Protocol for the Examination of Specimens from Patients with Cancers of the Nasopharynx

Version: 1.0.0.0
Protocol Posting Date: April 2026

CAP Laboratory Accreditation Program Protocol Required Use Date: January 2027
The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes specimens designated nasopharynx
Tumor Type	**Description**
Carcinoma	Includes squamous cell carcinoma and neuroendocrine carcinoma

This protocol is NOT required for accreditation purposes for the following:

Procedure
Biopsy
Primary resection specimen with no residual cancer (e.g., following neoadjuvant therapy)
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Sarcoma (consider the Soft Tissue or Bone protocol)
Hematologic malignancies (consider the Precursor and Mature Lymphoid Malignancies, Myeloid and Mixed / Ambiguous Lineage Neoplasms, and Plasma Cell Malignancies protocols)
Mucosal melanoma (consider the Head and Neck Mucosal Melanoma protocol)
Salivary glands (consider the Salivary Gland protocol)

Version Contributors

Committee Authors: Raja R. Seethala, MD, FCAP*, Nicole A. Cipriani, MD, FCAP*, Lananh Nguyen, MD, MSc, FCAP, Rashmi Samdani, MD, FCAP, Michael A. Berman, MD, FCAP, Jason R. Pettus, MD, FCAP
Expert Panel Contributors: Justin A. Bishop, MD, William C. Faquin, MD, PhD, Shao Hui Huang, MD, Nora Katabi, MD, William Lydiatt, MD, Brian O'Sullivan, MB BCh, Snehal Patel, MD, Lindsay Williams, MD, Keluo Yao, MD, FCAP

* Denotes primary author.
For any questions or comments, contact: cancerprotocols@cap.org.

Glossary:

Author: Expert who is designated by the chair of the Cancer Committee.
Expert Panel Contributors: Includes members of other CAP committees or external subject matter experts who contribute to the current version of the protocol.

Accreditation Requirements

Synoptic reporting with core and conditional data elements for designated specimen types* is required for accreditation.

- Data elements designated as core must be reported.
- Data elements designated as conditional only need to be reported if applicable.
- Data elements designated as optional are identified with "+". Although not required for accreditation, they may be considered for reporting.

This protocol is not required for recurrent or metastatic tumors resected at a different time than the primary tumor. This protocol is also not required for pathology reviews performed at a second institution (i.e., second opinion and referrals to another institution).
Full accreditation requirements can be found on the CAP website under Accreditation Checklists.
A list of core and conditional data elements can be found in the Summary of Required Elements under Resources on the CAP Cancer Protocols website.
**Includes definitive primary cancer resection and pediatric biopsy tumor types.*

Synoptic Reporting

All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
    - Anatomic site or specimen, laterality, and procedure
    - Pathologic Stage Classification (pTNM) elements
    - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location
- Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e., all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

V 1.0.0.0

- New protocol established to replace the retired Pharynx protocol, resulting from the separation of select Head and Neck protocols

Reporting Template

Protocol Posting Date: April 2026
Select a single response unless otherwise indicated.
CASE SUMMARY: (NASOPHARYNX)
Standard(s): AJCC 9

SPECIMEN

Procedure (select all that apply)
___ Excision: _____
___ Neck (lymph node) dissection (specify): _____
___ Other (specify): _____
___ Not specified

TUMOR

Multiple Primary Sites (required only if applicable)#
 # Please complete a separate checklist for each primary site
___ Not applicable (no additional primary site(s) present)
___ Present: _____

Tumor Focality
___ Unifocal
___ Multifocal: _____
___ Cannot be determined (explain): _____

Nasopharynx Tumor Subsite(s) (Note A) (select all that apply)
___ Superior wall
___ Posterior wall
___ Nasopharyngeal tonsils (adenoids)
___ Anterior wall
___ Lateral wall (including lateral pharyngeal recess, [i.e., Rosenmüller fossa])
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Not specified

Tumor Laterality (select all that apply)
___ Left
___ Right
___ Midline
___ Not specified

Tumor Size
___ Greatest dimension in Centimeters (cm): _____ cm
___ Cannot be determined (explain): _____

Histologic Type (Note B)

Carcinomas of the Nasopharynx

___ Squamous cell carcinoma, keratinizing, NOS
___ Squamous cell carcinoma, non-keratinizing, NOS
___ Basaloid squamous cell carcinoma
___ Low-grade nasopharyngeal papillary adenocarcinoma

Neuroendocrine

___ Neuroendocrine tumor, grade 1
___ Neuroendocrine tumor, grade 2
___ Neuroendocrine tumor, grade 3
___ Neuroendocrine carcinoma, small cell type
___ Neuroendocrine carcinoma, large cell type
___ Combined (or composite) neuroendocrine carcinoma

Type of Combined Histology# (select all that apply)

 # Please note that the user must select at least one neuroendocrine type and at least one carcinoma type from the list below.

___ Squamous cell carcinoma: _____
___ Adenocarcinoma: _____
___ Neuroendocrine carcinoma, small cell type
___ Neuroendocrine carcinoma, large cell type
___ Other (specify): _____

Other

___ Other histologic type not listed (specify): _____
___ Carcinoma, type cannot be determined: _____

+Histologic Type Comment: _____

Tumor Extent (specify other structures involved) (required only if pT defined elements are applicable): _____

Lymphatic and / or Vascular Invasion (Note C)

___ Not identified
___ Present: _____
___ Cannot be determined (explain): _____

Perineural Invasion (Note C)

___ Not identified
___ Present
___ Cannot be determined (explain): _____

+Tumor Comment: _____

MARGINS (Note D)

Specimen Margin Status for Invasive Tumor

___ All specimen margins negative for invasive tumor

Distance from Invasive Tumor to Closest Specimen Margin
Specify in Millimeters (mm)
___ Exact distance: _____ mm
___ Greater than: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined (explain): _____
Closest Specimen Margin(s) to Invasive Tumor (use orientation when provided)
___ Specify location(s) of closest specimen margin(s): _____
___ Cannot be determined (explain): _____
+Other Close Specimen Margin(s) to Invasive Tumor
___ Specify location(s) and distance(s) of other close specimen margin(s): _____
___ Cannot be determined: _____
___ Invasive tumor present at specimen margin(s)
Specimen Margin(s) Involved by Invasive Tumor (use orientation when provided)
___ Specify involved specimen margin(s): _____
___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Margin Comment: _____

REGIONAL LYMPH NODES (Note E)

Regional Lymph Node Status
___ Not applicable (no regional lymph nodes submitted or found)
___ Regional lymph nodes present
___ All regional lymph nodes negative for tumor
___ Tumor present in regional lymph node(s)
Number of Lymph Nodes with Tumor
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
Laterality of Lymph Node(s) with Tumor
___ Ipsilateral (including midline): _____
___ Contralateral: _____
___ Bilateral: _____
___ Cannot be determined (explain): _____
+Nodal Site(s) with Tumor (select all that apply)
___ Intraparotid: _____
___ Periparotid: _____
___ Level I: _____
___ Level II: _____
___ Level III: _____
___ Level IV: _____

___ Level V: _____
___ Other (specify): _____
___ Cannot be determined: _____

Size of Largest Nodal Metastatic Deposit
Specify in Centimeters (cm)
___ Exact size: _____ cm
___ At least: _____ cm
___ Greater than: _____ cm
___ Less than: _____ cm
___ Other (specify): _____
___ Cannot be determined (explain): _____

Extranodal Extension (ENE)
___ Not identified
___ Present

+Distance of ENE from Lymph Node Capsule
Specify in Millimeters (mm)
___ Exact distance: _____ mm
___ Greater than 2 mm (major ENE)
___ Less than or equal to 2 mm (minor ENE)
___ Less than 1 mm (minor ENE)
___ Other (specify): _____
___ Cannot be determined: _____

___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

Number of Lymph Nodes Examined
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Regional Lymph Node Comment: _____

DISTANT METASTASIS

Number of Metastatic Lesions (required only if applicable)
___ Not applicable
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

Distant Site(s) Involved, if applicable (select all that apply)
___ Not applicable
___ Lung: _____

___ Bone: _____
___ Brain: _____
___ Liver: _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

pTNM CLASSIFICATION (AJCC Version 9) (Note F)

Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.

Modified Classification (required only if applicable) (select all that apply)

___ Not applicable
___ y (post-neoadjuvant therapy)
___ r (recurrence)

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor, but EBV-positive cervical node(s) involvement
___ pTis: Carcinoma in situ
___ pT1: Tumor confined to nasopharynx; OR Tumor with extension to any of the following without parapharyngeal involvement: oropharynx or nasal cavity
___ pT2: Tumor with extension to any of the following: Parapharyngeal space; or adjacent soft tissue involvement of medial pterygoid, lateral pterygoid, prevertebral muscles
___ pT3: Tumor with unequivocal infiltration into any of the following bony structures: Skull base (including pterygoid structures); or paranasal sinuses; or cervical vertebrae
___ pT4: Tumor with any of the following: Intracranial extension; or unequivocal radiological and / or clinical involvement of cranial nerves; or involvement of hypopharynx; or involvement of orbit (including inferior orbital fissure); or involvement of parotid gland; or extensive soft tissue infiltration beyond the anterolateral surface of the lateral pterygoid muscle

T Suffix (required only if applicable)

___ Not applicable
___ (m) multiple primary synchronous tumors in a single organ

pN Category

___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)
___ pN0: No tumor involvement of regional lymph node(s)
___ pN1: Tumor involvement of any of the following: Unilateral cervical lymph node(s) or unilateral or bilateral retropharyngeal lymph node(s); AND all of the following: Less than or equal to 6 cm in greatest dimension; and above the caudal border of cricoid cartilage; and without advanced extranodal extension
___ pN2: Tumor involvement of bilateral cervical lymph nodes AND all of the following: Less than or equal to 6 cm in greatest dimension; and above the caudal border of cricoid cartilage; and without advanced extranodal extension
___ pN3: Tumor involvement of unilateral or bilateral cervical lymph node(s); AND any of the following:

Greater than 6 cm in greatest dimension; or extension below the caudal border of cricoid cartilage; or advanced radiologic extranodal extension with involvement of adjacent muscles, skin, and / or neurovascular bundle

pM Category (required only if confirmed pathologically)

___ Not applicable - pM cannot be determined from the submitted specimen(s)

pM1: Microscopic confirmation of distant metastasis

___ pM1a: Microscopic confirmation of less than or equal to 3 metastatic lesions in one or more organs / sites

___ pM1b: Microscopic confirmation of greater than 3 metastatic lesions in one or more organs / sites

___ pM1 (subgroup cannot be determined)

SPECIAL STUDIES

Pending biomarker studies should be listed in the Comments section of this report. For HPV status, p16 alone is insufficient as a surrogate marker. For reporting other molecular and biomarker testing results, the CAP Head and Neck Biomarker Template should be used.

Ancillary Studies Performed (required only if applicable) (select all that apply)

___ Not applicable

___ p16 IHC

p16 IHC

___ Negative (less than 50% moderate-to-strong nuclear and cytoplasmic staining)

___ Equivocal (less than 70% but greater than 50% moderate-to-strong nuclear and cytoplasmic staining)

___ Positive (greater than or equal to 70% moderate-to-strong nuclear and cytoplasmic staining)

___ Other (specify): _____

___ Cannot be determined (explain): _____

___ HPV E6 / E7 mRNA ISH

HPV E6 / E7 mRNA ISH

___ Negative (no signal)

___ Positive (cytoplasmic and / or nuclear signals)

Specify Subtypes (if available): _____

___ Cannot be determined (explain): _____

___ HPV-DNA ISH

HPV-DNA ISH

___ Negative (no nuclear signal)

___ Positive (punctate and / or diffuse nuclear staining)

Specify Subtypes (if available): _____

___ Cannot be determined (explain): _____

___ HPV-DNA PCR

HPV-DNA PCR

___ Negative

___ Positive

Specify Subtypes (if available): _____

___ Cannot be determined (explain): _____

___ HPV E6 / E7 mRNA RT-PCR
HPV E6 / E7 mRNA RT-PCR
___ Negative
___ Positive
Specify Subtypes (if available): _____
___ Cannot be determined (explain): _____
___ Epstein-Barr virus (EBV) testing
EBV Encoded mRNA (EBER) ISH
___ Negative (no nuclear signal)
___ Positive (nuclear signal)
___ Cannot be determined (explain): _____
___ Other studies (specify): _____
___ Pending studies (specify): _____
___ Not specified
___ Not performed: _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Anatomical Sites

The nasopharynx is situated behind the nasal cavity and above the soft palate; it begins anteriorly at the posterior choana and extends along the plane of the airway to the level of the free border of the soft palate.[1] The subsites of the nasopharynx include:

- Superior
- Posterior
- Lateral (including lateral pharyngeal recess, i.e., Rosenmüller fossa)
- Nasopharyngeal tonsils (adenoids)

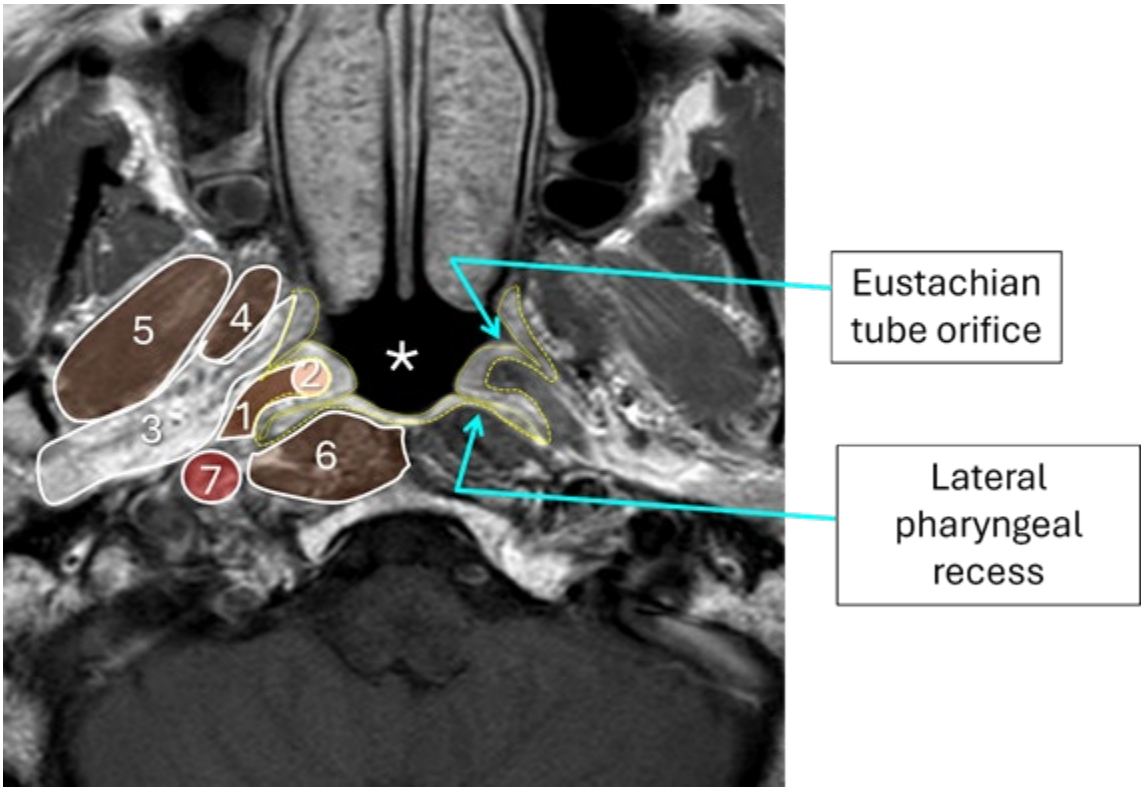

Figure 1: Lee AWM, Huang SH, Chua MLK, et al. Nasopharynx. In: Washington MK, ed. *AJCC Cancer Staging System.* Version 9. American College of Surgeons; 2025. Reproduced with permission.

The nasopharynx is associated with several key anatomic structures (Figure 1). This nasopharynx axial MRI shows:

1. Levator palatini muscle (brown)
2. Torus tubarius (pink), mucosa/submucosa outlined in yellow.
3. Parapharyngeal fat containing venous plexus and nerves (white)
4. Medial pterygoid muscle (brown)
5. Lateral pterygoid muscle (brown)
6. Prevertebral muscles (brown)
7. Carotid sheath (red)

References

1. Lee AWM, Huang SH, Chua MLK, et al. Nasopharynx. In: Washington MK, ed. *AJCC Cancer Staging System*. Version 9. American College of Surgeons; 2025.

B. Histologic Type and Grade

The WHO classification of nasopharyngeal carcinoma is shown below. There is no standard grading system for nasopharyngeal carcinoma.[1,2]

- Low-grade nasopharyngeal papillary adenocarcinoma
- Squamous cell carcinoma, keratinizing, NOS
- Squamous cell carcinoma, non-keratinizing, NOS
- Basaloid squamous cell carcinoma

Neuroendocrine Carcinoma

The recommended histologic classification for neuroendocrine neoplasms has been standardized across all head and neck sites.[2] The entities relevant to this protocol are listed below:

- Neuroendocrine tumor, grade 1-3
- Neuroendocrine carcinoma, small cell type
- Neuroendocrine carcinoma, large cell type

Additionally, composite tumors with non-neuroendocrine CA components exist throughout the upper aerodigestive tract. The carcinoma component can then be captured in this protocol accordingly.

References

1. Lee AWM, Huang SH, Chua MLK, et al. Nasopharynx. In: Washington MK, ed. *AJCC Cancer Staging System*. Version 9. American College of Surgeons; 2025.
2. WHO Classification of Tumours Editorial Board. *Head and neck tumours* [Internet; beta version ahead of print]. Lyon (France): International Agency for Research on Cancer; 2022 [cited 2026, Jan 26]. (WHO classification of tumours series, 5th ed.; vol. 9). Available from: https://tumourclassification.iarc.who.int/chapters/52

C. Lymphatic and/or Vascular Invasion and Perineural Invasion

Local lymphatic/vascular and perineural invasion are not well studied in nasopharyngeal carcinoma, as these are not typically resected as part of initial treatment. However, based on the high propensity for nodal involvement and proximity to named nerves, these parameters should still be reported in the rare tumors that are primarily resected.[1]

References

1. Lee AWM, Huang SH, Chua MLK, et al. Nasopharynx. In: Washington MK, ed. *AJCC Cancer Staging System*. Version 9. American College of Surgeons; 2025.

D. Margins and Orientation

Resections for nasopharyngeal carcinoma yielding an intact specimen are highly uncommon and almost exclusively post therapy. If measurable, in keeping with other sites, the distance from the nearest margin should be recorded.

Complex specimens should be examined and oriented with the assistance of the operating surgeon(s). Direct communication between the surgeon and pathologist is a critical component in specimen orientation and proper sectioning. Whenever possible, the tissue examination request form should include a drawing or photograph of the resected specimen showing the extent of the tumor and its relation to the anatomic structures of the region. The lines and extent of the resection can be depicted on preprinted adhesive labels and attached to the surgical pathology request forms.

E. Regional Lymph Nodes

Direct Extension of Tumor to Lymph Node
While data are essentially nonexistent for defining N status for lymph nodes involved by tumor via direct extension for head and neck cancers, the general convention based on other organ sites is to consider these positive for N categorization and counting purposes. It is recommended, however, to denote in the report the number of lymph nodes involved in this manner, as it may influence more nuanced management decisions.

Measurement of Tumor Metastasis
The cross-sectional diameter of the largest lymph node metastasis (not the lymph node itself) is measured in the gross specimen at the time of macroscopic examination or, if necessary, on the histologic slide at the time of microscopic examination.

Special Procedures for Lymph Nodes
Cervical nodal metastases may occur in the setting of an unknown primary carcinoma referred to as metastatic cervical carcinoma with an unknown primary (CUP).

Patients with EBV-associated cervical adenopathy without an identifiable primary are assigned a pT0 as per AJCC Version 9 TNM classification of nasopharyngeal carcinoma.[1] While a small subset of nasopharyngeal carcinomas is HPV-associated, HPV-associated tumors without a known primary are always assigned pT0 as per AJCC Version 9 TNM classification of HPV-associated oropharyngeal squamous cell carcinoma.[2]

Aside from these, no additional special techniques are required other than routine histology for the assessment of nodal metastases. Immunohistochemistry and polymerase chain reaction (PCR) to detect isolated tumor cells are considered investigational techniques at this time.

Regional Lymph Nodes (pN0): Isolated Tumor Cells
Isolated tumor cells (ITCs) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. The generic recommendation is that lymph nodes with ITCs found by either histologic examination, immunohistochemistry, or non-morphologic techniques (e.g., flow cytometry, DNA analysis, PCR amplification of a specific tumor marker) should be classified as N0 or M0, respectively.[3] Evidence for the validity of this practice in head and neck squamous cell carcinoma and other histologic subtypes is however lacking even on systematic review.[4,5] In fact, rare studies relevant to head and neck sites indicate that isolated tumor cells may actually be a poor prognosticator in terms of local control.[6]

Lymph Node Number

For assessment of pN, a selective neck dissection will ordinarily include 10 or more lymph nodes, and a comprehensive neck dissection (radical or modified radical neck dissection) will ordinarily include 15 or more lymph nodes. AJCC Version 9 now introduces a minimal requirement of 6 lymph nodes to be examined in order to assign a pN0 status.

Classification of Neck Dissection

1. Radical neck dissection
2. Modified radical neck dissection, internal jugular vein and/or sternocleidomastoid muscle spared
3. Selective neck dissection (SND), as specified by the surgeon (Figure 2), defined by dissection of less than the 5 traditional levels of a radical and modified radical neck dissection. The following dissections are now under this category:[7,8,9]
    1. Supraomohyoid neck dissection
    2. Posterolateral neck dissection
    3. Lateral neck dissection
    4. Central compartment neck dissection
4. Superselective neck dissection (SSND), a relatively new term defined by dissection of the fibrofatty elements of 2 or less levels[10]
5. Extended radical neck dissection, as specified by the surgeon

For purposes of pathologic evaluation, lymph nodes are organized by levels as shown in Figure 2.

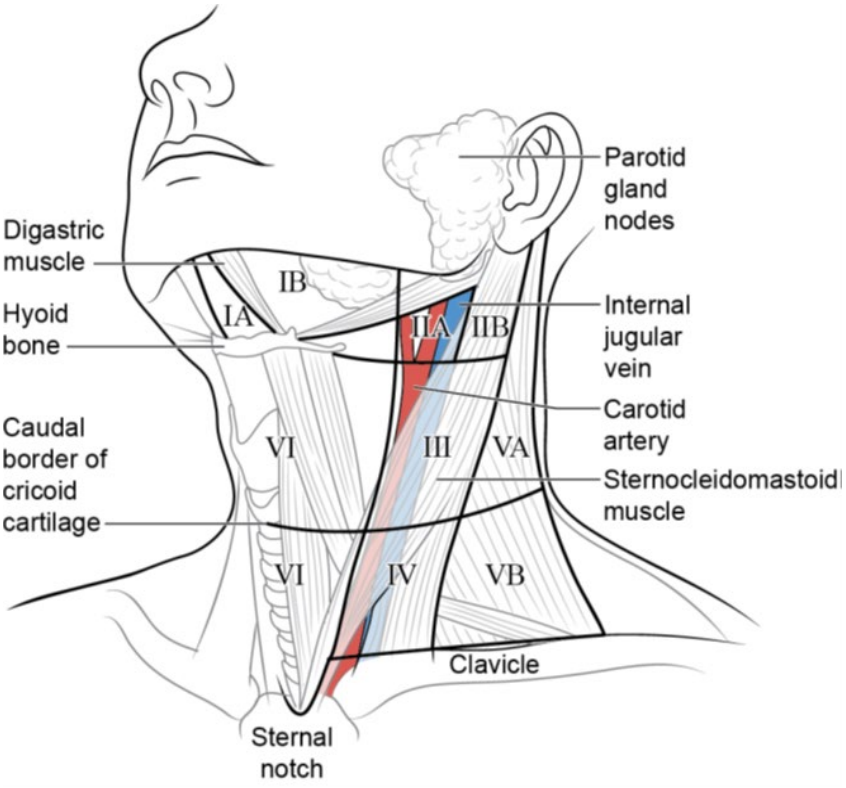

Figure 2. The six levels of the neck for describing the location of lymph nodes along with sublevels: Level IA, submental group; level IB, submandibular group; level IIA, upper jugular nodes along the carotid sheath, including the subdigastric group; level IIB, upper jugular nodes in the submuscular recess; level VA, spinal accessory nodes; and level VB, the supraclavicular and transverse cervical nodes. Evans M, Huang S, Ho A, et al. AJCC Protocol for Cancer Staging: Oropharynx (HPV-Associated). *American Joint Committee on Cancer*. Version 9. American College of Surgeons. 2025. Reproduced with permission.

In order for pathologists to properly identify these nodes, they must be familiar with the terminology of the regional lymph node groups and with the relationships of those groups to the regional anatomy. Which lymph node groups surgeons submit for histopathologic evaluation depends on the type of neck dissection they perform. Therefore, surgeons must supply information on the types of neck dissections that they perform and on the details of the local anatomy in the specimens they submit for examination or, in other manners, orient those specimens for pathologists.

If it is not possible to assess the levels of lymph nodes (for instance, when the anatomic landmarks in the excised specimens are not specified), then the lymph node levels may be estimated as follows: level II, upper third of internal jugular (IJ) vein or neck specimen; level III, middle third of IJ vein or neck specimen; level IV, lower third of IJ vein or neck specimen, all anterior to the sternocleidomastoid muscle.

Level I. Submental Group (Sublevel IA)
Lymph nodes within the triangular boundary of the anterior belly of the digastric muscles and the hyoid bone.

Level I. Submandibular Group (Sublevel IB)
Lymph nodes within the boundaries of the anterior and posterior bellies of the digastric muscle and the body of the mandible. The submandibular gland is included in the specimen when the lymph nodes within this triangle are removed.

Level II. Upper Jugular Group (Sublevels IIA and IIB)
Lymph nodes located around the upper third of the internal jugular vein and adjacent spinal accessory nerve extending from the level of the carotid bifurcation (surgical landmark) or hyoid bone (clinical landmark) to the skull base. The posterior boundary is the posterior border of the sternocleidomastoid muscle, and the anterior boundary is the lateral border of the stylohyoid muscle.

Level III. Middle Jugular Group
Lymph nodes located around the middle third of the internal jugular vein extending from the carotid bifurcation superiorly to the omohyoid muscle (surgical landmark), or cricothyroid notch (clinical landmark) inferiorly. The posterior boundary is the posterior border of the sternocleidomastoid muscle, and the anterior boundary is the lateral border of the sternohyoid muscle.

Level IV. Lower Jugular Group
Lymph nodes located around the lower third of the internal jugular vein extending from the omohyoid muscle superiorly to the clavicle inferiorly. The posterior boundary is the posterior border of the sternocleidomastoid muscle, and the anterior boundary is the lateral border of the sternohyoid muscle.

Level V. Posterior Triangle Group (Sublevels VA and VB)
This group comprises predominantly the lymph nodes located along the lower half of the spinal accessory nerve and the transverse cervical artery. The supraclavicular nodes are also included in this group. The posterior boundary of the posterior triangle is the anterior border of the trapezius muscle, the anterior boundary of the posterior triangle is the posterior border of the sternocleidomastoid muscle, and the inferior boundary of the posterior triangle is the clavicle.

Level VI. Anterior (Central) Compartment
Lymph nodes in this compartment include the pre- and paratracheal nodes, precricoid (Delphian) node, and the perithyroidal nodes, including the lymph nodes along the recurrent laryngeal nerve. The superior boundary is the hyoid bone, the inferior boundary is the suprasternal notch, the lateral boundaries are the common carotid arteries, and the posterior boundary by the prevertebral fascia.

Level VII. Superior Mediastinal Lymph Nodes
Metastases at level VII are considered regional lymph node metastases; all other mediastinal lymph node metastases are considered distant metastases.

Lymph node groups removed from areas not included in the above levels, e.g., scalene, suboccipital, and retropharyngeal, should be identified and reported from all levels separately. When staging lymph node involvement by metastases from nasopharyngeal carcinoma, lymph nodes below the caudal border of the cricoid cartilage include Levels IV and VA (see above). All cancers metastatic to these nodes are designated as N3. Midline nodes are considered ipsilateral nodes.

Extranodal Extension
Extranodal extension (ENE) is a core element for AJCC Version 9 pathological TNM classification of nasopharyngeal carcinoma and is critical for defining N category, however this is only if advanced as defined by structural involvement (adjacent muscles, skin and/or neurovascular bundle) and radiologically documented.

Other Elements
Anatomic compartment location of positive lymph nodes is now a non-core element, though this is still indirectly required to confirm caudal extension below cricoid cartilage.

References

1. Lee AWM, Huang SH, Chua MLK, et al. Nasopharynx. In: Washington MK, ed. *AJCC Cancer Staging System.* Version 9. American College of Surgeons; 2025.
2. Evans M, Huang S, Ho A, et al. AJCC Protocol for Cancer Staging: Oropharynx (HPV-Associated). *American Joint Committee on Cancer.* Version 9. American College of Surgeons. 2025.
3. Gress DM, Edge SB, Greene FL et al. General Information on Cancer Staging and End-Results Reporting. In: Amin MB, ed. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.
4. Singh A, Roy S, Tuljapurkar V, et al.Critical Review of the Current Evidence on Sentinel Node Biopsy in Oral Cancer. *Curr Oncol Rep*. 2022 Jun;24(6):783-791.
5. Liokatis P, Liokati I, et al. Prognostic role of lymph node micrometastasis in oral and oropharyngeal cancer: A systematic review. *Oral Oncol.* 2024 Jul; 154:106808.

6. Broglie MA, Haerle SK, Huber GF, Haile SR, Stoeckli SJ. Occult metastases detected by sentinel node biopsy in patients with early oral and oropharyngeal squamous cell carcinomas: *Impact on survival. Head Neck.* 2013;35(5):660-666.
7. Ferlito A, Robbins KT, Shah JP, et al. Proposal for a rational classification of neck dissections. *Head Neck.* 2011;33(3):445-450.
8. Robbins KT, Shaha AR, Medina JE, et al. Consensus statement on the classification and terminology of neck dissection. *Arch Otolaryngol Head Neck Surg.* 2008;134(5):536-538.
9. Seethala RR. Current state of neck dissection in the United States. *Head Neck Pathol.* 2009;3(3):238-245.
10. Suarez C, Rodrigo JP, Robbins KT, et al. Superselective neck dissection: rationale, indications, and results. *Eur Arch Otorhinolaryngol.* 2013.

F. pTNM Classification

The protocol recommends using the AJCC Version 9 pathological TNM classification of Nasopharyngeal Carcinoma for reporting.[1] Pathological T classification is unchanged. T2 denotes tumors with extension to parapharyngeal space and/or adjacent soft tissue involvement (medial pterygoid, lateral pterygoid, prevertebral muscles). There is some suggestion that up-classifying tumors with medial +/- lateral pterygoid involvement from T2 to T3 may be warranted constituting a more logical anatomic transition from T2 to T4, but this could not be validated for 9th version. Similarly, down-classification of T3 to T2 for 'early skull base invasion' could not be confirmed.[1,2] T4 indicates tumor with intracranial extension, involvement of cranial nerves (based on clinical evidence and/or unequivocal radiological evidence), hypopharynx, orbit, parotid gland, and/or extensive soft tissue infiltration beyond the lateral surface of the lateral pterygoid muscle.

For pN classification for Version 9, the N3 category now also includes advanced radiologic extranodal extension as defined previously.

M category for NPC is now stratified into M1a and M1b based on number of metastatic lesions. Specific site of involvement, particularly liver is of interest to further sub-stratify M category. However, there is currently insufficient evidence for this given the small size of the subset (~16%) with less than or equal to 3 metastatic lesions and liver involvement.[1,2]

TNM Descriptors[3]

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y”, “r”, and “a” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis. Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician’s responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.

The “m” suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or following initial multimodality therapy (i.e., neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM

categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor prior to multimodality therapy (i.e., before initiation of neoadjuvant therapy).

The “r” prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the “r” prefix: rTNM.

The “a” prefix designates the stage determined at autopsy: aTNM.

References

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3. Gress DM, Edge SB, Greene FL et al. General Information on Cancer Staging and End-Results Reporting. In: Amin MB, ed. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.