Protocol for the Examination of Specimens from Patients with Carcinomas of the Major and Minor Salivary Glands

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.

Procedure	Description
Resection	Includes specimens designated or containing parotid, submandibular, sublingual glands, or minor salivary / seromucinous glands of the upper aerodigestive tract up to the level of trachea and cervical esophagus
Tumor Type	**Description**
Carcinoma	Includes primary salivary gland 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 Bone or Soft Tissue protocols)
Bronchial or Lung (consider the Lung protocol)
External ear, including external auditory canal (consider the Cutaneous Carcinoma 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)
Neuroendocrine neoplasms (consider the corresponding mucosal or cutaneous (i.e., Merkel Cell) protocols)

Version Contributors

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Glossary:

Author: Expert who is designated by the chair of the Cancer Committee.
Expert Panel Contributor: 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 Major Salivary Gland protocol, resulting from the separation of select Head and Neck protocols
- AJCC Version 9 update to pTNM Classification

Reporting Template

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

SPECIMEN (Note A)

Procedure (select all that apply)
Major Salivary Glands
___ Parotidectomy, superficial
___ Parotidectomy, deep
___ Parotidectomy, total
___ Parotidectomy, NOS
___ Submandibular gland, resection
___ Sublingual gland, resection
Minor Salivary Glands
___ Glossectomy: _____
___ Buccal mucosal resection: _____
___ Mandibulectomy: _____
___ Maxillectomy: _____
___ Palatectomy
___ Tonsillectomy
___ Supraglottic laryngectomy
___ Supracricoid laryngectomy
___ Vertical hemilaryngectomy (specify side): _____
___ Partial laryngectomy (specify type): _____
___ Total laryngectomy
___ Laryngopharyngectomy
Other
___ Excision (specify type): _____
___ Neck (lymph node) dissection (specify laterality): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Not specified

TUMOR

Multiple Primary Sites (e.g., lower gingiva and floor of mouth) (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): _____

Tumor Site (Note A)

Major Salivary Gland

___ Parotid gland, superficial lobe: _____
___ Parotid gland, deep lobe: _____
___ Parotid gland, entire: _____
___ Parotid gland, NOS
___ Submandibular gland: _____
___ Sublingual gland: _____

Minor Salivary Gland

___ Oral cavity

+Tumor Subsite(s) (select all that apply)

___ Wet mucosa of upper lip
___ Wet mucosa of lower lip
___ Wet mucosa of lip, NOS
___ Lateral border of tongue
___ Ventral surface of tongue
___ Dorsal surface of tongue
___ Anterior two-thirds of tongue
___ Tongue, NOS
___ Upper gingiva
___ Lower gingiva
___ Gingiva, NOS
___ Anterior floor of mouth
___ Lateral floor of mouth
___ Hard palate
___ Buccal mucosa
___ Vestibule of mouth, maxillary
___ Vestibule of mouth, mandibular
___ Retromolar area
___ Other (specify): _____

___ Mandible (intraosseous)
___ Oropharynx

+Tumor Subsite(s) (select all that apply)

___ Palatine tonsil
___ Tonsillar pillar
___ Tonsillar fossa
___ Lingual tonsil
___ Tonsil, NOS
___ Base of tongue
___ Soft palate
___ Uvula
___ Lateral wall of oropharynx
___ Posterior wall of oropharynx
___ Vallecula
___ Epiglottis, anterior surface (lingual aspect)
___ Other (specify): _____

___ Hypopharynx
+Tumor Subsite(s) (select all that apply)
___ Pyriform sinus
___ Aryepiglottic fold, hypopharyngeal aspect
___ Postcricoid
___ Posterior wall of hypopharynx
___ Other (specify): _____
___ Supraglottic larynx
+Tumor Subsite(s) (select all that apply)
___ Epiglottis, posterior surface (laryngeal aspect)
___ Aryepiglottic folds, laryngeal aspect
___ False vocal cord
___ Ventricle
___ Other (specify): _____
___ Glottic larynx
+Tumor Subsite(s) (select all that apply)
___ True vocal cord
___ Anterior commissure
___ Posterior commissure
___ Other (specify): _____
___ Subglottic larynx
___ Trachea
___ Cervical esophagus
___ Nasopharynx
+Tumor Subsite(s) (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): _____
___ Nasal and paranasal sinuses
+Tumor Subsite(s) (select all that apply)
___ Nasal septum
___ Nasal floor
___ Nasal lateral wall
___ Nasal vestibule
___ Nasal cavity, NOS
___ Middle ear
___ Paranasal sinus(es), maxillary
___ Paranasal sinus(es), ethmoid
___ Paranasal sinus(es), frontal
___ Paranasal sinus(es), sphenoid
___ Other (specify): _____
___ Other (specify): _____
___ Not specified

Tumor Laterality
___ Right
___ Left
___ Midline
___ Not specified

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

Histologic Type (Note B)
___ Carcinoma ex pleomorphic adenoma
Architectural Type
Required in addition to carcinoma type
___ Minimally invasive
___ Invasive
___ Intracapsular (non-invasive)
___ Extent cannot be determined
Malignant Component Histologic Type(s) (select all that apply)
___ Salivary duct carcinoma
___ Myoepithelial carcinoma
___ Epithelial-myoepithelial carcinoma
___ Carcinosarcoma [sarcomatoid carcinoma]
___ Intraductal carcinoma
___ Other (specify): _____
___ Mucoepidermoid carcinoma
 # If multiple patterns are present, select the predominant pattern unless the solid pattern is greater than 30%, in which case the user should select the solid pattern.
___ Adenoid cystic carcinoma [tubular / cribriform]#
+Percentage of Solid Component for Adenoid Cystic Carcinoma
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined: _____
If multiple patterns are present, select the predominant pattern unless the solid pattern is greater than 30%, in which case the user should select the solid pattern.
___ Adenoid cystic carcinoma, solid##
+Percentage of Solid Component for Adenoid Cystic Carcinoma
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined: _____
___ Acinic cell carcinoma
___ Secretory carcinoma
___ Polymorphous adenocarcinoma, conventional
___ Polymorphous adenocarcinoma, cribriform subtype
+Percentage of Papillary Component for Polymorphous Adenocarcinoma
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined: _____

+Percentage of Cribriform Component for Polymorphous Adenocarcinoma
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined: _____
___ Salivary duct carcinoma
___ Epithelial-myoepithelial carcinoma
___ Hyalinizing clear cell carcinoma
___ Microsecretory adenocarcinoma
___ Intraductal carcinoma (specify subtype): _____
___ Basal cell adenocarcinoma
___ Carcinosarcoma
___ Mucinous adenocarcinoma, NOS
___ Mucinous adenocarcinoma, intraductal papillary mucinous neoplasia subtype
___ Mucinous adenocarcinoma, colloid / signet ring subtype
___ Sclerosing microcystic adenocarcinoma
___ Lymphoepithelial carcinoma
___ Myoepithelial carcinoma
___ Sebaceous adenocarcinoma
___ Sialoblastoma
Other
___ Other histologic type not listed (specify): _____
___ Carcinoma, type cannot be determined: _____

+Histologic Type Comment: _____

Grade / Intrinsic Biologic Potential (required only if applicable) (Note B)
___ Not applicable
___ Low
___ Intermediate
___ High / High-grade transformation
___ Cannot be assessed (explain): _____

Macroscopic Tumor Extent (select all that apply)
___ No gross extraparenchymal extension (for major salivary glands)
pT3
___ Extraparenchymal soft tissue
pT4a
___ Facial nerve
___ Skin
___ Ear canal
pT4b
___ Skull base
___ Pterygoid plates
___ Carotid artery encasement
Other
___ Other (specify): _____
___ Cannot be determined (explain): _____

Lymphatic and / or Vascular Invasion (Note C)
___ Not identified
___ Present: _____
___ Cannot be determined (explain): _____

Perineural Invasion (Note C)
___ Not identified
___ Present
+Extent / Type of Perineural Invasion#
 # Select the most aggressive type
___ Intratumoral
___ Extratumoral
___ Intraneural
+Specify Diameter of Involved Nerve in Millimeters (mm): _____ mm
___ Cannot be determined (explain): _____

+Tumor Comment: _____

MARGINS (Note D)

Specimen Margin Status
___ 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: _____
+Closest Specimen Margin(s) to Invasive Tumor
___ Specify location(s) of closest specimen margin(s): _____
___ Cannot be determined: _____
___ Invasive tumor present at specimen margin(s)
Specimen Margin(s) Involved by Invasive Tumor
___ Specify involved specimen margin(s): _____
___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Tumor Bed Margin Status (separately submitted)
___ Tumor bed margins assessed

Tumor Bed Margin Orientation
___ Oriented to true margin surface
___ Unoriented to true margin surface
___ Cannot be determined (explain): _____

Tumor Bed Margin Status for Invasive Tumor
___ All tumor bed margins negative for invasive tumor
+Distance from Invasive Tumor to True Margin Surface (pertinent to oriented specimens which are sectioned perpendicularly)
Specify in Millimeters (mm)
___ Exact distance: _____ mm
___ Greater than: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____
___ Invasive tumor present at tumor bed margin(s)
Tumor Bed Margin(s) Involved by Invasive Tumor (per part labeling)
___ Specify involved tumor bed margin(s): _____
___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Cannot be determined: _____
___ Not applicable

+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 (specify): _____ cm
___ At least: _____ cm
___ Greater than: _____ cm
___ Less than: _____ cm
___ Other (specify): _____
___ Cannot be determined: _____

Extranodal Extension (ENE) (Note E)
___ 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

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
___ pTis: Carcinoma in situ
 # Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues or nerve, except those listed under T4a and T4b. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.
___ pT1: Tumor is less than or equal to 2 cm in greatest dimension without extraparenchymal extension#
___ pT2: Tumor is greater than 2 cm but less than or equal to 4 cm in greatest dimension without extraparenchymal extension#
___ pT3: Tumor is greater than 4 cm and / or gross extraparenchymal extension (for major salivary glands)#
pT4: Tumor invades immediately and / or beyond adjacent structures
The following scenarios are not considered T category defining "bone invasion": 1) Destruction of intrinsic sinus bone in sinonasal primaries; 2) Erosion of cortical bone; 3) Primary intraosseous (central) salivary gland tumors.
___ pT4a: Tumor invades any immediately adjacent structures, including: skin, bone, cartilage, solid organ parenchyma, esophagus, trachea, named nerve##
___ pT4b: Tumor invades beyond any adjacent structures, including: encasement of carotid artery, base of skull invasion (except nasopharynx), spinal column invasion, intracranial invasion, orbital apex, prevertebral space, mediastinal structures, masticator space
___ pT4 (subcategory cannot be determined)

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 1-3 lymph node(s) without definitive pathological extranodal extension
___ pN2: Tumor involvement of greater than 3 lymph nodes OR Tumor involvement of any lymph node(s) with definitive pathological extranodal extension

pM Category (required only if confirmed pathologically)
___ Not applicable - pM cannot be determined from the submitted specimen(s)
___ pM1: Microscopic confirmation of distant metastasis

SPECIAL STUDIES
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.

COMMENTS
Comment(s): _____

Explanatory Notes

A. Anatomical Sites

The classification applies to both carcinomas of the major salivary glands: parotid, submandibular (submaxillary), and sublingual glands (Figure 1) and minor salivary glands (mucous-secreting glands in the lining membrane of the upper aerodigestive tract).[1]

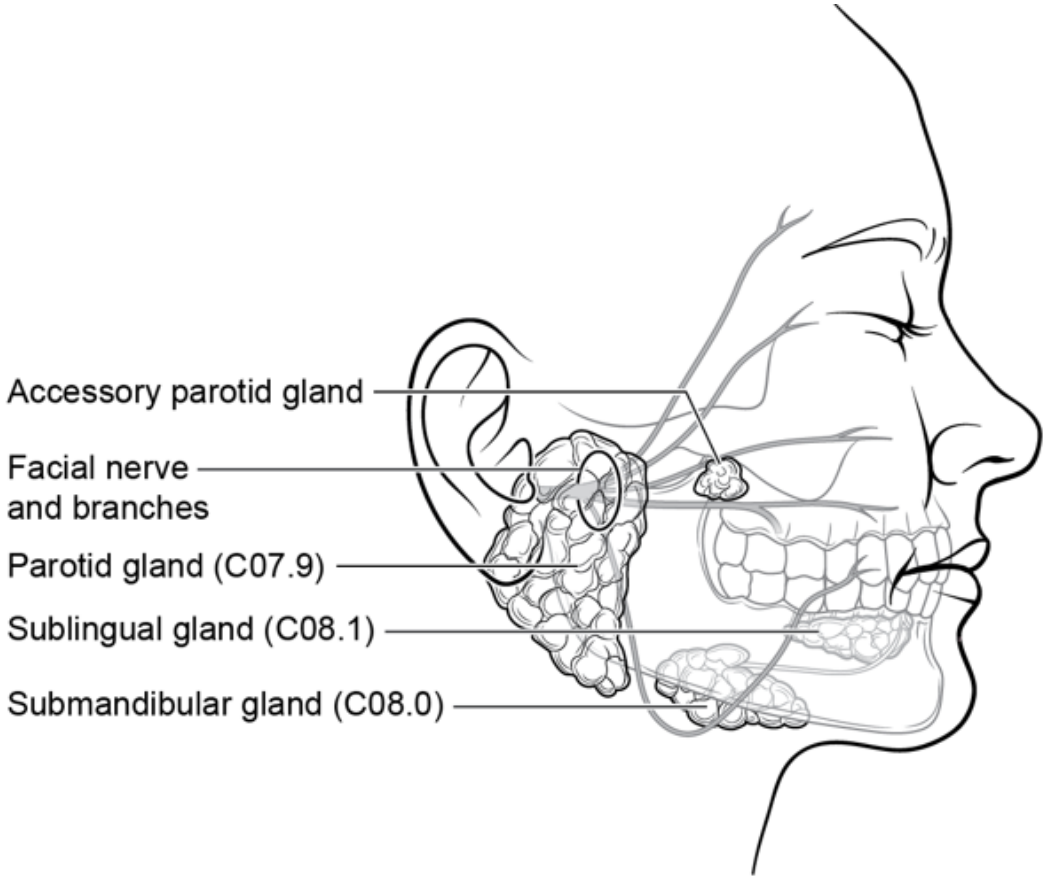

Figure 1. Anatomy of the major salivary glands. Ganly I, Huang SH, Glastonbury C, et al. American Joint Committee on Cancer (AJCC). 2025. *AJCC Protocol for Cancer Staging: Salivary Glands (Version 9).* Reproduced with permission © American College of Surgeons.

References

1. Ganly I, Huang SH, Glastonbury C, et al. American Joint Committee on Cancer (AJCC). 2025. *AJCC Protocol for Cancer Staging: Salivary Glands (Version 9)*.

B. Histologic Type and Grade

The histologic classification recommended is the WHO classification of salivary gland tumors.[1]

- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma

- Acinic cell carcinoma
- Secretory carcinoma
- Polymorphous adenocarcinoma, conventional (classic) and cribriform subtypes
- Salivary duct carcinoma
- Epithelial-myoepithelial carcinoma
- Hyalinizing clear cell carcinoma
- Microsecretory adenocarcinoma
- Intraductal carcinoma (with subtypes)
- Basal cell adenocarcinoma
- Carcinosarcoma
- Mucinous adenocarcinoma (with subtypes)
- Sclerosing microcystic adenocarcinoma
- Lymphoepithelial carcinoma
- Myoepithelial carcinoma (malignant myoepithelioma)
- Sebaceous adenocarcinoma
- Squamous cell carcinoma
- Sialoblastoma
- Carcinoma, not otherwise specified

Carcinoma ex pleomorphic adenoma, while part of the WHO classification, is regarded under AJCC Version 9 as a subclass with the classification based on the carcinoma type. This protocol thus captures Carcinoma ex pleomorphic adenoma separately.

The recommended histologic classification for neuroendocrine neoplasms has been standardized across all head and neck sites.[1] The entities relevant to this protocol are listed below:

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

Histologic Grade

The histologic (microscopic) grading of salivary gland carcinomas has been shown to correlate with stage, serve as an independent prognosticator, and serves to optimize therapy.[2,3,4] While a universal grading scheme is suboptimal given tumor specific nuances,[4] most carcinoma types can be stratified into low aggression and high aggression types based on a combination of histologic grade and intrinsic biologic behavior.[5] Carcinomas typically graded with a three-tiered schema (i.e., mucoepidermoid carcinoma, and carcinoma, not otherwise specified) can also be dichotomized by aggression. Included in high aggression is high-grade transformation (historically designated as dedifferentiation), the phenomenon of progression from a conventional, usually indolent phenotype to a pleomorphic aggressive morphology.

Carcinomas can be stratified by their risk for structural recurrence by a combination of category, subtype, and category specific grade[6] as in Table 1.

Table 1: Risk Stratification of Salivary Gland Carcinomas

Low Aggression	***High Aggression***
Mucoepidermoid carcinoma – Low grade	Mucoepidermoid carcinoma – High grade
Mucoepidermoid carcinoma – Intermediate grade*	
Acinic cell carcinoma – Conventional	Acinic cell carcinoma – High grade/HGT
Secretory carcinoma - Conventional	Secretory carcinoma – High grade/HGT
Microsecretory adenocarcinoma – Usual	Microsecretory adenocarcinoma – High grade/HGT
Polymorphous adenocarcinoma – Low grade, conventional	Polymorphous adenocarcinoma – High grade/HGT
Polymorphous adenocarcinoma – Low & intermediate grade, cribriform**	
Hyalinizing clear cell carcinoma – Conventional	Hyalinizing clear cell carcinoma – High grade/HGT
Basal cell adenocarcinoma – Conventional	Basal cell adenocarcinoma – High grade/HGT
Myoepithelial carcinoma – Low grade	Myoepithelial carcinoma – High grade
Epithelial-myoepithelial carcinoma – Conventional and subtypes	Epithelial-myoepithelial carcinoma – High grade/HGT
Sebaceous adenocarcinoma – Low grade	Sebaceous adenocarcinoma – High grade
	Adenoid cystic carcinoma – Solid/HGT
Adenoid cystic carcinoma – Tubular/cribriform^	
	Carcinosarcoma (sarcomatoid carcinoma)
Intraductal carcinoma, oncocytic and intercalated duct	
Intraductal carcinoma, apocrine	Salivary duct carcinoma
Mucinous adenocarcinoma “intraductal papillary mucinous neoplasm” type	Mucinous adenocarcinoma (not otherwise specified, and with colloid/signet ring features)
	Lymphoepithelial carcinoma
Sclerosing microcystic adenocarcinoma	
Sialoblastoma	
Carcinoma ex pleomorphic adenoma#	
Salivary carcinoma, NOS@	

Abbreviations: HGT-high-grade transformation. NOS-not otherwise specified
*Behavior varies with grading system or criteria
**The cribriform subtype of polymorphous adenocarcinoma has a high propensity for regional recurrence
^Adenoid cystic carcinoma though highly aggressive locally with capacity for distant spread, has somewhat lower risk for regional recurrence
#Carcinoma ex pleomorphic adenoma behavior is determined by carcinoma type and extent
@Salivary carcinoma, NOS behavior is determined by grade

A few outliers exist, however. For instance, the biological behavior of intermediate grade mucoepidermoid carcinoma may vary depending on grading system applied.[7,8,9] Adenoid cystic carcinoma can be parsed into low aggression and high aggression by proportion solid component (classically >30%, though reporting specific percentage is an optional data element) and/or high-grade transformation. While nodal metastasis is rare in tubular/cribriform (low aggression) adenoid cystic carcinoma and 5 year survival is favorable, all histologic patterns show high levels of local aggression and infiltration.[10] Conversely, the cribriform subtype of polymorphous adenocarcinoma has a favorable outcome and can be considered low aggression but has a high risk of regional (lymph node) spread. Papillary (>10%) and cribriform (>30%) seem to be adverse prognosticators in polymorphous adenocarcinoma independent of subtype and are optional to quantitate.[11]

Carcinoma ex pleomorphic adenoma is subclassified by histologic type and/or grade and extent of invasion, the latter including minimally invasive, invasive, and intracapsular (non-invasive) cancers. An optimal cut-off to define minimal invasion is not yet defined but 4 mm to 6 mm cutoffs are commonly utilized. 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 non-invasive and minimally invasive cancers apparently having a better prognosis than invasive cancers.[4,12,13] Carcinosarcoma is a rare subtype morphology that while currently separated, appears to almost invariably arise in the setting of a precursor pleomorphic adenoma, and should likely be regarded as a sarcomatoid carcinoma subtype ex pleomorphic adenoma.[14]

The WHO 5th edition has standardized the terminology for head and neck neuroendocrine neoplasms across all subsites.[15] Tumors previously designated as carcinoid and well-differentiated neuroendocrine carcinoma would now be considered grade 1 neuroendocrine tumors while atypical carcinoids/moderately-differentiated neuroendocrine carcinomas are now considered grade 2 neuroendocrine tumors. Grade 3 neuroendocrine tumor is a provisional category with no historical analogue. *It must be emphasized that this category in head and neck sites is provisional with no current evidence to support its use in head and neck sites.* Practically speaking, tumors that exceed the mitotic rate for grade 2 neuroendocrine tumors are usually more in keeping with neuroendocrine carcinomas (see below). Grading of neuroendocrine tumors is summarized in Table 2. Ki-67 proliferation indices are recommended for neuroendocrine tumors of head and neck, but are not required elements, and delineation of grade 1 and 2 at this site by proliferation index is not yet established.

Table 2: WHO Classification of Head and Neck Neuroendocrine Tumors

Neuroendocrine Tumor Grade	Mitoses per two mm^2	Necrosis
1	Less than 2	Absent
2	2-10	Present
3	*Undefined*	

Neuroendocrine carcinoma, small cell types and large cell types on the other hand, have not changed much in terms of their designation and reflect poorly differentiated neuroendocrine malignancies that were previously labeled small cell and large cell neuroendocrine carcinomas respectively. These characteristically show necrosis and have mitotic counts that exceed 10 per two mm^2. While neuroendocrine tumors and carcinomas are defined by neuroendocrine marker expression (synaptophysin, chromogranin, and/or INSM-1), other tumor types at each head and neck subsite may express these. Morphologic, other immunophenotypic, and molecular features would then supersede this neuroendocrine marker expression for classification.

Merkel cell carcinoma is a cutaneous neuroendocrine carcinoma, often driven by Merkel cell polyomavirus. Primary parotid Merkel cell carcinomas are described[16] and their definition is further obfuscated by the earlier description of a so called ‘Merkel cell’ subtype of primary parotid small cell neuroendocrine carcinoma that like Merkel cell carcinoma, expresses CK20 but are Merkel cell polyomavirus negative and do not show a UV molecular signature.[17] However, like squamous cell carcinoma of parotid, the idea of a primary parotid Merkel cell carcinoma should be viewed with heavy skepticism, and most are metastases from unknown primaries. This can often be resolved by a combination of detailed clinical history, and dermatologic examination.

References

1. 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 28]. (WHO classification of tumours series, 5th ed.; vol. 9). Available from: https://tumourclassification.iarc.who.int/chapters/52
2. Spiro RH, Thaler HT, Hicks WF, Kher UA, Huvos AH, Strong EW. The importance of clinical staging of minor salivary gland carcinoma. *Am J Surg*. 1991;162(4):330-336.
3. Kane WJ, McCaffrey TV, Olsen KD, Lewis JE. Primary parotid malignancies. A clinical and pathologic review. *Arch Otolaryngol Head Neck Surg.* 1991 Mar;117(3):307-15. doi: 10.1001/archotol.1991.01870150075010. PMID: 1998571.
4. Seethala RR. Histologic grading and prognostic biomarkers in salivary gland carcinomas. *Adv Anat Pathol*. 2011;18(1):29-45.
5. Ganly I, Huang SH, Glastonbury C, et al. American Joint Committee on Cancer (AJCC). 2025. *AJCC Protocol for Cancer Staging: Salivary Glands (Version 9)*.
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C. Lymphatic and/or Vascular Invasion and Perineural Invasion

Perineural invasion (neurotropism) in the primary salivary gland carcinomas is an adverse prognosticator and a required data element. Perineural invasion, especially of the facial nerve, is associated with recurrent tumor, occult metastases and decreased survival.[1,2] A systematic review and meta-analysis showed adverse outcomes in parotid tumors with perineural invasion by several oncologic endpoints.[3] The prognostic value of perineural invasion in minor salivary gland tumors is also supported.[4] Other parameters such as size of involved nerve may be relevant in certain histologic types such as adenoid cystic carcinoma and are retained as optional reporting elements.[5] Lymphatic and/or vascular invasion are also adverse prognosticators.[6,7]

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D. Margins and Orientation

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.[1,2,3] 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.

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.

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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 neck nodes positive for N categorization and counting purposes.

However, intraparotid lymph nodes involved in this manner should NOT be considered positive given that microanatomic boundaries (i.e., fascia, nodal capsules) are incomplete, and there is a higher likelihood of coincidental involvement in this manner.

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. Size is no longer part of salivary cancer N classification but is still important for clinical/radiologic correlation and is left as an optional reporting element.[1,2]

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.

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 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.[3,4] 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.[5]

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. AJCC Version 9 now introduces a minimal requirement of 6 lymph nodes to be examined in order to assign a pN0 status.[1] 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 2), defined by dissection of less than the 5 traditional levels of a radical and modified radical neck dissection. The following dissections are currently under this category:[2,3,4]
    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.[5]
5. Extended radical neck dissection, as specified by the surgeon

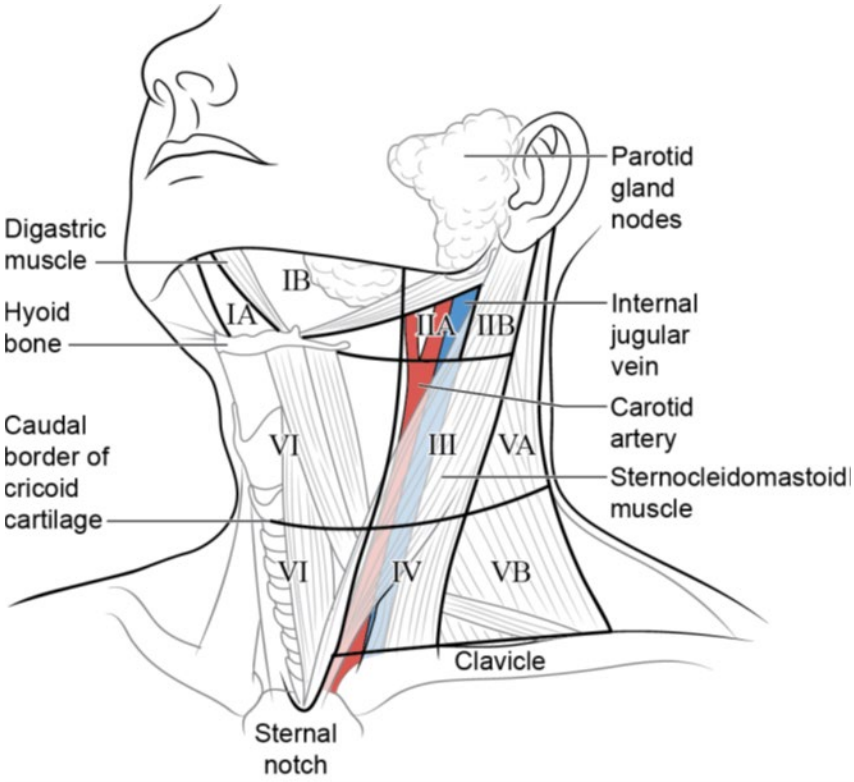

Figure 2. The six sublevels of the neck for describing the location of lymph nodes within levels I, II, and V. Level IA, submental group; level IB, submandibular group; level IIA, upper jugular nodes along the carotid sheath, including the subdigastric group; level IIB, upper jugular nodes in the submuscular recess; level

VA, spinal accessory nodes; and level VB, the supraclavicular and transverse cervical nodes. From: Ganly I, Huang SH, Glastonbury C, et al. American Joint Committee on Cancer (AJCC). 2025. *AJCC Protocol for Cancer Staging: Salivary Glands (Version 9)*. Reproduced with permission © American College of Surgeons.

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

Extranodal Extension[6]
Extranodal extension (ENE) remains a core element for AJCC Version 9 pathological TNM classification of salivary gland carcinoma.[1,7] Analysis of 8,401 surgically treated salivary gland carcinoma patients within the National Cancer Database and validation with a data set of 444 minor salivary gland carcinoma patients from Memorial Sloan Kettering Cancer Center support the inclusion of ENE in N-classification.[1]

Extranodal extension criteria and gross submission guidelines have been recently outlined by international consensus groups, HNCIG, and HN-CLEAR.[8,9] While these guidelines focus on squamous cell carcinoma, the same principles may be applied. Sampling should optimize surface area/perimeter examined, and to optimize this, serial sectioning is recommended for all lymph nodes above 5 mm. Grossly negative lymph nodes should be submitted entirely while grossly positive lymph nodes can be representatively submitted. However, focus on sampling of the nodal periphery is recommended to enrich for extranodal extension.[9]

Only definitive ENE as per HNCIG, HN-CLEAR[8,9] criteria should be recorded as positive. New terminology for microscopic expression includes:[9]

- ‘Matted’ where tumor crosses from one lymph node to another adjacent lymph node. This is considered ENE positive
- ‘Fused, adherent, confluent, and conglomerate’ lymph nodes refer to lymph nodes that are adherent based on inflammation and stromal reaction and show no transgression of tumor across capsules. These are considered ENE negative

Additionally, soft tissue deposits are considered ENE positive, while extranodal lymphatic/vascular invasion and perineural invasion are considered ENE negative but count towards lymphatic/vascular invasion and perineural invasion even if the primary tumor does not show this locally.

Other Elements
Anatomic compartment/extent of nodal disease[10] may also be prognostic in salivary cancers. Anatomic compartment location of positive lymph nodes is now a non-core element.
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F. pTNM Classification

The protocol recommends using the AJCC Version 9 pathological TNM classification of salivary gland carcinoma for reporting.[1]

Pathological T classification now incorporates minor salivary gland carcinomas. T classification of major salivary gland carcinomas is largely unchanged, while minor salivary gland carcinomas are categorized by size criteria alone for pT1-3. In other words, depth of invasion is not used in minor oral salivary gland carcinoma T classification. Tracheal, cervical esophageal, and intraosseous salivary type tumors used the minor salivary T classification as well. Pathological N categorization is considerably different. Size and laterality are no longer part of the Version 9 N classification, and the classification is simplified to numeric cutoffs for positive lymph node count and extranodal extension (1-3 for pN1, and >3 or extranodal extension for pN2).[1]

Tis

The concept of in-situ carcinoma of salivary gland is not well defined, and the categorization should be used sparingly. Intracapsular carcinoma ex pleomorphic adenoma, and intraductal carcinomas are the categories for which Tis can be considered. Even still, this should only be applied to intracapsular carcinoma ex pleomorphic adenoma with a ductal phenotype (i.e., not myoepithelial carcinoma) that is completely encapsulated/well demarcated and uninodular/unicystic for which the entire lesional border (preferably the entire lesion) has been sampled for histologic evaluation.

Extraparenchymal Extension
Extraparenchymal extension is relevant to major salivary glands and is clinical or macroscopic evidence of invasion of soft tissues or nerve (T3), except those listed under T4a and 4b. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.[1]

Intraparotid Lymph Nodes
By convention, a tumor arising from an intranodal parotid tissue should not be considered a metastasis (N0). However, if the tumor has spread via lymphatics into an intraparotid lymph node this would be considered positive with respect to determining N category.[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.[3] 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 (e.g., 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.

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 (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.

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