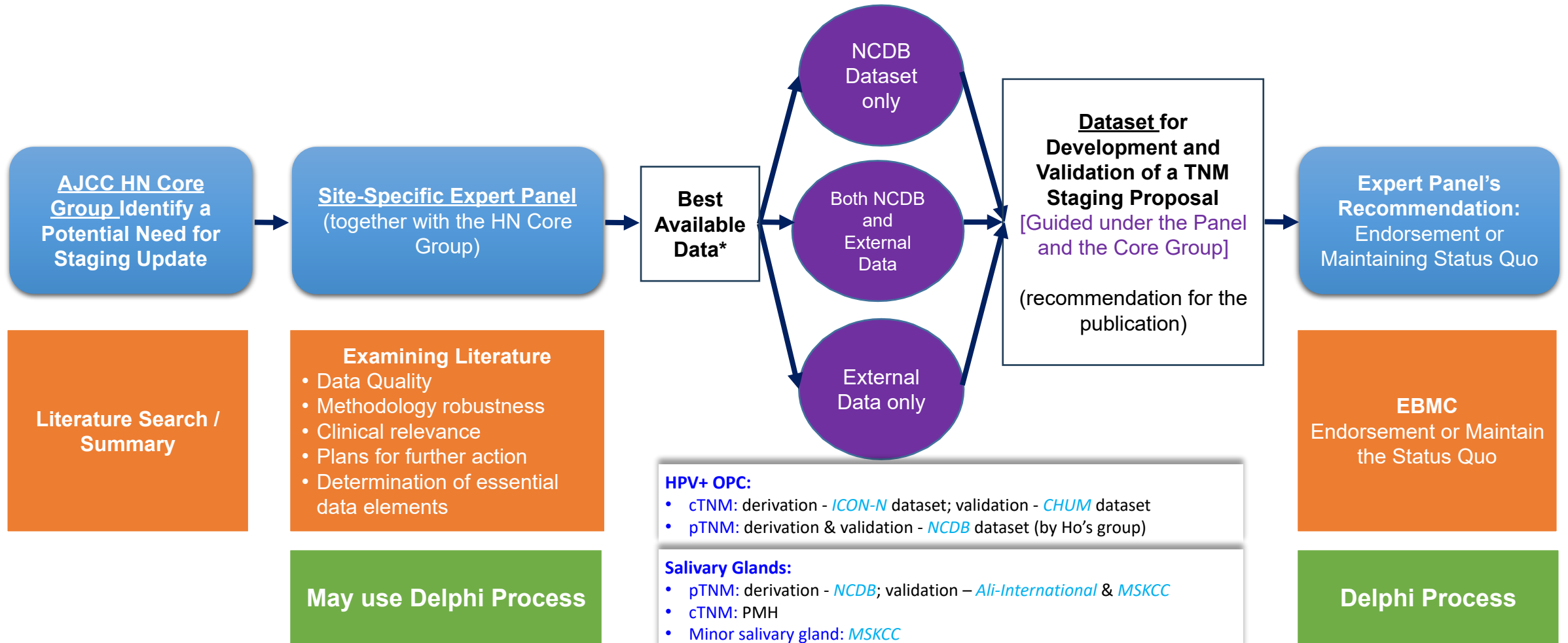


Raja Seethala
Pathology



Sophie Huang
Radiation Oncology & Data Science

AJCC HNC Staging Update Process



*Requirement of best dataset(s): contains minimal essential data elements

General Principles and Changes

- Principles
 - Consistent Application of Statistical Metrics to Determine Best Staging System
 - Simplification of Stage Groups and Categories (reduction of subgroups and subcategories)
 - Enhancement of criteria for iENE to augment cN status
- Changes
 - Standardization of Stage Group IV representing M+ disease
 - pN0 status defined by a minimum of 6 lymph nodes examined, else cN0
 - pN status determined by number and ENE rather than lymph node size or laterality

Human Papillomavirus (HPV) Associated Oropharyngeal Squamous Cell Carcinoma (OPSCC)

Summary of Changes

Summary of Changes at a Glance

Change	Details of Change	Level of Evidence
Title Change	Changed from HPV-Mediated (p16+) Oropharyngeal Cancer to Oropharynx (HPV-Associated)	N/A
Identification of Primary Site	Pharyngeal tonsil (adenoid) and tubal tonsils have been moved to the nasopharynx staging system Anterior surface of epiglottis has been included in this staging system and removed from the larynx staging system	N/A
Definition of Regional Lymph Nodes (N) Clinical N (cN)	• Addition of unequivocal imaging-detected extranodal extension (iENE) and/or clinical extranodal extension as a cN criterion: ▪ iENE or clinical ENE increases N1 and N2 by one category	II
Definition of Regional Lymph Nodes (N) Pathologic N (pN)	• Addition of definitive pathologic extranodal extension (pENE) as a pN criterion: ▪ pENE increases N1 and N2 by one category • Pathological N1 without definitive pENE is subdivided into N1a (single node without definitive pENE) and N1b (2-4 nodes without definitive pENE)	II
AJCC Pathological Prognostic Stage Groups	• Stage II is revised to include T0-T2 N2-N3 M0 or T3 N0-N2 M0 • Stage III is revised to include T3 N3 M0 or T4 Any N M0	II

Summary of Changes at a Glance – HPV status and Site

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HPV Status Assessment

Ground Truth:

High-risk transcriptionally active HPV (integrated)

AND

Oncogenic transformation

WITH

Localization to tumor

High Risk HPV E6/E7 mRNA

RT-PCR

NGS

mRNA-ISH

High Risk HPV DNA

PCR/Signal Amp

NGS

DNA-ISH

Cell Cycle Markers

P16

EMERGING

EMERGING

PERFORMANCE GRADIENT



Good

Bad

HPV Status Assessment



PERFORMANCE GRADIENT



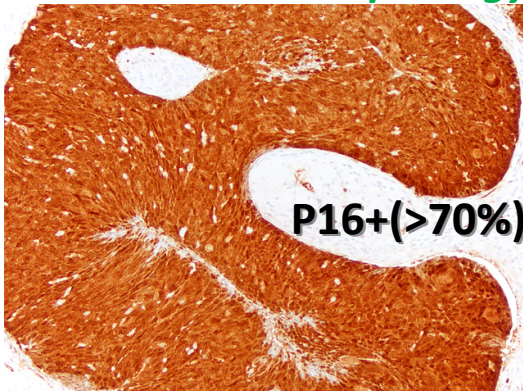
Good

Bad

P16 vs HPV DNA ISH vs HPV E6/E7 mRNA ISH CAP Updated Recommendations

P16

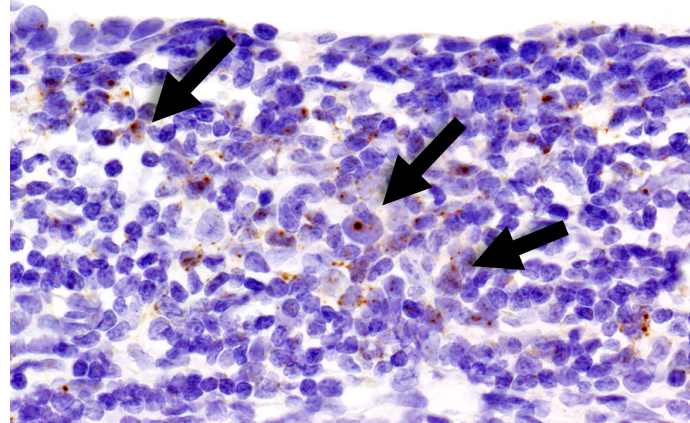
- Inexpensive
- Most available
- Excellent surrogate in most settings in US
- **Limitations (requiring specific testing)**
 - *Low attributable fraction*
 - *Non-Waldeyer ring subsites (e.g. uvula, soft palate)*
 - *Neck unknown primary*
 - *Discordant morphology*



HPV DNA ISH

- Direct but more expensive
- Not as sensitive or specific as RNA ISH; requires skill to perform and interpret
- Mostly discontinued
- **NOT RECOMMENDED (no advantage over RNA ISH)**

HPV DNA ISH (punctate integrated)

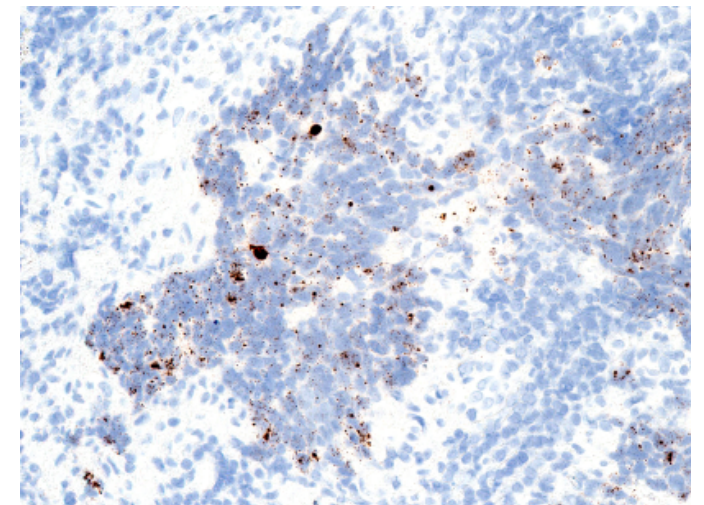


We had skill, but no longer needed

HPV RNA ISH

- Direct but more expensive
- Sensitive and specific; usually easy to interpret
- HR18 covers 18 HR HPV subtypes
- Availability increasing
- **Popular HPV specific testing verification**

HPV RNA ISH



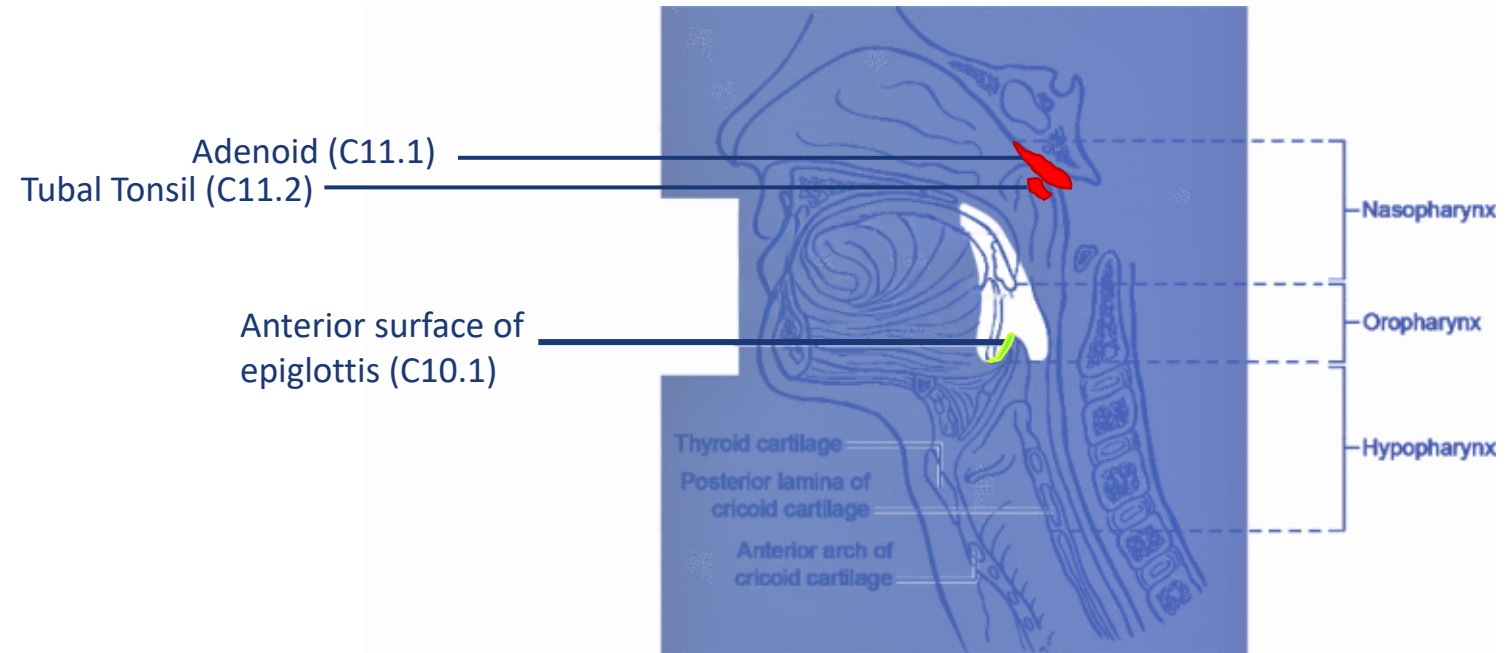
HPV Status Determination

- *Pathologist should integrate all testing information to report a final overall interpretation of HPV status for classification of a tumor as HPV associated vs HPV independent OPSCC*

Test Result	HPV Status
P16 positive alone – no caveats	HPV associated OPSCC
HPV specific test result positive	HPV associated OPSCC
P16 and HPV specific testing concordant	HPV associated OPSCC
No testing done	HPV independent OPSCC
P16 and HPV specific testing discordant	HPV independent OPSCC
P16 positive alone – caveats present	HPV independent OPSCC

Primary Site Changes

- Adenoid and tubal tonsils
– Nasopharynx
- Lingual surface of epiglottis - Oropharynx



Adapted from AJCC Cancer Staging System (2026)

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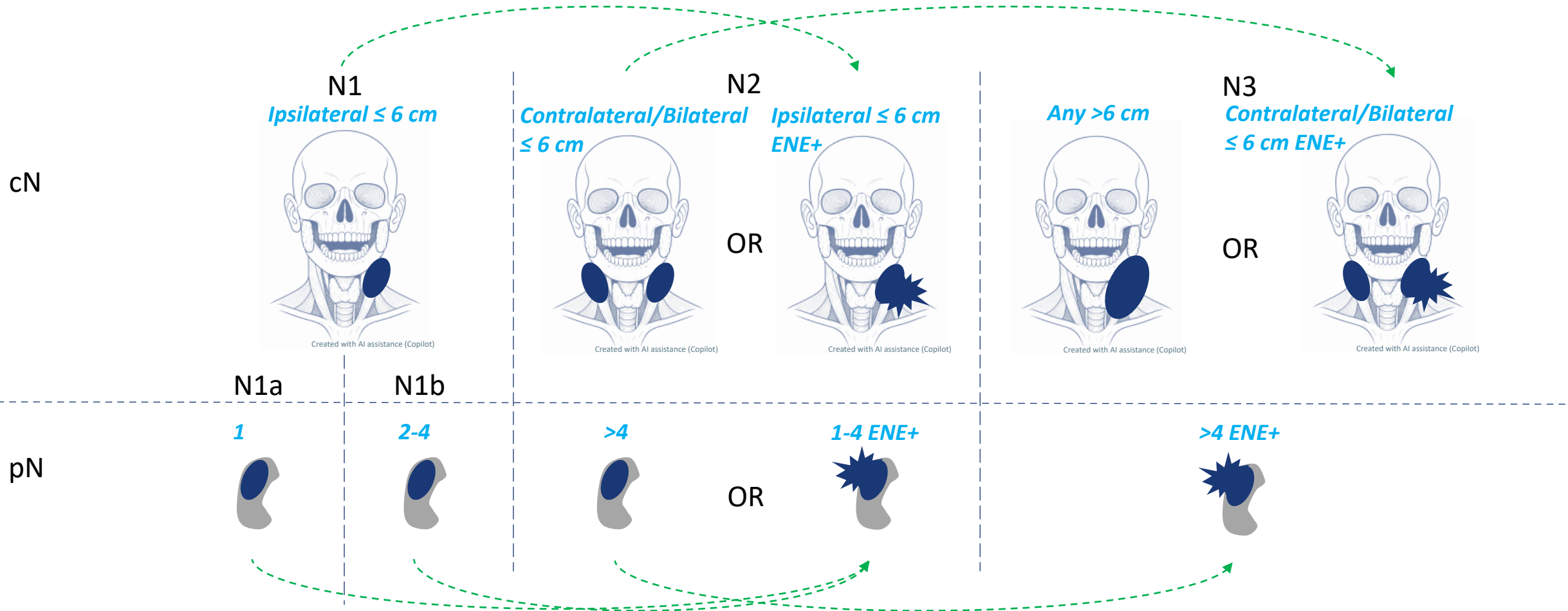
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Definition of Regional Lymph Nodes (N) at a Glance

cN Category	N Criteria
NX	Regional lymph nodes cannot be assessed
N0	No tumor involvement of regional lymph node(s)
N1	Tumor involvement of ipsilateral lymph node(s), all ≤ 6 cm in greatest dimension, without unequivocal imaging-detected and/or clinical extranodal extension
N2	Tumor involvement of ipsilateral lymph node(s), all ≤ 6 cm in greatest dimension, with unequivocal imaging-detected and/or clinical extranodal extension OR Tumor involvement of contralateral or bilateral lymph node(s), all ≤ 6 cm in greatest dimension without unequivocal imaging-detected and/or clinical extranodal extension
N3	Tumor involvement of lymph node(s) > 6 cm in greatest dimension OR Tumor involvement of contralateral or bilateral lymph node(s) with unequivocal imaging-detected and/or clinical extranodal extension
pN Category	N Criteria
NX	Regional lymph nodes cannot be assessed
N0	No tumor involvement of regional lymph node(s)
N1	Tumor involvement of 1-4 lymph nodes without definitive pathological extranodal extension
N1a	Tumor involvement of 1 lymph node without definitive pathological extranodal extension
N1b	Tumor involvement of 2-4 lymph nodes without definitive pathological extranodal extension
N2	Tumor involvement of 1-4 lymph nodes with definitive pathological extranodal extension OR Tumor involvement of > 4 lymph nodes without definitive pathological extranodal extension
N3	Tumor involvement of > 4 lymph nodes with definitive pathological extranodal extension

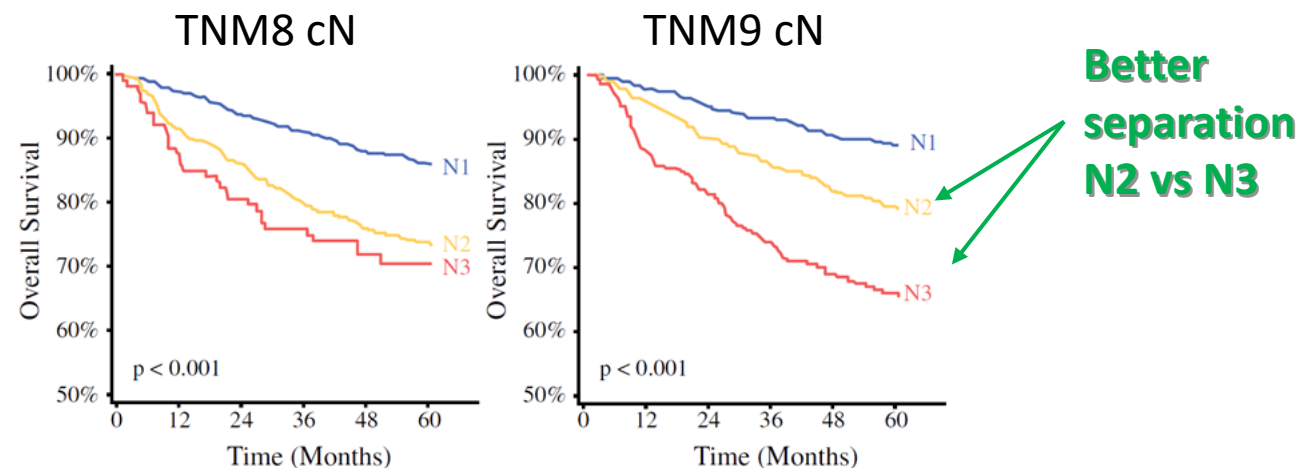
Definition of Regional Lymph Nodes (N) Revision

- cN size and laterality; pN number
- ENE+ upclassifies by one category

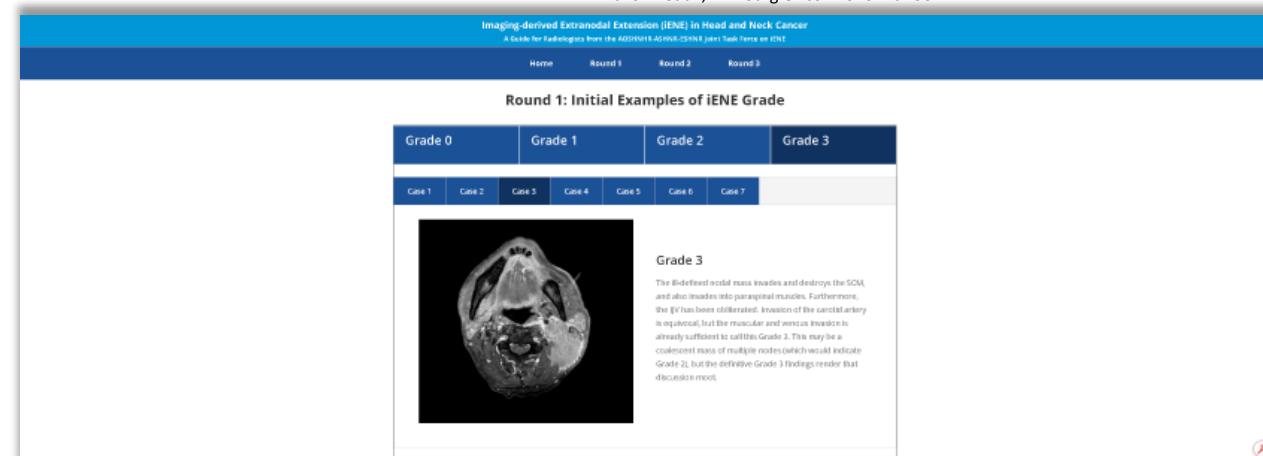


Rationale cN changes

- AJCC 8th ed - cN1 heterogeneous and over-represented
- iENE a powerful prognosticator
- Inclusion of ENE (iENE in particular) in cN categorization improves balance and separation of groups
- iENE training initiative to improve consistency
 - <https://ashnr.org/iene>
 - 3 grades of ENE by extent
 - Level of certainty (only unequivocal counts)

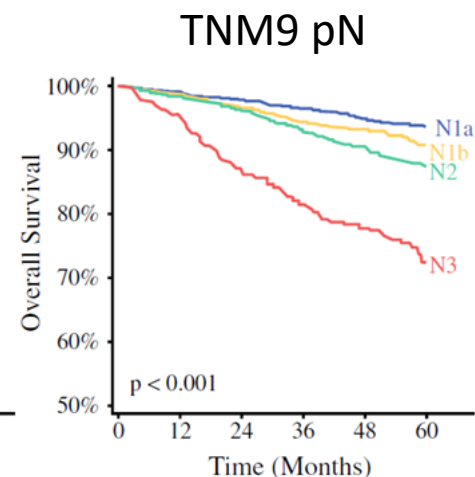
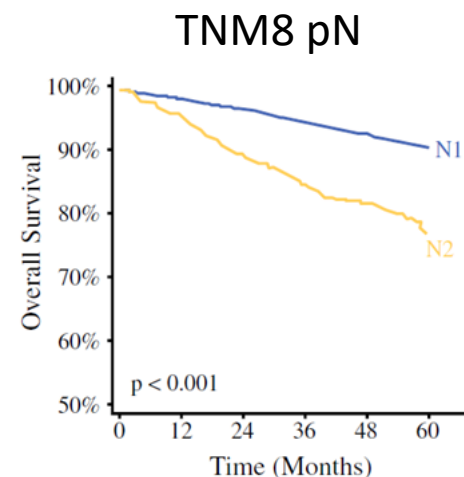


Evans M et al., Ann Surg Oncol. 2026 Mar 30.

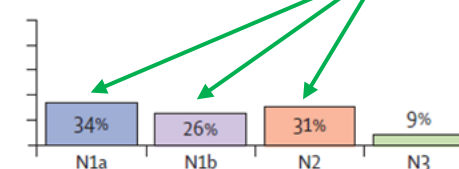
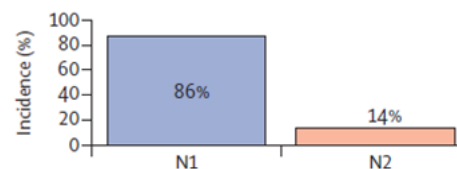


Rationale pN changes

- pENE re-emerges as a prognosticator
- Inclusion of ENE in pN categorization improves balance and stage grouping



Evans M et al., Ann Surg Oncol. 2026 Mar 30.



Better Balance

Ho AS et al., Lancet Oncol. 2025 Aug;26(8):1113-1122.

Guidelines for reporting pENE

- HN-CLEAR and HNCIG guidelines for lymph node grossing and reporting ENE

LETTER ▶ [Head Neck Pathol.](#) 2025 Feb 7;19(1):20. doi: [10.1007/s12105-025-01753-7](#) 

International Consensus Recommendations of Diagnostic Criteria and Terminologies for Extranodal Extension in Head and Neck Squamous Cell Carcinoma: An HN CLEAR Initiative (Update 1)

[Rita Gupta](#)^{1,2,3,21,22,23}, [Timothy Fielder](#)¹, [Munita Bai](#)⁴, [Simon I Chiosea](#)⁵, [Jane E Dahlstrom](#)^{6,7}, [Aanchal Kakkar](#)⁸, [Katalin Kiss](#)⁹, [Jan Laco](#)^{10,11}, [Neha Mittal](#)⁴, [Sunil Pasricha](#)¹², [Spinder Samra](#)¹³, [Nina Zidar](#)¹⁴, [Martin Bullock](#)¹⁵, [Rebecca Chernock](#)¹⁶, [William Faquin](#)¹⁷, [Shao Hui Huang](#)¹⁸, [Jean Yang](#)¹⁹, [Sun Och Yoon](#)²⁰

SERIES | [Head and Neck Cancer Consensus Recommendations](#) · Volume 25, Issue 7, E285-E296, July 2024

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Standardised definitions and diagnostic criteria for extranodal extension detected on histopathological examination in head and neck cancer: Head and Neck Cancer International Group consensus recommendations

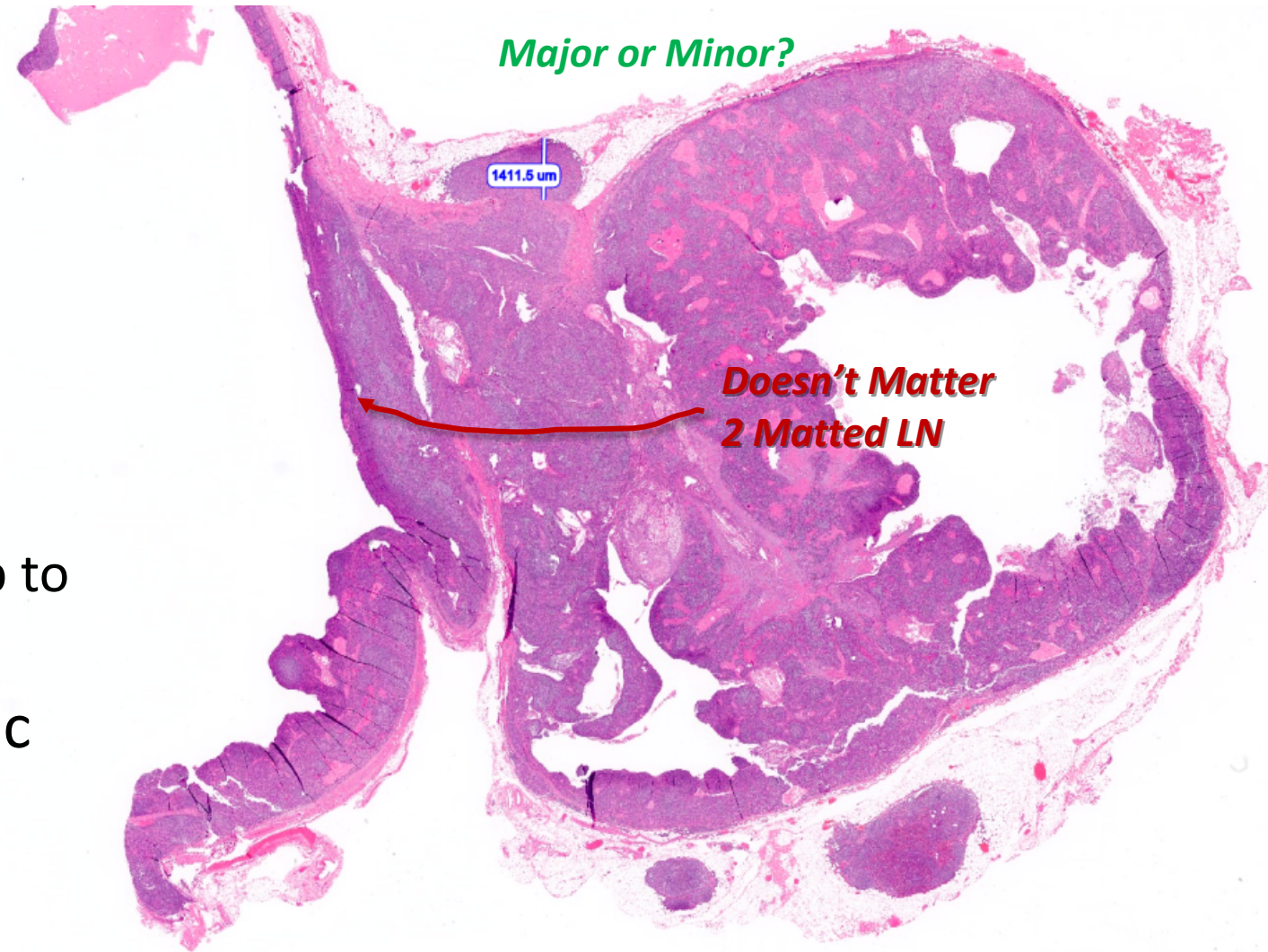
[Ahmad K Abou-Fouly, MD](#)^{a,1} · [Christina Henson, MD](#)^{b,1} · [Prof Rebecca D Chernock, MD](#)^c · [Shao Hui Huang, MD](#)^{4b} · [William M Lydiatt, MD](#)¹ · [Franklin McDowell, MRCJ](#) · et al · [Show more](#)



- New terminology
 - **‘Matted’** - tumor crosses from one lymph node to another adjacent lymph node. **ENE+**
 - **‘Fused, adherent, confluent, and conglomerate’** - lymph nodes that are adherent based on inflammation and stromal reaction and show no transgression of tumor across capsules **ENE-**
- Scenarios formally defined
 - Soft tissue deposits - **ENE+**
 - Extranodal PNI, LVI – **ENE-** but count towards parameter if not identified in primary (i.e. LVI+, PNI+)

Unresolved Issue Extent of ENE

- Qualitative Major ENE
 - Gross ENE
 - Soft tissue deposits
 - Matted LN
- Major vs Minor
 - Generic – 2mm
 - Clinical Trials – 1mm
 - Optimal – Unclear (possibly up to 4mm)
- NCDB – insufficient prognostic value currently
- CAP – remain optional



Salivary Gland

Summary of Changes

Summary of Changes at a Glance

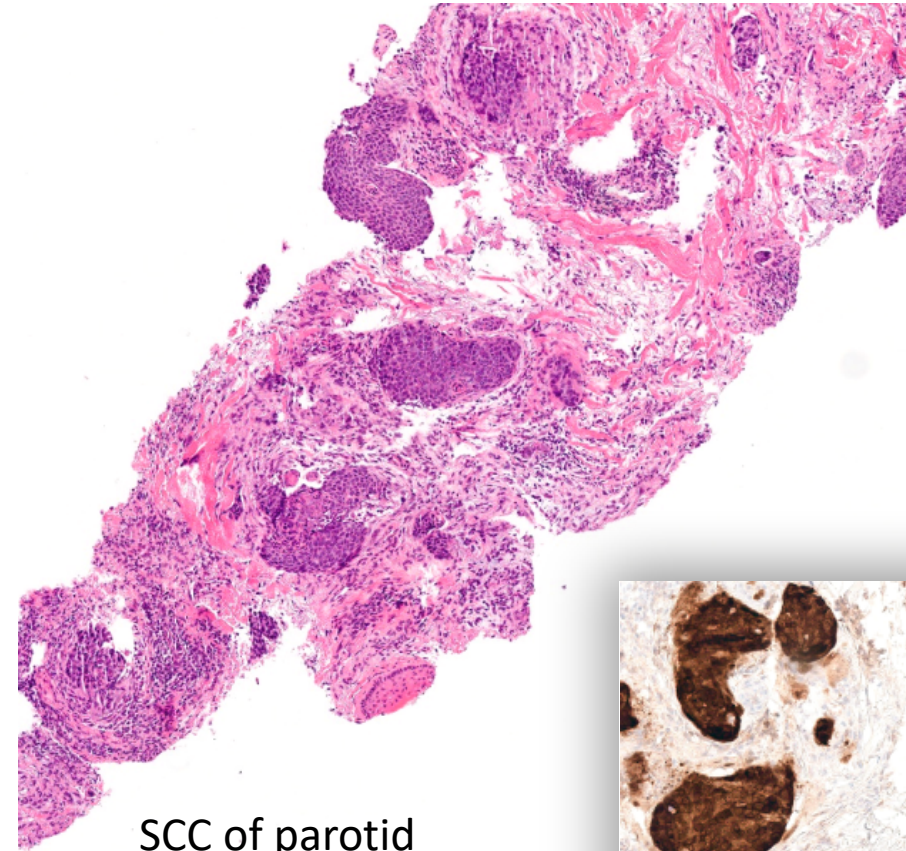
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Identification of Primary Site	Includes major and minor salivary glands	III
Histopathologic Type	• Removal of squamous cell carcinoma (SCC), neuroendocrine, basosquamous cell since they are not typical salivary gland origin • Almost all SCCs in salivary gland are metastatic nodes from a skin primary or rarely from a mucosal primary	II
Definition of Primary Tumor (T)	• Consolidation of major and minor salivary gland T category definitions • Clarification of the definition of: ▪ Extraparenchymal extension for T3 ▪ Bone invasion for T4	III
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AJCC Prognostic Stage Groups	• Confinement of M0 disease in Stages I, II, IIIA and IIIB, while reserving stage IV for M1 disease • Stage I: T1 N0 • Stage II: T2 N0 • Stage IIIA: T1-T2 N1 or T3-T4 N0 • Stage IIIB: T1-T2 N2 or T3-T4 N1-N2	I

Summary of Changes at a Glance – Histo and T

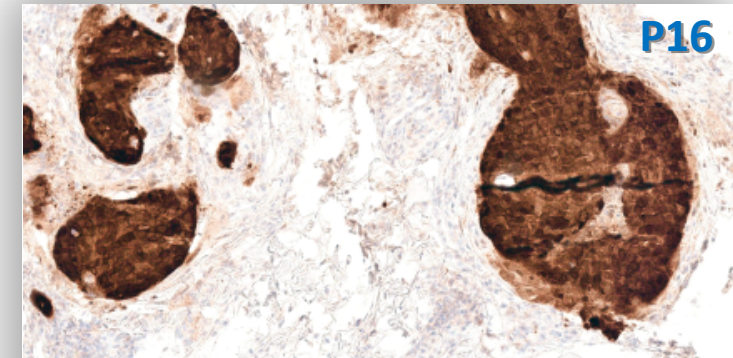
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Histopathological Type

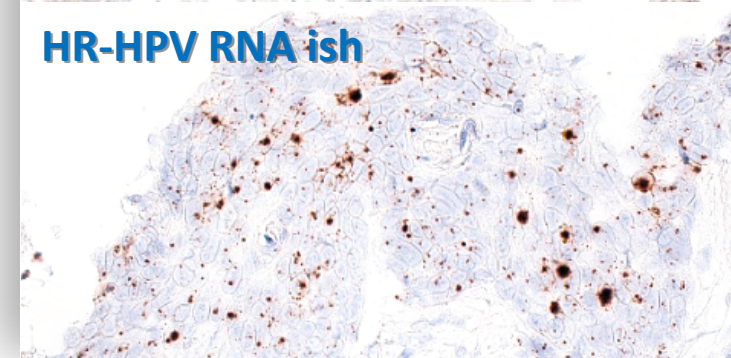
- Removal of
 - Squamous cell carcinoma (SCC)
 - Almost all SCCs in salivary gland are metastatic nodes from a skin primary or rarely from a mucosal primary
 - Neuroendocrine carcinoma
 - Majority of neuroendocrine carcinomas are also metastases (usually from Merkel cell carcinoma)
 - Basosquamous carcinoma
 - This is related to cutaneous basal cell carcinoma (*as opposed to salivary basal cell adenocarcinoma*) and is definitionally extension from skin or metastasis



SCC of parotid
(Metastasis-HPV
associated)



HR-HPV RNA ish



Behavioral Stratification of Salivary Gland Carcinomas (Based on WHO 5th Edition)

• Low Aggression	• High Aggression
• Mucoepidermoid carcinoma – Low grade	• Mucoepidermoid carcinoma – High grade
• Mucoepidermoid carcinoma – Intermediate grade (depends on grading scheme)	
• Acinic cell carcinoma – Conventional	• Acinic cell carcinoma – High grade/HGT
• Secretory carcinoma - Conventional	• Secretory carcinoma – High grade/HGT
• Microsecretory adenocarcinoma – Usual	• Microsecretory adenocarcinoma – High grade/HGT
• Polymorphous adenocarcinoma – Low grade, conventional	• Polymorphous adenocarcinoma – High grade/HGT
• Polymorphous adenocarcinoma – Low & intermediate grade, cribriform (high risk for nodal disease)	
• Hyalinizing clear cell carcinoma – Conventional	• Hyalinizing clear cell carcinoma – High grade/HGT
• Basal cell adenocarcinoma – Conventional-all patterns	• Basal cell adenocarcinoma – High grade/HGT
• Myoepithelial carcinoma – Low grade	• Myoepithelial carcinoma – High grade
• Epithelial-myoepithelial carcinoma – Conventional and subtypes	• Epithelial-myoepithelial carcinoma – High grade/HGT
• Sebaceous adenocarcinoma – Low grade	• Sebaceous adenocarcinoma – High grade
	• Adenoid cystic carcinoma – Solid/HGT
• Adenoid cystic carcinoma – Tubular/cribriform (low risk for nodal disease)	
	• Carcinosarcoma
	• Squamous cell carcinoma
• Intraductal carcinoma, oncocytic and intercalated duct	• Frankly invasive non-apocrine carcinoma ex intraductal carcinoma
• Intraductal carcinoma, apocrine	• Apocrine (salivary duct) carcinoma
• Salivary gland “intraductal papillary mucinous neoplasm”	• Mucinous adenocarcinoma
• Carcinoma ex lymphadenoma	• Lymphoepithelial carcinoma
• Sclerosing microcystic adenocarcinoma	
• Sialoblastoma	
• Carcinoma ex pleomorphic adenoma – Aggression is determined by type of carcinoma and extent of invasion	
• Salivary carcinoma, NOS – Aggression depends on grade	

Almost
invariably
metastasis

Disposition of Carcinoma ex Pleomorphic Adenoma (CAxPA)

- Removed from protocol as a distinct type
 - Characterizes a critical pathogenesis/subclass but not a specific entity
 - Classification based on carcinoma type and grade arising from pleomorphic adenoma
- For pathologists – CAP protocols will still capture CAxPA in a separate field set with emphasis on type, grade and extent.

Site: e.g. Head and Neck
Category: e.g. Salivary Gland Tumors
Family (class): e.g. Malignant Epithelial Tumors
Type: Carcinoma ex PA

PREVIOUS

Site: e.g. Head and Neck
Category: e.g. Salivary Gland Tumors
Family (class): e.g. Malignant Epithelial Tumors
Sub class: Carcinoma ex PA
Type: Epithelial-Myoepithelial Carcinoma

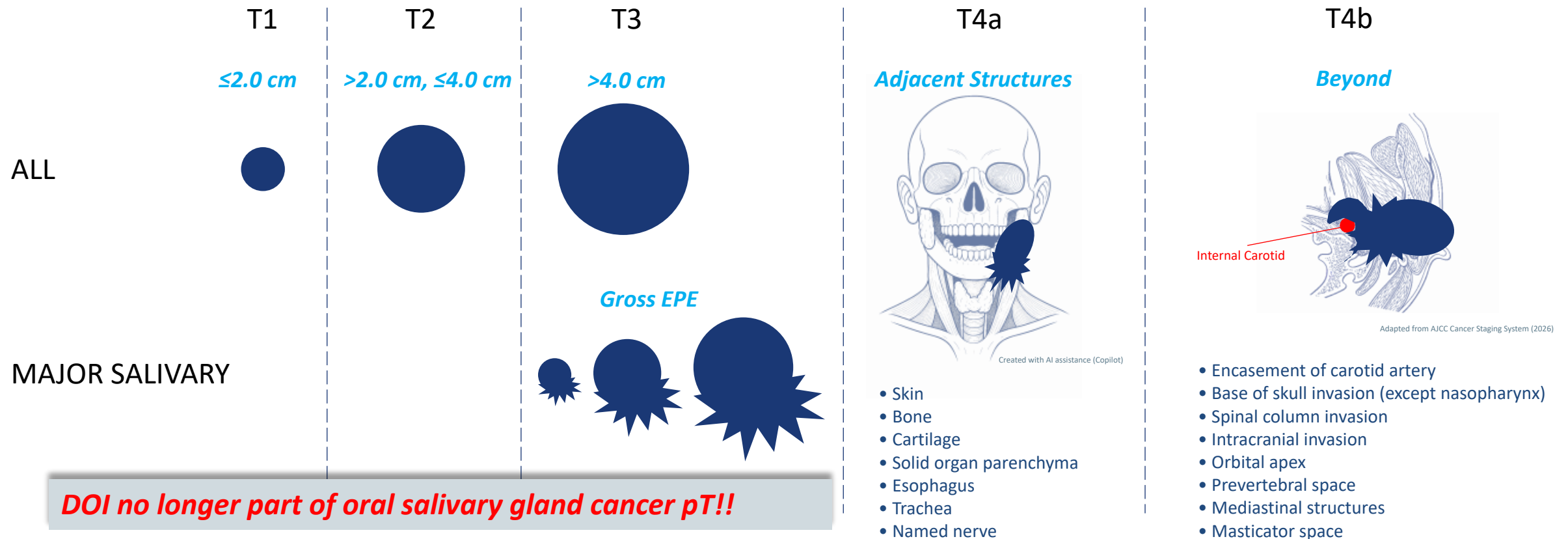
FOR AJCC v9

Definition of Primary Tumor (T) at a Glance

T Category		T Criteria
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis		Carcinoma <i>in situ</i>
T1		Tumor ≤ 2 cm in greatest dimension without extraparenchymal extension ^β
T2		Tumor > 2 cm but ≤ 4 cm in greatest dimension without extraparenchymal extension ^β
T3		• Tumor > 4 cm in greatest dimension and/or • Gross extraparenchymal extension (for major salivary glands) ^β
T4		Tumor invades immediately and/or beyond adjacent structures
	T4a	Tumor invades any immediately adjacent structures including: • Skin • Bone ^{ββ} • Cartilage • Solid organ parenchyma • Esophagus • Trachea • Named nerve
	T4b	Tumor invades beyond any adjacent structures including: • Encasement of carotid artery • Base of skull invasion (except nasopharynx) • Spinal column invasion • Intracranial invasion • Orbital apex • Prevertebral space • Mediastinal structures • Masticator space
^β Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues or nerve, except those listed under T4a and T4b. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes. ^{ββ} The following scenarios are not considered T category defining "bone invasion": 1) Destruction of intrinsic sinus bone in sinonasal primaries; 2) Erosion of cortical bone; 3) Primary intraosseous (central) salivary gland tumors.		

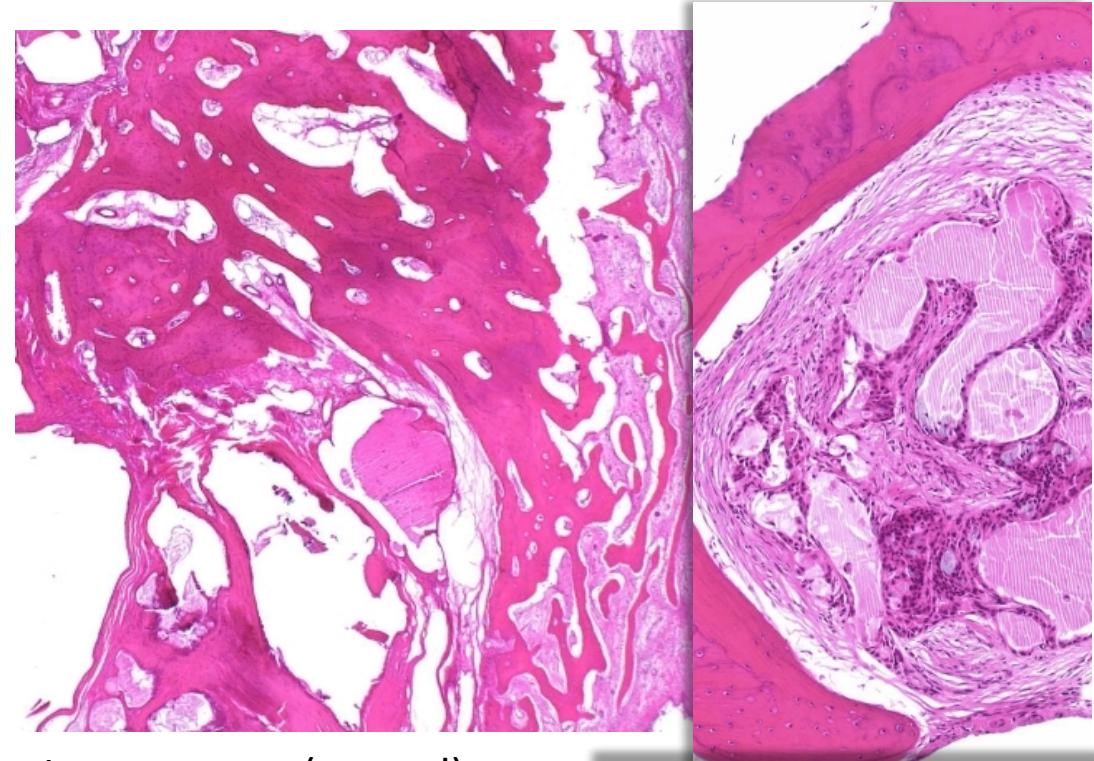
Definition of Primary Tumor (T) Site Consolidation

- Consolidation of major and minor salivary gland T category definitions
- **NEW:** middle ear, cervical esophagus, trachea and intraosseous jaw now included



Definition of Primary Tumor (T)

- Clarification of the definition of:
 - Extraparenchymal extension for T3
 - Major salivary gland cancers
 - Clinical(radiologic) and/or macroscopic extension
 - Soft tissue or “non-named nerve”
 - Bone invasion for T4 (*What are the exceptions?*)
 - All sites – Bone erosion (without invasion)
 - Sinonasal - intrinsic sinus bone destruction
 - *Primary intraosseous tumors*



Intraosseous (central)
mucoepidermoid
carcinoma (*not pT4a*)



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AJCC Prognostic Stage Groups	• Confinement of M0 disease in Stages I, II, IIIA and IIIB, while reserving stage IV for M1 disease • Stage I: T1 N0 • Stage II: T2 N0 • Stage IIIA: T1-T2 N1 or T3-T4 N0 • Stage IIIB: T1-T2 N2 or T3-T4 N1-N2	I

Summary of Changes at a Glance – N

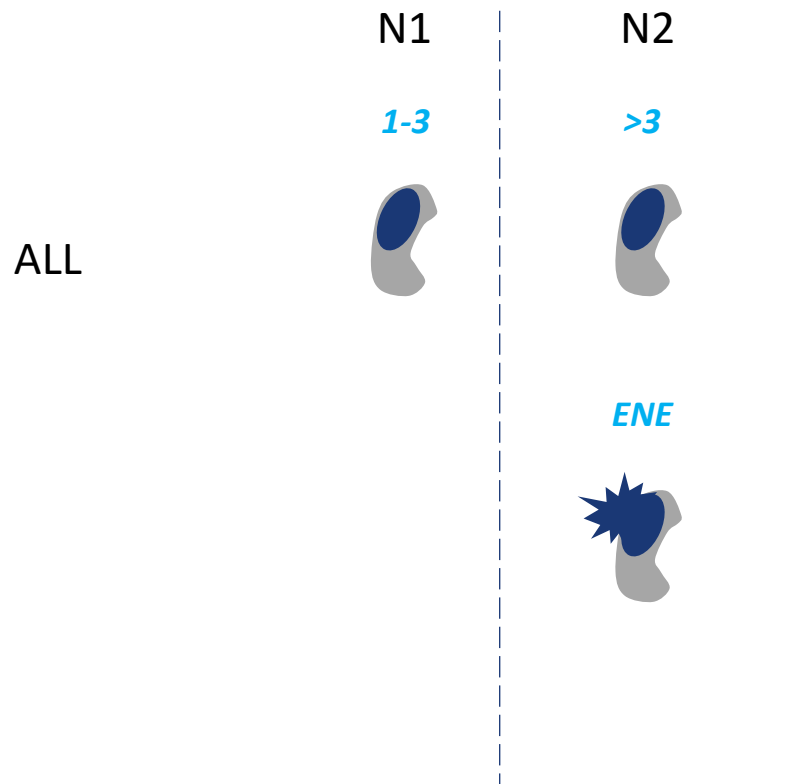
Change	Details of Change	Level of Evidence
Title Change	Changed from Major Salivary Glands to Salivary Glands as the staging system now includes minor salivary glands	N/A
Identification of Primary Site	Includes major and minor salivary glands	III
Histopathologic Type	• Removal of squamous cell carcinoma (SCC), neuroendocrine, basosquamous cell since they are not typical salivary gland origin • Almost all SCCs in salivary gland are metastatic nodes from a skin primary or rarely from a mucosal primary	II
Definition of Primary Tumor (T)	• Consolidation of major and minor salivary gland T category definitions • Clarification of the definition of: • Extraparenchymal extension for T3 • Bone invasion for T4	III
Definition of Regional Lymph Nodes (N) Clinical N (cN)	• Replacement of laterality with lymph node number (1-3 vs > 3) • Elimination of the N3 category • Addition of imaging-detected extranodal extension (iENE) in addition to clinical ENE as a cN criteria: • N1: 1-3 lymph nodes involved, without unequivocal iENE and/or clinical ENE • N2: > 3 lymph nodes involved, or any lymph node with unequivocal iENE and/or clinical ENE	I
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Definition of Regional Lymph Nodes (N) at a Glance

N Category	N Criteria
NX	Regional lymph nodes cannot be assessed
N0	No tumor involvement of regional lymph node(s)
N1	Tumor involvement of 1-3 lymph node(s), without definitive pathological extranodal extension
N2	Tumor involvement of > 3 lymph nodes OR Tumor involvement of any lymph node(s) with definitive pathological extranodal extension

Definition of Regional Lymph Nodes (N) Revision

- Number of lymph nodes, not size
- ENE+ is N2 defining regardless of number



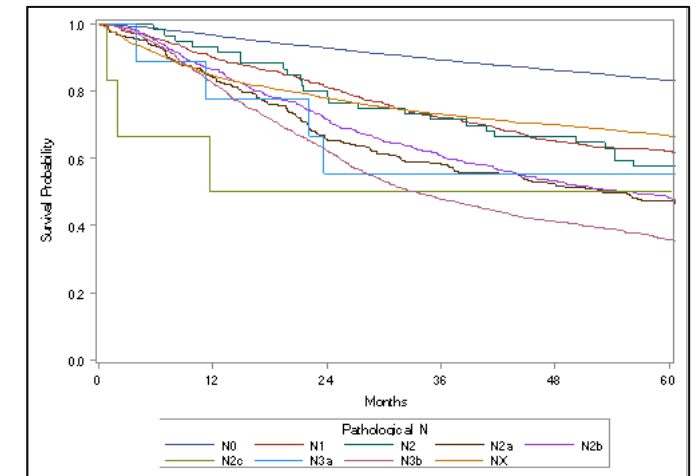
RATIONALE:

AJCC 8th ed N was awkward
had poor discriminatory
performance

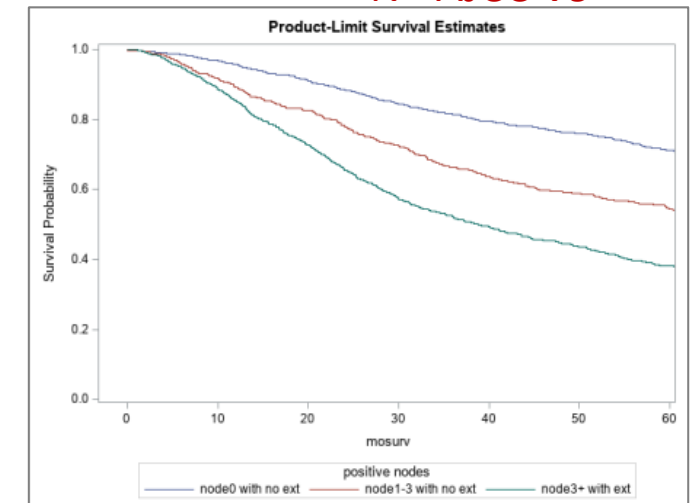
SOLUTION:

Number of positive LN and
ENE simpler with improved
performance

N –AJCC 8TH ED

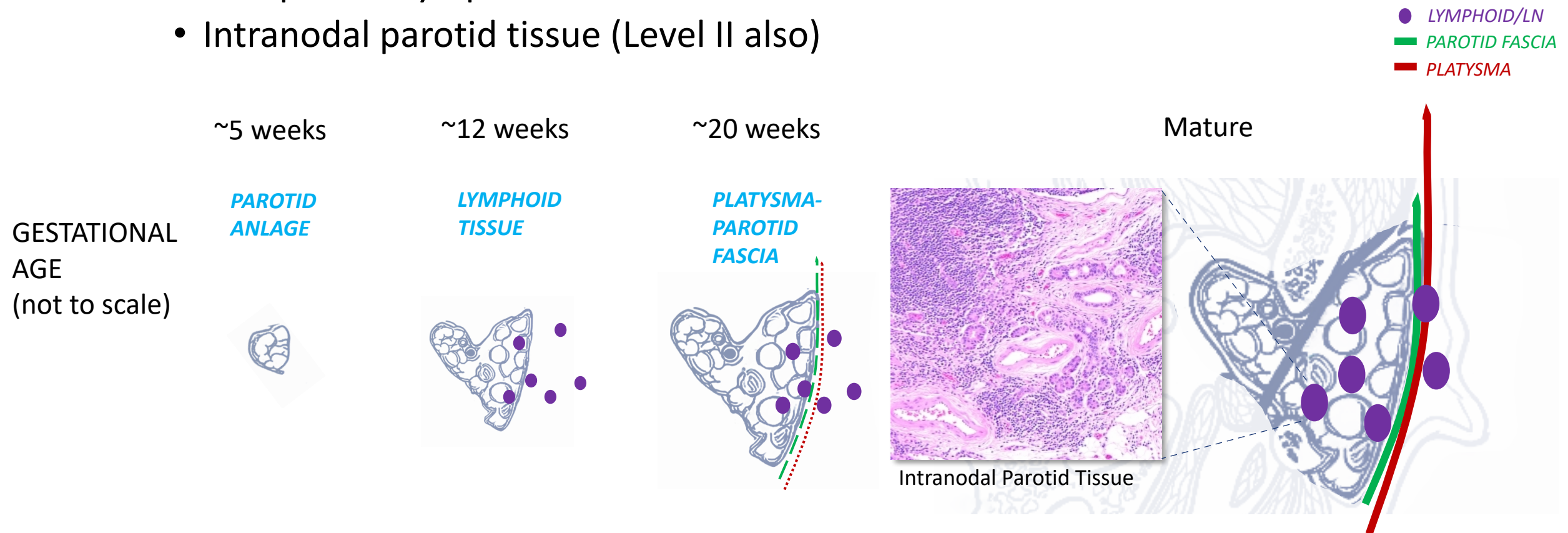


N –AJCC V9



Special Consideration: Intra/Periparotid Lymph Nodes

- Parotid Embryology – First to form last to encapsulate
- Lymphoid tissue intermingles with parotid prior to encapsulation
 - Intraparotid lymph nodes
 - Intranodal parotid tissue (Level II also)

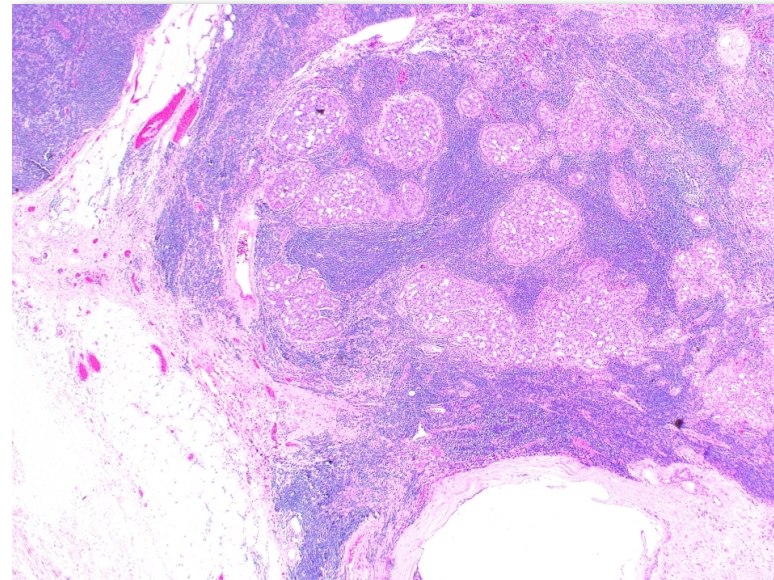
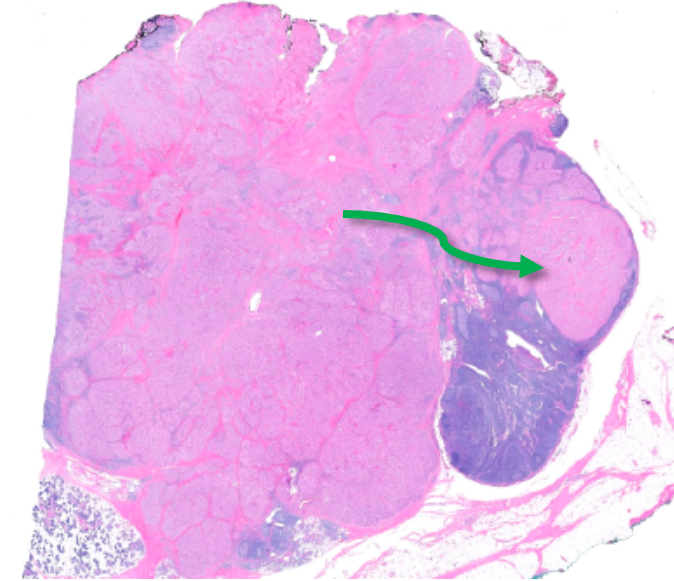


Adapted from AJCC Cancer Staging System (2026)

N Category Consequences

- Direct extension
 - Likely not equivalent to positive LN by lymphatic spread
 - Convention **STILL** Count as positive LN
- Intranodal primary parotid tumor
 - Arise from intranodal parotid tissue
 - **NOT** a metastasis and does not count as positive LN

Oncocytic
Mucoepidermoid
Carcinoma direct
extension into LN
(N+)



Primary Intranodal
Acinic Cell Carcinoma
(not N+)

Take Home Points

- AJCC v9 for Head and Neck now has a more standardized process of approaching and updating TNM and stage grouping
- HPV terminology and status aligns with WHO definitions and CAP guidelines
 - P16 is an adequate surrogate with caveat scenarios
 - Discordant testing results and no testing results would default to HPV independent
- WHO salivary gland histologic types are dichotomized by aggression
 - Key histologic types (i.e. squamous cell carcinoma) are generally considered metastasis and excluded from v9 derivation
 - Carcinoma ex PA is not an entity, the appropriate classification is by carcinoma type
- Both major and minor salivary cancers are unified into one staging system necessitating T3 and T4a definition refinements
- ENE is critical to both HPV OPSCC and salivary cancer N categorization; extent of ENE remains under investigation

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- Donna Gress
- Dr. Nicole Cipriani
- AJCC Core HN Task Force and Staff
- CAP Protocol Authors and Staff

<https://www.cap.org/protocols-and-guidelines/cancer-reporting-tools/cancer-protocol-templates>

Latest News and Resources

OPEN ALL ▲ CLOSE ALL ▼

April 2026 ▲

On April 1, 2026, the College of American Pathologists (CAP) released updates to the CAP Cancer Protocols, with changes across 11 protocols and retiring two protocols. Key highlights include:

- 1. Head and Neck Protocol Restructuring:** Retirement of the Pharynx and Major Salivary Gland protocols, replaced with several new site-specific protocols including HPV-Associated Oropharynx, HPV-Independent Oropharynx and Hypopharynx, Nasopharynx, Salivary Gland, and Mucosal Melanoma.
- 2. AJCC Staging Updates:** Implementation of AJCC Version 9 staging for select Head and Neck protocols, including HPV-Associated Oropharynx, Nasopharynx, and Salivary Gland.
- 3. Reporting Element Updates:** Addition of the Tumor Bed Margin Status section and expanded lymph node reporting elements in several Head and Neck protocols, with some elements moving from conditionally required to required (core).
- 4. Head and Neck Biomarker Updates:** Removal of certain HPV and HER2 interpretation questions, addition of defined HER2 scoring criteria and additional antibodies, and terminology updates related to SWI/SNF complex-deficient sinonasal carcinoma.
- 5. Protocol Content and Terminology Improvements:** Updates across several protocols including refined tumor site and histologic type questions, improved nodal terminology for SNOMED coding, and removal of select grading and perineural invasion elements.
- 6. Merkel Cell Carcinoma Updates:** WHO 5th edition content updates, addition of Locoregional Cutaneous Metastases as a required reporting element, and new optional biomarker-related questions including MCPyV status.

THANK YOU