Protocol for the Examination of Specimens From Patients With Carcinomas of the Major Salivary Glands

Version: SalivaryGland 4.0.0.0 **Protocol Posting Date:** June 2017
Includes pTNM requirements from the 8th Edition, AJCC Staging Manual

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

Procedure	Description
Resection	Includes specimens designated or containing parotid, submandibular, sublingual glands
Tumor Type	**Description**
Carcinoma	Includes primary salivary gland carcinoma and neuroendocrine carcinoma

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

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

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

Tumor Type
Minor salivary gland carcinoma (consider the Lip and Oral Cavity, Nasal Cavity and Paranasal Sinuses, Pharynx, or Larynx protocols)
Sarcoma (consider the Soft Tissue protocol)
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)

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Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is “not applicable” or “cannot be determined.”
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with “+” and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

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 must 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.

CAP Laboratory Accreditation Program Protocol Required Use Date: March 2018*

** Beginning January 1, 2018, the 8th edition AJCC Staging Manual should be used for reporting pTNM.*

CAP Salivary Gland Protocol Summary of Changes

The following data elements were modified:
Pathologic Stage Classification (pTNM, AJCC 8th Edition)

The following data element was added:
High Grade Transformation

The following data elements were deleted:
Specimen Description
Tumor Description
Clinical History

Surgical Pathology Cancer Case Summary

Protocol posting date: June 2017

MAJOR SALIVARY GLANDS:

Select a single response unless otherwise indicated.

Procedure (select all that apply)
___ Excision
___ Parotidectomy, superficial
___ Parotidectomy, deep
___ Parotidectomy, total
___ Parotidectomy, not specified
___ Resection, submandibular gland
___ Resection, sublingual gland
___ Neck (lymph node) dissection (specify): ______________________________
___ Other (specify): ______________________________
___ Not specified

Tumor Site (Note A)
___ Parotid gland
+ ___ Superficial lobe
+ ___ Deep lobe
+ ___ Entire parotid gland
___ Submandibular gland
___ Sublingual gland
___ Other (specify): ______________________________
___ Not specified

Tumor Laterality
___ Right
___ Left
___ Bilateral
___ Not specified

Tumor Focality
___ Unifocal
___ Multifocal
___ Cannot be determined

Tumor Size
Greatest dimension (centimeters): ___ cm
+ Additional dimensions (centimeters): ___ x ___ cm
___ Cannot be determined (explain): ______________________________________

Histologic Type (Note B)
___ Mucoepidermoid carcinoma, low grade
___ Mucoepidermoid carcinoma, intermediate grade
___ Mucoepidermoid carcinoma, high grade
___ Adenoid cystic carcinoma, tubular pattern[#]
+ Specify percentage of solid component: ____%
___ Adenoid cystic carcinoma, cribriform pattern[#]
+ Specify percentage of solid component: ____%
___ Adenoid cystic carcinoma, solid pattern[#]

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.

+ Specify percentage of solid component: ____%
___ Acinic cell carcinoma
___ Polymorphous adenocarcinoma, classic, low grade
___ Polymorphous adenocarcinoma, classic, intermediate grade
___ Polymorphous adenocarcinoma, classic, high grade
___ Polymorphous adenocarcinoma, cribriform (cribriform adenocarcinoma of salivary origin), low grade
___ Polymorphous adenocarcinoma, cribriform (cribriform adenocarcinoma of salivary origin), intermediate grade
___ Polymorphous adenocarcinoma, cribriform (cribriform adenocarcinoma of salivary origin), high grade
___ (Mammary analogue) Secretory carcinoma
___ Salivary duct carcinoma
___ Epithelial-myoepithelial carcinoma
___ (Hyalinizing) clear cell carcinoma
___ Adenocarcinoma, not otherwise specified, low grade
___ Adenocarcinoma, not otherwise specified, intermediate grade
___ Adenocarcinoma, not otherwise specified, high grade
___ Basal cell adenocarcinoma
___ Carcinosarcoma (true malignant mixed tumor)
___ Intraductal carcinoma, low grade
___ Intraductal carcinoma, high grade
___ Lymphoepithelial carcinoma
___ Myoepithelial carcinoma
___ Oncocytic carcinoma
___ Poorly differentiated carcinoma, small cell neuroendocrine
___ Poorly differentiated carcinoma, large cell neuroendocrine
___ Poorly differentiated carcinoma, undifferentiated
___ Sebaceous adenocarcinoma
___ Squamous cell carcinoma, primary
Preexisting pleomorphic adenoma component (required in addition to salivary carcinoma type, if applicable)
___ Carcinoma ex pleomorphic adenoma, minimally invasive
___ Carcinoma ex pleomorphic adenoma, invasive
___ Carcinoma ex pleomorphic adenoma, intracapsular (noninvasive)

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

[#] Note: If multiple patterns present, select predominant pattern unless solid pattern is greater than 30%, in which case should select solid pattern.

+ High-Grade Transformation (if applicable)
+ ___ Present
+ ___ Not identified

Tumor Extension
Macroscopic Tumor Extension (specify): ___________________________

Margins (Note C)
___ Cannot be assessed
___ Uninvolved by carcinoma
Distance of tumor from closest margin (millimeters): ___ mm
Specify margin, if possible: ______________________________
___ Involved by carcinoma
Specify margin(s), if possible: ______________________________

Lymphovascular Invasion
___ Not identified
___ Present

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.

___ Cannot be determined

Perineural Invasion (Note D)
___ Not identified
___ Present
___ Cannot be determined

Regional Lymph Nodes (Note E)

___ No lymph nodes submitted or found

Lymph Node Examination (required only if lymph nodes present in specimen)

Number of Lymph Nodes Involved: ________
___ Number cannot be determined (explain): ____________________________

Number of Lymph Nodes Examined: _______
___ Number cannot be determined (explain): ____________________________

Lymph Node Metastasis (required only if lymph nodes involved)

Laterality of Lymph Nodes Involved
___ Ipsilateral (including midline)
___ Contralateral
___ Bilateral
___ Cannot be determined

Size of Largest Metastatic Deposit (centimeters): ____ cm

Extranodal Extension (ENE)
___ Not identified
___ Present
 + Distance from lymph node capsule (millimeters): _____ mm
 +___ ENE_{ma} (>2 mm)
 +___ ENE_{mi} (≤2 mm)
___ Cannot be determined

Pathologic Stage Classification (pTNM, AJCC 8th Edition) (Note F)

Note: Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. Only the applicable T, N, or M category is required for reporting; their definitions need not be included in the report. The categories (with modifiers when applicable) can be listed on 1 line or more than 1 line.

Note: The phrases in italics include clinical findings required for AJCC staging. This clinical information may not be available to the pathologist. However, if known, these findings should be incorporated into the pathologic staging.

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple primary tumors)
___ r (recurrent)
___ y (posttreatment)

Primary Tumor (pT)
___ pTX: Primary tumor cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ
___ pT1: Tumor 2 cm or smaller in greatest dimension *without extraparenchymal extension*[#]

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.

___ pT2: Tumor larger than 2 cm but not larger than 4 cm in greatest dimension *without extraparenchymal extension*#
___ pT3: Tumor larger than 4 cm and/or tumor *having extraparenchymal extension*#
___ pT4: Moderately advanced or very advanced disease
___ pT4a: Moderately advanced disease. Tumor invades skin, mandible, ear canal, and/or facial nerve.
___ pT4b: Very advanced disease. Tumor invades skull base and/or pterygoid plates and/or encases carotid artery

 # Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.

Regional Lymph Nodes (pN)# (Note E)
___ 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 and ENE(−); *or* in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(−)
___ pN2a: Metastasis in single ipsilateral 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: Metastasis in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(−)
___ pN2c: Metastasis in bilateral or contralateral lymph nodes, 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 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 3 cm or smaller 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(+)

 # Midline nodes are considered ipsilateral nodes.

Note: Pathological ENE should be recorded as ENE(−) or ENE(+).

Note: Measurement of the metastatic focus in the lymph nodes is based on the largest metastatic deposit size, which may include matted or fused lymph nodes.

Distant Metastasis (pM) (required only if confirmed pathologically in this case)
___ pM1: Distant metastasis
Specify site(s), if known: ____________________________

+ Additional Pathologic Findings (select all that apply)
+ ___ Sialadenitis
+ ___ Tumor associated lymphoid proliferation (TALP)
+ ___ Other (specify): ____________________________

+ Ancillary Studies

Note: For reporting molecular testing and other cancer biomarker testing results, the CAP Head and Neck Biomarker Template should be used. Pending biomarker studies should be listed in the Comments section of this report.

+ Comment(s)

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.

Explanatory Notes

Scope of Guidelines

The reporting of major salivary gland cancer is facilitated by the provision of a case summary illustrating the features required for comprehensive patient care. However, there are many cases in which the individual practicalities of applying such a case summary may not be straightforward. Common examples include finding the prescribed number of lymph nodes, trying to determine the levels of the radical neck dissection, and determining if isolated tumor cells in a lymph node represent metastatic disease. Case summaries have evolved to include clinical, radiographic, morphologic, immunohistochemical, and molecular results in an effort to guide clinical management. Adjuvant and neoadjuvant therapy can significantly alter histologic findings, making accurate classification an increasingly complex and demanding task. This protocol tries to remain simple while still incorporating important pathologic features as proposed by the American Joint Committee on Cancer (AJCC) cancer staging manual,[1] the World Health Organization (WHO) classification of tumors, the TNM classification, the American College of Surgeons Commission on Cancer, and the International Union on Cancer (UICC). This protocol is to be used as a guide and resource, an adjunct to diagnosing and managing cancers of the oral cavity in a standardized manner. It should not be used as a substitute for dissection or grossing techniques and does not give histologic parameters to reach the diagnosis. Subjectivity is always a factor, and elements listed are not meant to be arbitrary but are meant to provide uniformity of reporting across all the disciplines that use the information. It is a foundation of practical information that will help to meet the requirements of daily practice to benefit both clinicians and patients alike.

A. Primary Site (Figure 1)

The classification applies only to carcinomas of the major salivary glands: parotid, submandibular (submaxillary), and sublingual glands.[2] Tumors arising in minor salivary glands (mucous-secreting glands in the lining membrane of the upper aerodigestive tract) are staged according to the classification schemes corresponding to the anatomic sites in which they reside, eg, oral cavity, pharynx, sinonasal tract.

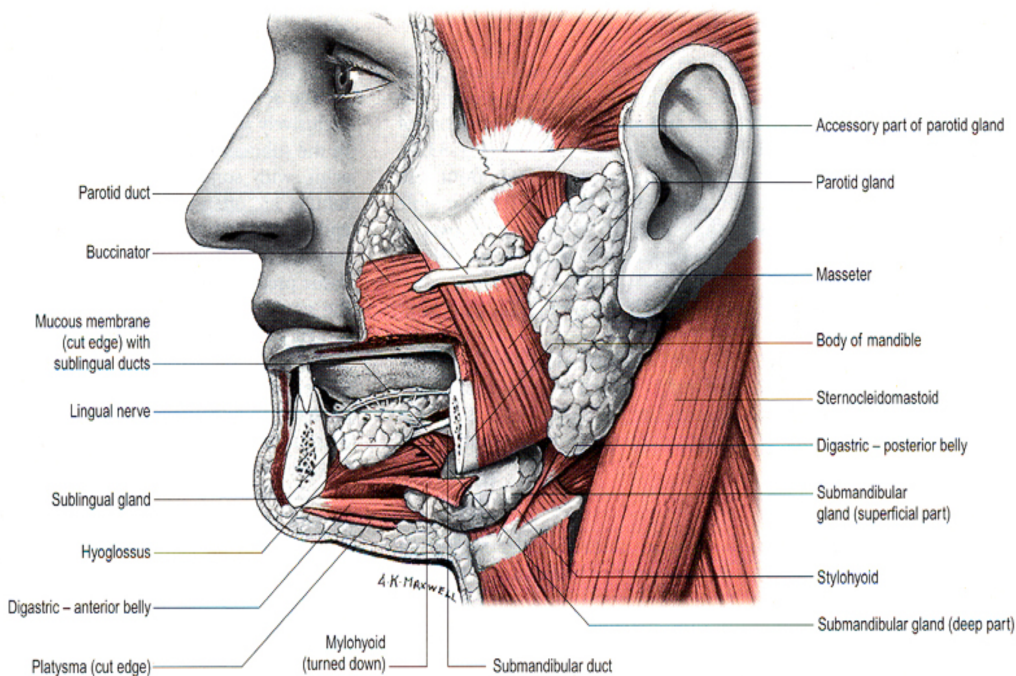

Figure 1. Anatomy of the major salivary glands. From: *Gray's Anatomy*. 39th ed. Edinburgh: Elsevier Churchill Livingstone; 2005. Reproduced with permission © Elsevier.

B. Histologic Type and Grade

The histologic classification recommended is the WHO classification of salivary gland tumors.[3]

Mucoepidermoid carcinoma
Adenoid cystic carcinoma
Acinic cell carcinoma
Polymorphous adenocarcinoma
(Mammary analogue) secretory carcinoma
Salivary duct carcinoma
Carcinoma ex pleomorphic adenoma
Epithelial-myoepithelial carcinoma
(Hyalinizing) clear cell carcinoma
Adenocarcinoma, not otherwise specified[#]
Basal cell adenocarcinoma
Carcinosarcoma
Intraductal carcinoma
Lymphoepithelial carcinoma
Myoepithelial carcinoma
Oncocytic carcinoma
Poorly differentiated carcinoma
    Large cell neuroendocrine carcinoma
    Small cell neuroendocrine carcinoma
    Undifferentiated carcinoma
Sebaceous adenocarcinoma
Squamous cell carcinoma

[#] *Includes cystadenocarcinoma, intestinal type adenocarcinoma, and mucinous adenocarcinoma*

In this current classification, sialoblastoma is designated as a tumor of uncertain malignant potential. Metastasizing pleomorphic adenoma has been collapsed under pleomorphic adenoma.[3] Since the biologic behavior of these still overlaps with the other malignant tumors, these can be reported under "other."

Histologic Grade

The histologic (microscopic) grading of salivary gland carcinomas has been shown to be an independent predictor of behavior and plays a role in optimizing therapy. Further, there is often a positive correlation between histologic grade and clinical stage.[4-7] However, most salivary gland carcinoma types have an intrinsic biologic behavior, and attempted application of a universal grading scheme is merely a crude surrogate.[6] Thus, a generic grading scheme is no longer recommended for salivary gland carcinomas.[2] Carcinoma types for which grading systems exist and are relevant are incorporated into histologic type. The 3 major categories that are amenable to grading include adenoid cystic carcinoma, mucoepidermoid carcinoma, and adenocarcinoma, not otherwise specified.[5,6,8]

In some carcinomas, histologic grading may be based on growth pattern, such as in adenoid cystic carcinoma, for which a histologic high-grade variant has been recognized based on the percentage of solid growth.[8] Those adenoid cystic carcinomas showing 30% or greater of solid growth pattern are considered to be histologically high-grade carcinomas. The histologic grading of mucoepidermoid carcinoma includes a combination of growth pattern characteristics (eg, cystic, solid, neurotropism) and cytomorphologic findings (eg, anaplasia, mitoses, necrosis).[9-11] Adenocarcinomas, not otherwise specified, do not have a formalized grading scheme and are graded intuitively based on cytomorphologic features.[6] Polymorphous adenocarcinomas are to be graded as per current WHO recommendations, though these are also graded intuitively as there are no listed criteria.

Carcinoma ex pleomorphic adenoma is subclassifed by histologic type and or grade and extent of invasion, the latter including minimally invasive, widely invasive, and intracapsular (noninvasive) cancers. Previously the cut-off for minimal invasion was designated as 1.5 mm; however, more recent studies have shown a favorable prognosis even with cut-offs of 4 mm to 6 mm.[12] Thus, there is no agreement on an optimal cut-off. However, from a practical standpoint, the terms *intracapsular* and *minimally invasive* should only be applied to uninodular tumors (as opposed to carcinomas arising in multinodular recurrent pleomorphic adenomas) with a well-delineated interface for which the entire lesional border has been microscopically evaluated. Prognosis has been linked to degree of invasion with noninvasive and minimally invasive cancers apparently having a better prognosis than invasive cancers.[6,12,13]

C. Surgical Margins
Complete surgical excision to include cancer-free surgical margins is the primary mode of therapy for salivary gland cancers, as retrospective studies have shown an increased risk for recurrence and decreased survival with positive surgical margins.[14-16] The need for additional surgery is determined on the basis of histopathologic review; positive surgical margins are an indication for additional resection to ensure total tumor removal.

Orientation of Specimen
Complex specimens should be examined and oriented with the assistance of attending surgeons. 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 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.

D. Perineural Invasion
The presence of perineural invasion (neurotropism) is an important predictor of poor prognosis in head and neck cancer of virtually all sites.[17] The majority of studies evaluating the influence of perineural invasion on therapy and prognosis are limited to head and neck squamous cell carcinoma. However, relative to salivary gland carcinomas, facial nerve dysfunction and perineural involvement are factors influencing the indication for neck dissection, postoperative radiation therapy, and survival rate. Perineural invasion (neurotropism) in the primary salivary gland carcinomas, especially the facial nerve, is associated with recurrent tumor[18] and decreased survival. Further, facial nerve involvement by carcinoma has been found to be predictive of occult metastases.[19] Among other prognostic indicators, perineural invasion in minor salivary gland tumors has been shown to be statistically significant to the outcome.[20] Given the significance relative to prognosis and treatment, perineural invasion is a required data element in the reporting of salivary gland carcinomas.

E. Lymph Nodes

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.[17,21]

Special Procedures for Lymph Nodes
At the current time, no additional special techniques should be used 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.

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. Examination of fewer tumor-free nodes still mandates a pN0 designation.

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. While the generic recommendation is that for lymph nodes with ITCs found by either histologic examination, immunohistochemistry, or nonmorphologic techniques (eg, flow cytometry, DNA analysis, PCR amplification of a specific tumor marker), they should be classified as N0 or M0, respectively.[22,23] Evidence for the validity of this practice in head and neck squamous cell carcinoma and other histologic subtypes is lacking. 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.[24]

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

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 3), 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[21,25,26]:
    a. Supraomohyoid neck dissection
    b. Posterolateral neck dissection
    c. Lateral neck dissection
    d. 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.[27]
5. Extended radical neck dissection, as specified by the surgeon

Figure 2. The six sublevels of the neck for describing the location of lymph nodes within levels I, II, and V. 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. From: Flint PW, et al, eds. *Cummings Otolaryngology: Head and Neck Surgery.* 5th ed. Philadelphia, PA; Saunders: 2010. Reproduced with permission © Elsevier.

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 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 sternohyoid 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, eg, scalene, suboccipital, and retropharyngeal, should be identified and reported from all levels separately. Midline nodes are considered ipsilateral nodes.

Extranodal Extension
The status of cervical lymph nodes is the single most important prognostic factor in aerodigestive cancer. For uniformity and based on existing evidence (albeit a much smaller scale),[28] these principles are applied to salivary gland carcinomas as well. All macroscopically negative or equivocal lymph nodes should be submitted in toto. Grossly positive nodes may be partially submitted for microscopic documentation of metastasis. Reporting of lymph nodes containing metastasis should include whether there is presence or absence of extranodal extension (ENE),[29] which is now part of N staging. This finding consists of extension of metastatic tumor, present within the confines of the lymph node, through the lymph node capsule into the surrounding connective tissue, with or without associated stromal reaction. A distance of extension from the native lymph node capsule is now suggested (but not yet required) with the proposed stratification of ENE into ENE_{ma} (>2 mm) and ENE_{mi} (≤2 mm).[30-33] However, pitfalls in the measurement (ie, in larger, matted lymph nodes, in nodes post fine-needle aspiration, and in nodes with near total replacement of lymph node architecture) and the disposition of soft tissue deposits is still not resolved. In general, absence of ENE in a large (>3 cm) lymph node, especially with traversing fibrous bands,

should be viewed with skepticism. Soft tissue deposits for lymph node metastases based on limited studies appear to be the equivalent of a positive lymph node with ENE and should be recorded as such.[34]

F. TNM and Stage Groupings

The protocol recommends the TNM staging system of the American Joint Committee on Cancer and the International Union Against Cancer for salivary gland cancer.[2]

There are no significant changes to T stage in the AJCC 8th edition for major salivary gland. Carcinomas for which the Tis designation may be applied include some intracapsular carcinomas ex pleomorphic adenoma, and intraductal carcinomas. However, as with squamous cell carcinoma of the head and neck sites (excluding nasopharynx and human papillomavirus (HPV)-related carcinomas), N stage now incorporates extranodal extension.[2]

Extraparenchymal Extension

Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues or nerve (T1, T2, T3), except those listed under T4a and 4b. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.[2]

By AJCC/UICC convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and based on clinical stage information supplemented/modified by operative findings and gross and microscopic evaluation of the resected specimens[1]. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

Stage Groupings for Carcinomas

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1,T2,T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1,T2,T3,T4a	N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

TNM Descriptors

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.

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 (ie, 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 (ie, 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.

Additional Descriptors

Residual Tumor (R)
Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

RX Presence of residual tumor cannot be assessed
R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

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