

Protocol for the Examination of Specimens from Patients with Cancers of the Lip and Oral Cavity

Protocol applies to carcinomas arising from the lip and oral cavity including squamous cell carcinoma and minor salivary gland carcinoma. Mucosal melanoma is included. This protocol does not apply to lymphoma or sarcoma.

Based on:

AJCC/UICC TNM, 8th edition
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None

Summary of Changes:

This protocol is revised to the 8th edition of the AJCC Cancer Staging Manual and the current version of the CAP Cancer Protocol LipOralCavity 4.0.0.1.

Procedures Covered in this Protocol:

- Excision
- Glossectomy
- Buccal Mucosal Resection
- Mandibulectomy
- Maxillectomy
- Palatectomy
- Neck (Lymph Node) Dissection

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**AAPA Macroscopic Examination Guidelines:
Utilization of the *CAP Cancer Protocols* at the Surgical Gross Bench**

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The purpose of the Protocols is to support Laboratory Personnel engaged in the macroscopic examination of cancer resection specimens. The Protocols are based on specified relevant source documents, drafted by pathologists' assistant experts, and supported by information provided by the College of American Pathologists (CAP) and the American Joint Committee on Cancer (AJCC). These Protocols are intended to serve patients by ensuring that the macroscopic examination of cancer resection specimens is compliant with CAP Cancer Protocols, the AJCC Cancer Staging Manual, and provide optimization of the pre-analytic steps necessary to promote appropriate molecular studies.

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Molecular and Immunohistochemistry Considerations:

It is well established that human papillomavirus (HPV) plays a pathogenic role in a subset of head and neck cancers, termed HPV-associated head and neck squamous cell carcinoma (HPVHNSCC). Present in most oropharyngeal carcinomas, positivity for high risk HPV16 was detected in 93% of cases. These carcinomas arise predominantly from the palatine tonsils and lingual tonsils of the oropharynx (e.g., tonsil or base of tongue) and are nonkeratinizing carcinomas characterized by a basaloid cell type. Initial presentation may include metastatic cancer to a cervical neck lymph node from an unknown primary site, also known as a metastatic cervical carcinoma with an unknown primary (MCCUP). Among the methods of detecting HPV16, polymerase chain reaction (PCR), fluorescence in-situ hybridization (FISH) and p16 immunohistochemical stain may all be utilized.

PCR has high sensitivity, but lower specificity, giving rise to false positives. FISH has lower specificity than PCR but enables visualization of tumor cells and localization of positivity. P16 is now a mainstay of HPVHNSCC of the head and neck with its high sensitivity and high specificity.

Immunohistochemical staining including S-100, HMB-45, Melanin-A, MITF, and PNL-2 will help confirm a mucosal melanoma diagnosis.

These tests can be performed on formalin-fixed, paraffin embedded tissue sections. The macroscopic description should provide the fixative used. 10% neutral buffered formalin is the preferred fixative. It is recommended that the duration of fixation be provided as well.

PROCEDURES AND GENERAL ANATOMIC CONSIDERATIONS:

■ **Procedures Covered by this Protocol:**

- Excision
- Glossectomy
- Buccal mucosal resection
- Mandibulectomy (partial and total)
- Maxillectomy (partial and total)
- Palatotomy (partial and total)
- Neck (lymph node) dissection
- Other (specify)

■ **Specimen Size and Extent of Resection:**

- Provide three dimensions with orientation, if specified.
- Identify and name all anatomic components of the specimen; including teeth if applicable.
- Identify, name and provide three dimensions of any additional structures received.

■ **Specimen Orientation:**

Complex specimens should be examined and oriented with the assistance of the surgeon. Consequently, communication between the surgeon and pathologist is a critical component in specimen orientation and proper sectioning. An illustration or photograph of the resected specimen demonstrating the extent of the tumor and its relation to the anatomic structures of the region may prove an invaluable adjunct to the final pathology report.

■ **Specimen Integrity and Adequacy:**

Provide an assessment of the specimen integrity. Note areas of disruption and relationship to the lesion. Identify and describe any defects or disruptions. *

- Specify if specimen is intact or fragmented.

**Statements should include, with as much clarity as can be provided, the anatomic location of the defect(s) or disruption(s), and should also incorporate statements, which assess the relationships of any defect(s) or disruption(s) to the tumor. If these involve the tumor and hinder evaluation of the final surgical margins, this must be stated. Consultation with the surgeon for clarification should be considered, as well as differential application of ink to the margins in the area affected by the defect as this may assist in creating a post-surgical treatment plan.*

TUMOR ("T" of TNM)

■ **Tumor Size and Thickness:**

- Three dimensions of each tumor in cm.
- Measure tumor thickness in mm.

■ **Tumor Laterality:**

- Right
- Left
- Midline

■ **Tumor Focality:**

- State if unifocal or multifocal.

■ **Tumor Description (include macroscopic features):**

- Polypoid
- Exophytic
- Endophytic
- Sessile
- Ulcerated
 - Specify if the surface mucosa is intact or ulcerated
- Other (specify)

■ **Tumor Site(s):** (*Figures 1A and 1B*)

- Lip
 - External upper lip (exclude vermillion border)
 - External lower lip (exclude vermillion border)
 - Mucosa of upper lip
 - Mucosa of lower lip
 - Commissure of lip
- Oral Cavity
 - Buccal Mucosa
 - Mucosa of upper and lower lips
 - Cheek mucosa
 - Retromolar areas
 - Bucco-alveolar sulci, upper and lower (vestibule of mouth)
 - Upper alveolus and gingiva (upper gum)
 - Lower alveolus and gingiva (lower gum)
 - Hard palate
 - Tongue
 - Dorsal surface and lateral borders anterior to circumvallate papillae (anterior two-thirds)
 - Inferior (ventral) surface

- Floor of mouth
- Bone Involvement
 - Mandible
 - Maxilla
 - Base of skull
- Other
 - Alveolar nerve
 - Salivary gland
 - Skin of face (e.g., chin, cheek, nose)

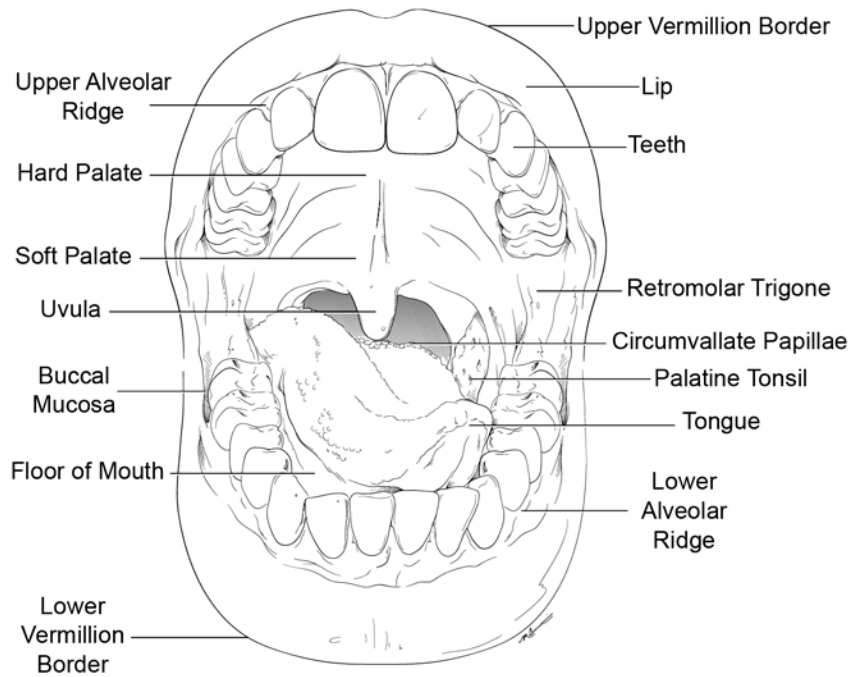


Figure 1A: Anterior View of the Oral Cavity

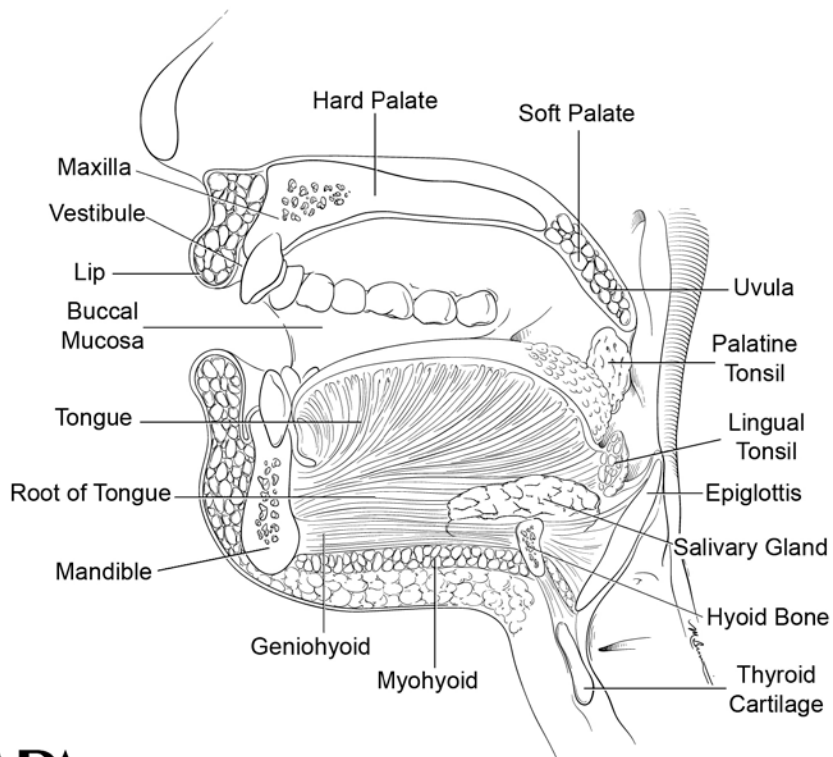


Figure 1B: Sagittal View of the Oral Cavity

■ **Tumor Depth of Invasion (DOI), Relationship to Attached Organs / Structures, and Specimen Examination Guidelines:** (*Figure 2*)

Depth of invasion (DOI), measured from the tumor mucosal surface to the deepest point, correlates with predicted regional lymphatic spread and is an important predictor of clinical outcome.

- Submit 2 mm to 3 mm consecutive sections through the tumor to facilitate locating the deepest point of invasion and maximum tumor dimension.
- Macroscopic examination of consecutive sections through the lesion and measuring tumor thickness from a histologic section with the least amount of tangential artifact should aid in accurately measuring tumor thickness.
- **Exophytic tumors:** measure the tumor thickness from the surface of the tumor exclusive of the keratin layer to the deepest area of invasion.
 - This measurement is better characterized as tumor thickness rather than depth of invasion.
- **Ulcerated tumors:** measure from the ulcer base to the deepest area of invasion, as well as from the surface of the most lateral extent of the invasive tumor to the deepest area.
- **Endophytic tumors:** measure from the perpendicular surface of the invasive tumor to the deepest area of invasion. The measurement should not be done on tangential sections or in lesions without a clearly recognizable surface component.

Involvement of the retromolar trigone is of particular clinical significance, as it carries a more unfavorable prognosis due its mandible proximity.

Perineural Invasion:

The most significant prognostic factor is the presence of perineural invasion (neurotropism), an important predictor of poor prognosis in head and neck cancer of virtually all sites. The presence of perineural invasion in the primary cancer is associated with poor local disease control and regional control, as well as being associated with metastasis to regional lymph nodes.

■ **Explanatory Notes:**

The microscopic measurement of tumor thickness or depth of invasion (DOI) has long been considered a valuable parameter for predicting regional nodal involvement and survival in oral cavity squamous cell carcinoma. Proper macroscopic examination techniques (avoidance of tangential cuts and serial sectioning of the lesion at 2-3 mm intervals) will facilitate subsequent microscopic assessment. DOI should be distinguished from tumor thickness, and its determination is predicted on invasion beneath the plane defined by surrounding normal mucosa.

Thickness is usually measured from the mucosal surface of the tumor to the deepest point of tissue invasion in a perpendicular fashion with an optical micrometer or transparent ruler overlaid on the slide, while DOI is measured from the basement membrane of adjacent normal mucosa to the deepest point of invasion of the tumor.

Depth of invasion assesses the invasiveness of a carcinoma, regardless of any exophytic component.

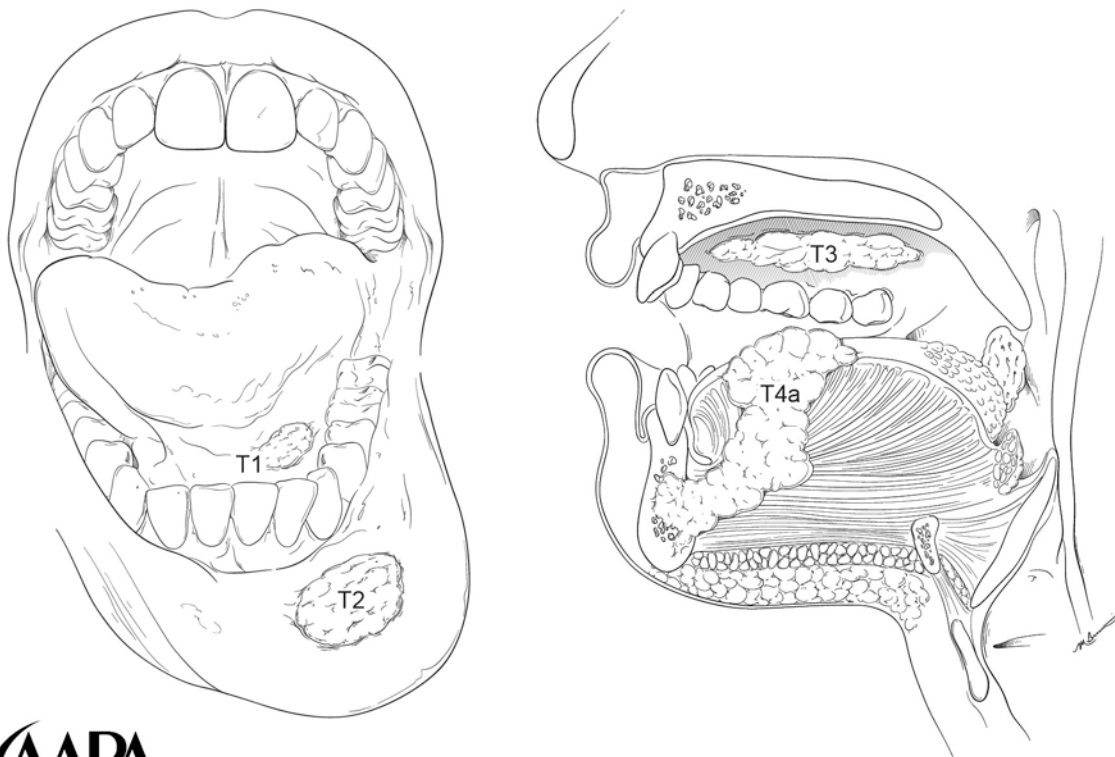


Figure 2: Lip and Oral Cavity - T1-T4 Criteria

- T1: Tumor ≤ 2 cm, with depth of invasion (DOI)* ≤ 5 mm
T2: Tumor ≤ 2 cm with DOI* > 5 mm or tumor > 2 cm and < 4 cm with DOI* < 10 mm
T3: Tumor > 2 cm and < 4 cm with DOI* > 10 mm or tumor > 4 cm with DOI* < 10 mm
T4a: Moderately advanced local disease
Tumor > 4 cm with DOI* > 10 mm
or tumor invades adjacent structures only (e.g., through cortical bone of the mandible or maxilla, or involves the maxillary sinus or skin of the face)
Note: Superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumor as T4.

* DOI is depth of invasion and not tumor thickness.

Definition of Primary Tumor (pT)

pT Category	pT Criteria
pTX	Primary tumor cannot be assessed
pTis	Carcinoma <i>in situ</i>
pT1	Tumor ≤ 2 cm, with depth of invasion (DOI)* ≤ 5 mm
pT2	Tumor ≤ 2 cm with DOI* > 5 mm or tumor > 2 cm and < 4 cm with DOI* < 10 mm
pT3	Tumor > 2 cm and < 4 cm with DOI* > 10 mm or tumor > 4 cm with DOI* < 10 mm
pT4	Moderately advanced or very advanced local disease
pT4a	Moderately advanced local disease Tumor > 4 cm with DOI* > 10 mm or tumor invades adjacent structures only (e.g., through cortical bone of the mandible or maxilla, or involves the maxillary sinus or skin of the face) Note: Superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumor as T4.
pT4b	Very advanced local disease. Tumor invades masticator space, pterygoid plates, or skull base, and/or encases the internal carotid artery

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**DOI is depth of invasion and not tumor thickness.*

TNM Categorization for Mucosal Melanoma:

Mucosal melanoma is an aggressive neoplasm that calls for separate consideration. Approximately two-thirds of these lesions arise in the sinonasal tract; one quarter are found in the oral cavity, and the remainder occur only sporadically in other mucosal sites of the head and neck. Even small cancers behave aggressively with advanced initial presentation, high rates of recurrence and death. To reflect this aggressive behavior, primary cancers limited to the mucosa are considered T3 lesions.

Definition of Primary Tumor (pT)

pT Category	pT Criteria
pT3	Tumors limited to the mucosa and immediately underlying soft tissue, regardless of thickness or greatest dimension; for example, polypoid nasal disease, pigmented or nonpigmented lesions of the oral cavity, pharynx, or larynx
pT4	Moderately advanced or very advanced disease
pT4a	Moderately advanced disease. Tumor involving deep soft tissue, cartilage, bone, or overlying skin
pT4b	Very advanced disease. Tumor involving brain, dura, skull base, lower cranial nerves (IX, X, XI, XII), masticator space, carotid artery, prevertebral space, or mediastinal structures

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TNM Descriptors:

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y” and “r” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

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.

Residual Tumor (R) Category

The absence or presence of residual tumor at the primary tumor site after treatment is denoted by the symbol R. The R categories for the primary tumor site are as follows:

R	R Definition
RX	Presence of residual tumor cannot be assessed
R0	No residual tumor
R1	Microscopic residual tumor
R2	Macroscopic residual tumor at the primary cancer site or regional nodal sites

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■ **Margins:**

Surgical Margins:

All specimens should be oriented appropriately, the soft tissue margins applied with ink, and the mucosal and soft tissue margins evaluated.

- State if margins are macroscopically involved or uninvolved by tumor.
- If the margin is involved by tumor, specify the margin, per orientation, if possible, or after consultation with the surgeon.
 - If the tumor macroscopically approximates a margin to < 1 mm to 2 mm, radial (perpendicular) sections should be taken.
- Specify location and measurement of closest margin, per orientation, if possible or after consultation with the surgeon.
 - If the tumor is relatively distant from a margin, shave sections may be taken, however, radial (perpendicular) sections are recommended. *
- Sections should also be evaluated to assess for carcinoma in situ or high-grade dysplasia.

**It is recommended to take radial (perpendicular) margins whenever possible, even when margins are distant from the tumor. With this technique, the distance to occult tumor or dysplasia, if present, can still be measured. Bone margins may be taken en face, and the gingival margin close to bone/tooth must be scraped or shaved off and then can only be submitted en face.*

Note: Tumor or carcinoma in situ/high-grade dysplasia with close margins is a predictor of local recurrence. Measure as accurately as possible to the margin. In general, close margins are defined as 5 mm and 2 mm with respect to glottis larynx. An ideal therapeutic margin is 10 mm but often, resections are 2 mm to 3 mm which is compounded by a peri-tumoral zone of dysplastic or hypertrophic mucosa.

Tumor Bed Margins: (separately submitted) (required for squamous cell carcinoma only)

- Specify if the specimen is oriented or unoriented to the true margin surface.
- Specify if the specimen is uninvolved by tumor.
 - Specify the distance to the true margin surface in mm (if oriented and sectioned perpendicularly).
- Specify if the specimen is involved by tumor.
- Specify the margin(s), per specimen labeling, if possible.

Worst Pattern of Invasion (WPOI):

WPOI is a validated outcome predictor for oral cavity squamous carcinoma patients. The recommendation is whether or not WPOI-5 is present. WPOI-5 is defined as a tumor dispersion >/ 1mm between tumor satellites. Tumor dispersion is assessed at the advancing of a tumor edge. The most common WPOI-5 phenotype is tumor dispersion through soft tissue. Dispersed extratumoral perineural invasion, or extratumoral lymphovascular invasion, also can qualify for classification as WPOI-5.

LYMPH NODES ("N" of TNM)

■ **Lymph Nodes:** (if applicable)

The status of cervical lymph nodes is the single most important prognostic factor in aerodigestive cancer. Mucosal cancer of the oral cavity may spread to regional lymph nodes. Tumors of each anatomic site have their own predictable patterns of regional spread.

Definition of Regional Lymph Node (pN)

Pathological N (pN)

pN Category	pN Criteria
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(-)
pN2	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+); or larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension, ENE(-); or in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(-)
pN2a	Metastasis in single ipsilateral lymph node 3 cm or smaller in greatest dimension and ENE(+); or a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(-)
pN2b	Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(-)
pN2c	Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(-)
pN3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-); or metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); or multiple ipsilateral, contralateral or bilateral nodes any with ENE(+); or a single contralateral node of any size and ENE(+)
pN3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(-)
pN3b	Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); or multiple ipsilateral, contralateral or bilateral nodes any with ENE(+); or a single contralateral node of any size and ENE(+)

Note: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+).

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Note: Anterior Superior mediastinal lymph nodes (level VII) are considered regional lymph nodes. Midline nodes are considered ipsilateral nodes.

Definition of Regional Lymph Node for Mucosal Melanoma (pN)

pN Category	pN Criteria
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastases
pN1	Regional lymph node metastases present

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Regional Lymph Nodes:

Lip

- Submental nodes
- Submandibular nodes
- Jugular nodes

Hard Palate

- Buccinator nodes
- Pre-vascular facial nodes
- Submandibular nodes
- Jugular nodes
- Retropharyngeal nodes (occasional)

Anterior Oral Tongue

- Bilateral cervical nodes
- Lower jugular nodes (occasional)

Lymph Node Submission:

Dissection of 18 lymph nodes has been proposed for the oral cavity but has not yet been validated.

- Specify number of lymph nodes involved by tumor.
 - Specify laterality of lymph nodes involved.
 - Ipsilateral (including midline)
 - Contralateral
 - Bilateral
 - Cannot be determined
- Specify number of lymph nodes examined.

Macroscopically positive lymph nodes:

- Count and submit representative sections of all macroscopically positive lymph nodes.
- Measure the lymph nodes in three dimensions.
- Section the lymph node along the long axis.
- Measure the size of the nodal 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, and the size of lymph node metastasis affects stage.

- State if lymph nodes appear matted; if suspected, submit sections to assess for lymph node matting.
- If suspected, additional sections should be submitted to assess for extranodal extension. *
- Take steps to ensure that an accurate lymph node count can be rendered.

**Extranodal extension (ENE) is metastatic tumor present within the confines of the lymph node, through the lymph node capsule into the surrounding connective tissue. A distance of extension from the native lymph node capsule is suggested but not yet required.*

Involvement of internodal fat resulting in loss of the normal oval-to-round nodal shape suggests extranodal tumor spread.

Extranodal extension and size of matted nodes do not have bearing on stage for mucosal melanoma.

Macroscopically negative lymph nodes:

- Count and submit macroscopically negative or equivocal smaller lymph nodes in toto and larger lymph nodes entirely.
- Measure the lymph nodes in three dimensions.
- Section the lymph nodes along the long axis.
- Take steps to ensure that an accurate lymph node count can be rendered; and submit using methods that will disclose the size of a metastasis (long axis sectioning, sequential sectioning, etc).

Non-regional lymph nodes:

Delineation as to what constitutes non-regional is still unspecified. The above procedure may be employed for more distant level lymph nodes.

■ **Explanatory Notes:**

Extranodal extension, a predictor of regional relapse and a criterion for postoperative radiotherapy is indicated by lymph node matting. Lymph nodes over 3 cm in greatest dimension may represent a confluence of lymph nodes which already display tumor extension into surrounding tissue. Consequently, extra sampling of macroscopically positive lymph nodes may be necessary to rule out extranodal extension, even if not macroscopically evident.

In a previously treated patient, lymph nodes appearing macroscopically positive may actually be fibrotic or cystic without gross tumor. Thus, in this setting, generous sampling is recommended.

Classification of Neck Dissection:

- Radical neck dissection
Includes 22 or more lymph nodes
- Modified radical neck dissection, internal jugular vein and/or sternocleidomastoid muscle spared
Includes 15 or more lymph nodes
- Selective neck dissection (SND), as specified by surgeon, defined by dissection of less than the 5 traditional levels of a radical or modified radical neck dissection
Includes 15 or more lymph nodes
 - Supraomohyoid neck dissection
 - Posterolateral neck dissection
 - Lateral neck dissection
 - Central compartment neck dissection
- Superselective neck dissection, as specified by the surgeon – “SSND” defined by dissection of the fibrofatty elements of 2 levels or less
- Extended radical neck dissections, as specified by surgeon

For purposes of pathologic evaluation, lymph nodes are organized by levels. (Figure 3)

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.

Other Lymph Nodes

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.

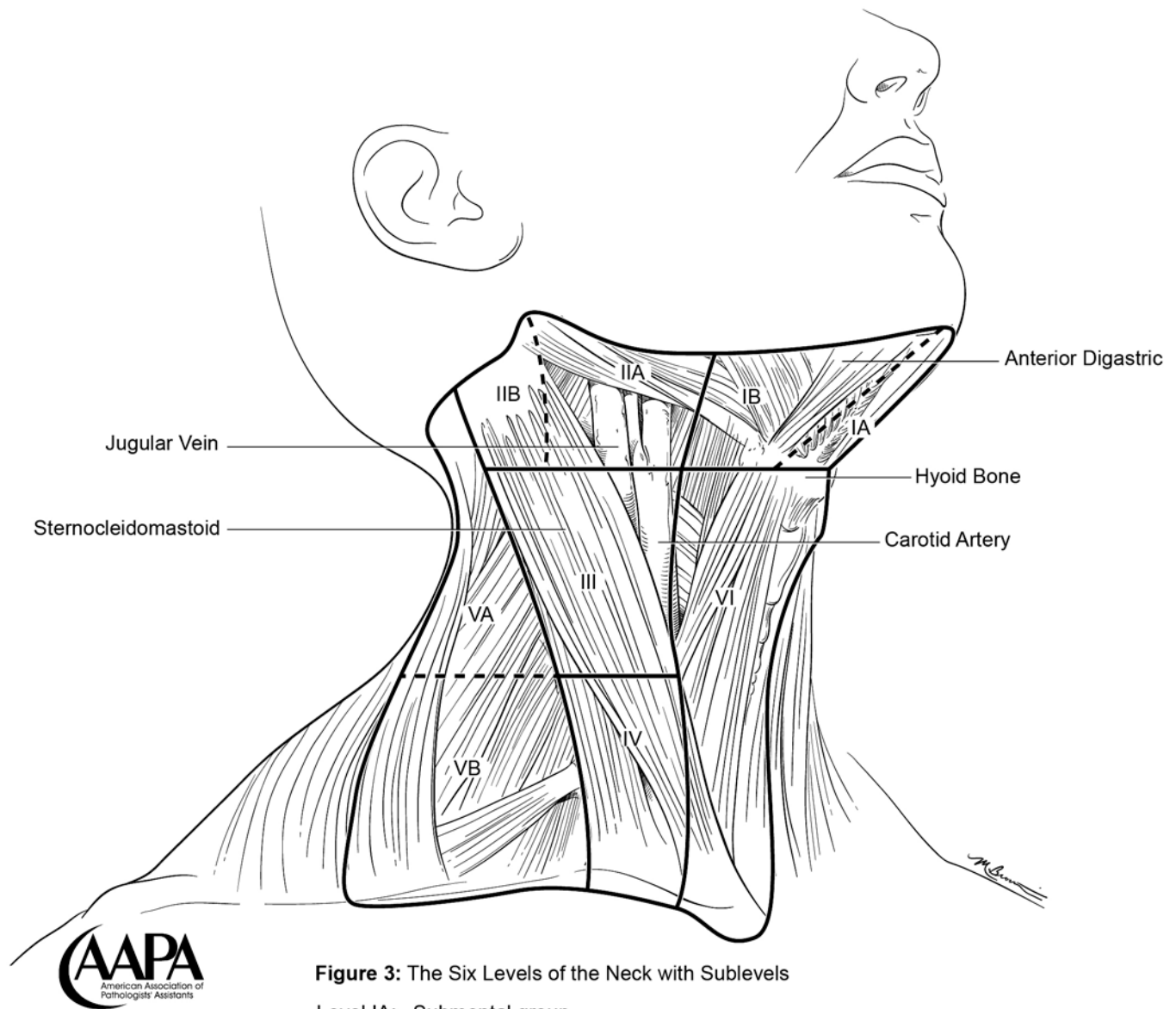


Figure 3: The Six Levels of the Neck with Sublevels

- 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 III: Middle jugular group
- Level IV: Lower jugular group
- Level VA: Spinal accessory nodes
- Level VB: Supraclavicular and transverse cervical nodes
- Level VI: Anterior (central) compartment

Note: 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*

METASTASIS ("M" of TNM)

■ **Metastasis:**

Definition of Distant Metastases (pM) (required only if confirmed pathologically)

pM Category	pM Criteria
M0	No distant metastases
pM1	Distant metastasis

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- The lungs are the most common site of distant metastases.
- Skeletal and hepatic metastases occur less often.
- Mediastinal lymph node metastases are considered distant metastases, except level VII lymph nodes (anterior superior mediastinal lymph nodes cephalad to the innominate artery).

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