

Upper Aerodigestive Tract (Including Salivary Glands)

Protocol applies to all invasive carcinomas of the upper aerodigestive tract including the oral cavity (including lip and tongue), pharynx (oropharynx, hypopharynx, nasopharynx), larynx, paranasal sinuses, and salivary glands.

*Protocol revision date: January 2004
Based on AJCC/UICC TNM, 6th edition*

Procedures

- **Cytology** (No Accompanying Checklist)
- **Biopsy**
- **Resection**

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Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2004
Applies to invasive cancers only
Based on AJCC/UICC TNM, 6th edition*

**UPPER AERODIGESTIVE TRACT AND MINOR SALIVARY GLANDS:
Incisional and Excisional Biopsy/Resection**

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC**Specimen Type**

- Incisional biopsy
 Excisional biopsy
 Resection (specify type): _____
 Other (specify): _____
 Not specified

Tumor Site

- Lip
 Oral cavity
 Pharynx, oropharynx
 Pharynx, hypopharynx
 Pharynx, nasopharynx
 Larynx, supraglottis
 Larynx, glottis
 Larynx, subglottis
 Paranasal sinus(es), maxillary
 Paranasal sinus(es), ethmoid
 Other (specify): _____
 Not specified

Tumor Size

Greatest dimension: ___ cm

*Additional dimensions: ___ x ___ cm

Cannot be determined (see Comment)

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MICROSCOPIC**Histologic Type**Carcinomas of the Upper Aerodigestive Tract

Squamous cell carcinoma, conventional

Squamous Cell Carcinoma, Variant

- Verrucous carcinoma
 Spindle cell squamous carcinoma
 Adenosquamous carcinoma
 Basaloid squamous cell carcinoma
 Papillary squamous cell carcinoma

Lymphoepithelioma-like carcinoma (non-nasopharyngeal)

Sinonasal Carcinoma

- Keratinizing sinonasal carcinoma
 Non-keratinizing sinonasal carcinoma (Transitional type)
 Undifferentiated sinonasal carcinoma (SNUC)

Nasopharyngeal Carcinoma

- Keratinizing nasopharyngeal carcinoma
 Non-keratinizing nasopharyngeal carcinoma
 Non-keratinizing nasopharyngeal carcinoma, differentiated
 Non-keratinizing nasopharyngeal carcinoma, undifferentiated (lymphoepithelioma)
 Non-keratinizing nasopharyngeal carcinoma, mixed differentiated and undifferentiated

Adenocarcinoma, salivary gland type (specify type):

Adenocarcinoma, Non-salivary Gland Type

- Papillary adenocarcinoma
 Intestinal-type adenocarcinoma
 Adenocarcinoma, not otherwise specified (NOS)

Neuroendocrine carcinoma

- Typical carcinoid tumor (well differentiated neuroendocrine carcinoma)
 Atypical carcinoid tumor (moderately differentiated neuroendocrine carcinoma)
 Small cell carcinoma (poorly differentiated neuroendocrine carcinoma)

Other (specify): _____

Carcinoma, type cannot be determined

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Carcinomas of Minor Salivary Glands

- Acinic cell carcinoma
- Adenoid cystic carcinoma
- Adenocarcinoma, not otherwise specified (NOS)
- Adenocarcinoma, low grade
- Adenocarcinoma, intermediate grade
- Adenocarcinoma, high grade
- Adenosquamous carcinoma
- Squamous cell carcinoma
- Carcinoma ex pleomorphic adenoma (malignant mixed tumor)
- Carcinosarcoma (true malignant mixed tumor)
- Mucoepidermoid carcinoma, low grade
- Mucoepidermoid carcinoma, intermediate grade
- Mucoepidermoid carcinoma, high grade
- Polymorphous low-grade adenocarcinoma
- Epithelial-myoepithelial carcinoma
- Basal cell adenocarcinoma
- Sebaceous carcinoma
- Cystadenocarcinoma
- Mucinous carcinoma (colloid carcinoma)
- Oncocytic carcinoma
- Salivary duct carcinoma
- Myoepithelial carcinoma (malignant myoepithelioma)
- Small cell carcinoma
- Undifferentiated carcinoma
- Other (specify): _____
- Carcinoma, type cannot be determined

Histologic Grade

- Not applicable
- GX: Cannot be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated
- Other (specify): _____

Pathologic Staging (pTNM) (see appropriate site below)

Note: The phrases in italics include clinical findings required for AJCC staging. This clinical information may be unknown to the pathologist. It is included here only for the sake of completeness.

Primary Tumor (pT): Lip and Oral Cavity

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor 2 cm or less in greatest dimension
- ___ pT2: Tumor more than 2 cm but not more than 4 cm in greatest dimension
- ___ pT3: Tumor more than 4 cm in greatest dimension
- ___ pT4: Lip: Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, ie, chin or nose
- ___ pT4a: Oral cavity: Tumor invades adjacent structures (eg, through cortical bone, into deep [extrinsic] muscle of tongue [genioglossus, hyoglossus, palatoglossus, and styloglossus], maxillary sinus, skin of face)
- ___ pT4b: Tumor invades masticator space, pterygoid plates, or skull base, and/or encases internal carotid artery

Primary Tumor (pT): Oropharynx

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor 2 cm or less in greatest dimension
- ___ pT2: Tumor more than 2 cm but not more than 4 cm in greatest dimension
- ___ pT3: Tumor more than 4 cm in greatest dimension
- ___ pT4a: Tumor invades larynx, deep/extrinsic muscle of tongue, medial pterygoid muscles, hard palate, or mandible
- ___ pT4b: Tumor invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base, or encases carotid artery

Primary Tumor (pT): Hypopharynx

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor limited to 1 subsite of hypopharynx and 2 cm or less in greatest dimension
- ___ pT2: Tumor invades more than 1 subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest dimension *without fixation of hemilarynx*
- ___ pT3: Tumor measures more than 4 cm in greatest dimension *or with fixation of hemilarynx*
- ___ pT4a: Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, esophagus, or central compartment soft tissue

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___ pT4b: Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

Primary Tumor (pT): Nasopharynx

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor confined to nasopharynx
- ___ pT2: Tumor extends to soft tissue
- ___ pT2a: Tumor extends to the oropharynx and/or nasal cavity without parapharyngeal extension
- ___ pT2b: Any tumor with parapharyngeal extension
- ___ pT3: Tumor invades bony structures and/or paranasal sinuses
- ___ pT4: Tumor with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx, orbit, or masticator space

Primary Tumor (pT): Supraglottis

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor limited to 1 subsite of supraglottis *with normal vocal cord mobility*
- ___ pT2: Tumor invades mucosa of more than 1 adjacent subsite of supraglottis or glottis or region outside the supraglottis (eg, mucosa of base of tongue, vallecula, medial wall of pyriform sinus) *without fixation of the larynx*
- ___ pT3: Tumor limited to larynx *with vocal cord fixation* and/or invades any of the following: postcricoid area, pre-epiglottic tissues, paraglottic space, and/or minor thyroid cartilage erosion (eg, inner cortex)
- ___ pT4a: Tumor invades through thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle of tongue, strap muscles, thyroid, or esophagus)
- ___ pT4b: Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Primary Tumor (pT): Glottis

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor limited to the vocal cords (may involve anterior or posterior commissure) *with normal mobility*
- ___ pT1a: Tumor limited to 1 vocal cord
- ___ pT1b: Tumor involves both vocal cords
- ___ pT2: Tumor extends to supraglottis and/or subglottis *and/or with impaired vocal cord mobility*
- ___ pT3: Tumor limited to the larynx *with vocal cord fixation* and/or invades paraglottic space, and/or minor thyroid cartilage erosion (eg, inner cortex)
- ___ pT4a: Tumor invades through thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)
- ___ pT4b: Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

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Primary Tumor (pT): Subglottis

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor limited to subglottis
- ___ pT2: Tumor extends to vocal cord(s) *with normal or impaired mobility*
- ___ pT3: Tumor limited to larynx *with vocal cord fixation*
- ___ pT4a: Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (eg, trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)
- ___ pT4b: Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Primary Tumor (pT): Maxillary Sinus

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor limited to the maxillary sinus mucosa with no erosion or destruction of bone
- ___ pT2: Tumor causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
- ___ pT3: Tumor invades any of the following: bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, ethmoid sinuses
- ___ pT4a: Tumor invades anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinuses
- ___ pT4b: Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V₂), nasopharynx, or clivus

Primary Tumor (pT): Nasal Cavity and Ethmoid Sinus

- ___ pTX: Cannot be assessed
- ___ pT0: No evidence of primary tumor
- ___ pTis: Carcinoma in situ
- ___ pT1: Tumor restricted to any 1 subsite, with or without bony invasion
- ___ pT2: Tumor invading 2 subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bony invasion
- ___ pT3: Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate
- ___ pT4a: Tumor invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses
- ___ pT4b: Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than (V₂), nasopharynx, or clivus

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Regional Lymph Nodes (pN): All Aerodigestive Sites Except Nasopharynx

- pNX: Cannot be assessed
 pN0: No regional lymph node metastasis
 pN1: Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
 pN2a: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
 pN2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
 pN2c: Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
 pN3: Metastasis in a lymph node more than 6 cm in greatest dimension
 Specify: Number examined: ____
 Number involved: ____

Regional Lymph Nodes (pN): Nasopharynx

- pNX: Cannot be assessed
 pN0: No regional lymph node metastasis
 pN1: Unilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa
 pN2: Bilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa
 pN3: Metastasis in a lymph node greater than 6 cm and/or to supraclavicular fossa
 pN3a: Greater than 6 cm in dimension
 pN3b: Extension to the supraclavicular fossa
 Specify: Number examined: ____
 Number involved: ____

*Extra-capsular Extension of Nodal Tumor

- * Absent
 * Present
 * Indeterminate

Distant Metastasis (pM)

- pMX: Cannot be assessed
 pM1: Distant metastasis
 *Specify site(s), if known: _____

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Margins (check all that apply)

- Cannot be assessed
- Margins uninvolved by tumor
 Distance of tumor from closest margin: ____ mm
 Specify margin, if possible: _____
- Carcinoma in situ absent
- Carcinoma in situ present
- Carcinoma in situ, not applicable
- Margin(s) involved by tumor
 Specify location(s), if possible: _____
- Not applicable

***Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)**

- * Absent
- * Present
- * Indeterminate

Perineural Invasion

- Absent
- Present

***Additional Pathologic Findings (check all that apply)**

- * None identified
- * Carcinoma in situ
- * Inflammation (specify type): _____
- * Epithelial hyperplasia
- * Epithelial dysplasia
- * Other (specify): _____

***Comment(s)**

Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2004
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MAJOR SALIVARY GLANDS: Resection

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Tumor Site

- Resection, submandibular gland
- Resection, sublingual gland
- Superficial parotidectomy
- Total parotidectomy
- Other (specify): _____
- Not specified

Laterality

- Right
- Left
- Not specified

Tumor Size

- Greatest dimension: ____ cm
*Additional dimension: ____ x ____ cm
 Cannot be determined (see Comment)

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MICROSCOPIC**Histologic Type**

- Acinic cell carcinoma
- Adenoid cystic carcinoma
- Adenocarcinoma not otherwise specified (NOS)
- Squamous cell carcinoma
- Carcinoma ex pleomorphic adenoma (malignant mixed tumor)
- Carcinosarcoma (true malignant mixed tumor)
- Mucoepidermoid carcinoma, low grade
- Mucoepidermoid carcinoma, intermediate grade
- Mucoepidermoid carcinoma, high grade
- Polymorphous low-grade adenocarcinoma
- Epithelial-myoepithelial carcinoma
- Basal cell adenocarcinoma
- Sebaceous carcinoma
- Cystadenocarcinoma
- Mucinous carcinoma (colloid carcinoma)
- Oncocytic carcinoma
- Salivary duct carcinoma
- Myoepithelial carcinoma (malignant myoepithelioma)
- Small cell carcinoma
- Undifferentiated carcinoma
- Other (specify): _____
- Carcinoma, type cannot be determined

Histologic Grade (if appropriate)

- Not applicable
- GX: Cannot be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated
- Other (specify): _____

Pathologic Staging (pTNM)

Note: The phrases in italics include clinical findings required for AJCC staging. This clinical information may be unknown to the pathologist. It is included here only for the sake of completeness.

Primary Tumor (pT)

- ___ pTX: Cannot be assessed
 ___ pT0: No evidence of primary tumor
 ___ pT1: Tumor 2 cm or less in greatest dimension *without extraparenchymal extension*
 ___ pT2: Tumor more than 2 cm but not more than 4 cm in greatest dimension *without extraparenchymal extension*
 ___ pT3: Tumor more than 4 cm and/or tumor *having extraparenchymal extension*
 ___ pT4a: Tumor invades skin, mandible, ear canal, and/or facial nerve.
 ___ pT4b: Tumor invades skull base and/or pterygoid plates and/or encases carotid artery

Regional Lymph Nodes (pN)

- ___ pNX: Cannot be assessed
 ___ pN0: No regional lymph node metastasis
 ___ pN1: Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
 ___ pN2a: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
 ___ pN2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
 ___ pN2c: Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
 ___ pN3: Metastasis in a lymph node more than 6 cm in greatest dimension
 Specify: Number examined: ___
 Number involved: ___

***Extracapsular Extension of Nodal Tumor**

- * ___ Absent
 * ___ Present
 * ___ Indeterminate

Distant Metastasis (pM)

- ___ pMX: Cannot be assessed
 ___ pM1: Distant metastasis
 *Specify site(s), if known: _____

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Margins

Cannot be assessed

Margins uninvolved by tumor

Distance of tumor from closest margin: ____ mm

Specify margin, if possible: _____

Margin(s) involved by tumor

Specify location(s), if possible: _____

***Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)**

* Absent

* Present

* Indeterminate

Perineural Invasion

Absent

Present

***Additional Pathologic Findings**

*Specify: _____

***Comment(s)**

Background Documentation

Protocol revision date: January 2004

I. Cytologic Material

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)/clinic(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) surgery and date(s)
 - (2) radiation and date(s)
 - (3) chemotherapy and date(s)
 - (4) others (eg, hyperthermia, photodynamic therapy)
 - b. Clinical findings (eg, imaging studies)
 - c. Clinical diagnoses
 - d. Procedure (eg, fine-needle aspiration [FNA])
 - e. Anatomic site(s) of specimen(s) (eg, tongue, tonsil, pharynx, epiglottis, false cord, true cord; specify right, left, midline)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Number of slides received
 - c. Quantity and appearance of fluid specimen, if appropriate
 - d. Other (eg, tissue received for cytologic preparation)
 - e. Results of intraprocedural consultation with clinician (eg, rapid/ immediate interpretation)
2. Material submitted for microscopic evaluation (eg, smear, cytocentrifuge, touch or filter preparation, other liquid-based cytology preparations, cell block)
3. Special studies (specify)

C. Microscopic Evaluation

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
2. Tumor, if present
 - a. Histologic type, if possible (Note **A**)
 - b. Other characteristics (eg, nuclear grade, necrosis)
 - c. Indeterminate as to the presence of tumor
3. Presence and description of effects of previous treatment, if present and evaluable
4. Additional pathologic findings, if present
5. Results/status of special studies (specify)
6. Comments
 - a. Correlation with intra procedural consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

II. Biopsy

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)/clinic(s)
3. Date of procedure
4. Other clinical information that may assist the pathologist interpret the biopsy
 - a. Relevant history
 - (1) surgery and date(s)
 - (2) radiation and date(s)
 - (3) chemotherapy and date(s)
 - (4) others (eg, hyperthermia, photodynamic therapy)
 - b. Clinical findings (eg, imaging studies)
 - c. Clinical diagnosis
 - d. Procedure
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s) (eg, tongue, tonsil, pharynx, epiglottis, false cord, true cord; specify right, left, midline)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Size (3 dimensions)
 - c. Results of intraoperative consultation
2. Tissue(s) submitted for microscopic evaluation (all or selected samples)
3. Special studies (specify)

C. Microscopic Evaluation

1. Tumor, if present
 - a. Histologic type (Note **A**)
 - b. Histologic grade (Note **B**)
 - c. Extent of invasion
 - (1) noninvasive (in situ)
 - (2) subepithelial connective tissue (depth of invasion from the basement membrane in millimeters: lip and tongue cancer only)
 - (3) muscle, when applicable
 - (4) bone or cartilage, when applicable
 - (5) indeterminate (state reasons)
 - d. Lymphovascular invasion, if identified
 - e. Perineural invasion, if identified
2. Tissue changes adjacent to the tumor, if present
 - a. Dysplasia or atypia
 - b. Carcinoma in situ (CIS)
 - c. Others (eg, hyperkeratosis, radiation change, scar)
3. Presence and description of effects of previous treatment, if present and evaluable
4. Results/status of special studies (specify)

5. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

III. Resection

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)/clinic(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous diagnoses
 - (2) previous cervical lymph node biopsy, if applicable
 - (3) surgery and date(s)
 - (4) radiation and date(s)
 - (5) chemotherapy and date(s)
 - (6) others (eg, hyperthermia, photodynamic therapy)
 - b. Relevant physical, radiologic, and laboratory findings
 - c. Clinical diagnosis
 - d. Procedure
 - (1) excision (eg, right hemiglossectomy)
 - (2) all anatomical structures removed (Note **C**)
 - (3) lymph node dissection (Note **D**)
 - e. Operative findings (documentation of areas of concern marked by surgeon)
 - f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Size (3 dimensions)
 - c. Constituent organs/tissues submitted en bloc or separately
 - d. Margins (tumor present/absent, distance from free margin)
 - (1) note areas designated by surgeon
 - (2) ink margin(s) of clinical relevance
 - e. Neck contents accompanying specimen in continuity or separately (specify)
 - f. Results of intraoperative consultation
2. Neoplasm
 - a. Anatomical site(s) involved by tumor
 - b. Size (3 dimensions) (Note **E**)
 - c. Pattern of growth
 - (1) exophytic
 - (2) endophytic
 - (3) others
 - d. Anatomic extent (structures involved by tumor and depth of invasion) (Note **E**)

- e. Relation to margins
- f. Additional tumors (describe each primary tumor, as above)
 - (1) size
 - (2) number
 - (3) location
3. Additional pathologic findings, if present
 - a. Abnormal mucosa (eg, leukoplakia)
 - b. Other lesions (eg, scar)
4. Lymph nodes submitted as part of specimen
 - a. Location by levels (Note **F**)
 - b. Number, each level (Note **G**)
 - c. Description of lymph nodes containing tumor
 - (1) matted
 - (2) gross metastasis
 - (3) size of largest metastasis in a lymph node containing metastatic tumor (Note **H**)
 - (4) extranodal extension
 - (5) gross involvement of adjacent nerve or vessel (eg, internal jugular vein)
5. Separately submitted lymph nodes (according to the regional lymph node groups or levels, as designated by surgeon) (Note **F**)
6. Other separately submitted organ(s)/tissue(s)
 - a. Location, as specified by surgeon
 - b. Description
 - (1) salivary gland
 - (2) thyroid
 - (3) parathyroid
 - (4) others
 - c. Involvement by tumor
7. Tissue submitted for microscopic evaluation
 - a. Tumor, representative
 - b. Tumor at point of deepest penetration
 - c. Interface of tumor with adjacent nontumorous mucosa/tissue
 - d. Mucosa/tissue remote from cancer
 - e. Margin(s) of resection
 - f. Areas designated by surgeon
 - g. Areas with additional pathologic findings
 - h. Other organ(s)/tissue(s)
8. Special studies (specify)

C. Microscopic Evaluation

1. Tumor, if present
 - a. Histologic type (Note **A**)
 - b. Histologic grade (Note **B**)
 - c. Location
 - d. Extent of invasion (Note **E**)
 - (1) noninvasive (carcinoma in situ)
 - (2) subepithelial connective tissue depth of invasion (from the basement membrane, in millimeters: lip and tongue cancer only)
 - (3) muscle, if applicable
 - (4) bone or cartilage, if applicable

- (5) adjacent structures
- e. Lymphovascular invasion
- f. Perineural invasion (designate the name of nerve, if applicable)
- 2. Margins
 - a. Tumor present
 - b. Tumor absent, margin width (in millimeters)
 - c. Margins pushing or invasive
- 3. Status of area(s) marked by surgeon
- 4. Presence and description of effects of previous treatment, if present and evaluable
- 5. Additional pathologic findings, if present
 - a. Dysplasia or atypia
 - b. Carcinoma in situ (CIS)
 - c. Others (eg, radiation changes or scars)
- 6. Lymph nodes
 - a. Site(s) (according to levels) (Note **F**)
 - (1) included in specimen (report according to level)
 - (2) separately submitted (report as specified)
 - b. Number
 - (1) total number, according to level
 - (2) number involved by tumor according to level
 - i. number involved by viable tumor
 - ii. number involved by evidence of treated (eg, radiated) nonviable tumor (eg, keratin and parakeratotic debris, fibrosis, necrotic cells consistent with tumor cells)
 - (3) size of largest metastasis in a lymph node containing metastatic tumor (Note **H**)
 - c. Extracapsular extension
 - (1) number involved by tumor, according to level
- 7. Results/status of special studies (specify)
- 8. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Histological Type

A modification of the World Health Organization (WHO) classification of carcinomas of the head and neck is shown below. This list may not be complete. This protocol applies only to carcinomas and does not apply to melanomas, lymphomas, or sarcomas.

Carcinomas of Upper Aerodigestive Tract

Squamous cell carcinoma, conventional

Squamous cell carcinoma, variant (see below)

Verrucous carcinoma

Spindle cell squamous carcinoma

Adenosquamous carcinoma

Basaloid squamous cell carcinoma

- Papillary squamous cell carcinoma
- Lymphoepithelioma-like carcinoma (non-nasopharyngeal)[#]
- Sinonasal carcinoma
 - Keratinizing
 - Non-keratinizing (transitional-type)
 - Undifferentiated sinonasal carcinoma (SNUC)[#]
- Nasopharyngeal carcinoma
 - Keratinizing
 - Non-keratinizing
 - Differentiated nasopharyngeal carcinoma (specify)
 - Undifferentiated nasopharyngeal carcinoma (lymphoepithelioma)
 - Mixed differentiated and undifferentiated nasopharyngeal carcinoma (specify types)
- Adenocarcinoma
 - Salivary gland type (specify)
 - Non-salivary gland type
 - Papillary adenocarcinoma
 - Intestinal-type adenocarcinoma
 - Not otherwise specified (NOS)
- Neuroendocrine carcinoma
 - Typical carcinoid tumor (well differentiated neuroendocrine carcinoma)
 - Atypical carcinoid (moderately differentiated neuroendocrine carcinoma)
 - Small cell carcinoma (poorly differentiated neuroendocrine carcinoma)
- Other[#]

[#] Diagnoses not included in WHO classification.

Carcinomas of the Major and Minor Salivary Glands

The histologic classification recommended is a modification of the WHO classification of salivary gland tumors. The major malignant varieties include the following:

- Acinic cell carcinoma
- Adenoid cystic carcinoma
- Adenocarcinoma (not otherwise specified [NOS])
- Adenosquamous carcinoma (minor salivary gland only)
- Squamous cell carcinoma
- Carcinoma ex pleomorphic adenoma (malignant mixed tumor)
 - Non-invasive/minimally invasive (carcinoma in situ ex pleomorphic adenoma)
 - Invasive
- Carcinosarcoma (true malignant mixed tumor)
- Mucoepidermoid carcinoma
 - Low grade
 - Intermediate grade
 - High grade
- Polymorphous low-grade adenocarcinoma
- Epithelial-myoepithelial carcinoma
- Basal cell adenocarcinoma
- Sebaceous carcinoma
- Cystadenocarcinoma

Mucinous carcinoma (colloid carcinoma)
 Oncocytic carcinoma
 Salivary duct carcinoma
 Myoepithelial carcinoma (malignant myoepithelioma)
 Small cell carcinoma
 Undifferentiated carcinoma[#]
 Other

[#] Diagnosis not included in WHO classification.

B. Histologic Grade

For histologic types of carcinomas that are amenable to grading, 3 histologic grades are suggested, as shown below. When a tumor manifests more than 1 grade of differentiation, the surgical report must designate both the highest and the most prevalent tumor grades.

Grade X	Cannot be assessed
Grade 1	Well differentiated
Grade 2	Moderately differentiated
Grade 3	Poorly differentiated

This grading system does not apply to all salivary gland tumors. When attempting to grade salivary gland tumors, pathologists are referred to the references on tumor grading listed below.

C. Orientation of Specimen

Complex specimens should be examined and oriented with the assistance of attending surgeons. Optimally, attending surgeons should submit diagrams illustrating graphically the extents of the tumors and the lines of resections, as shown in Figure 1.

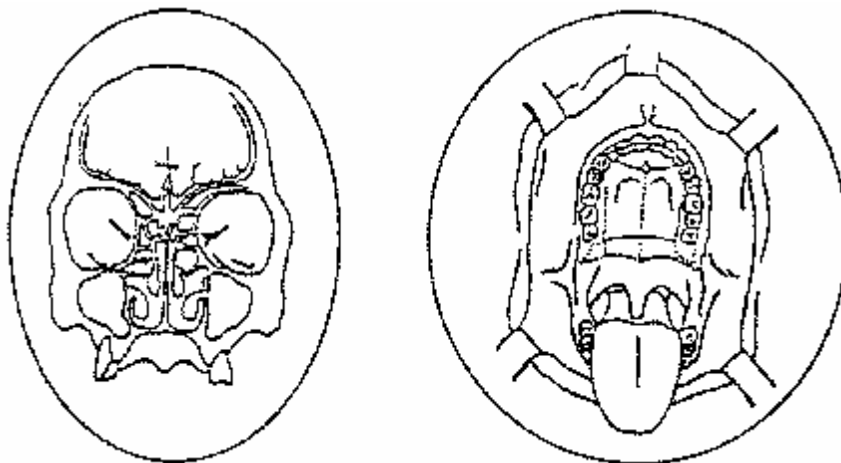


Figure 1. Whenever possible, the tissue examination request form should include a drawing of the resected specimen showing the extent of the tumor and its relation to the anatomic structures of the region. The lines and extent of the resection can be depicted on preprinted adhesive labels, as shown in the figure, and attached to the surgical pathology request forms.

D. 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, as specified by the surgeon
 - a. Supraomohyoid neck dissection
 - b. Posterolateral neck dissection
 - c. Lateral neck dissection
 - d. Central compartment neck dissection
 - e. Others
4. Extended radical neck dissection, as specified by the surgeon

E. TNM and Stage Groupings

The protocol recommends the TNM staging system of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) for head and neck cancer.^{1,2} Separate categories and stage grouping classifications for the various specific sites of the aerodigestive tract (including salivary glands) are enumerated individually below.

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 is based on gross and microscopic examination. 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.

Lip and Oral CavityAnatomical Sites and Subsites for Lip and Oral Cavity*Lip*

- External upper lip (vermillion border)
- External lower lip (vermillion border)
- Commissures

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 vallate papillae
 (anterior two-thirds)

 Inferior (ventral) surface

Floor of mouth

Primary Tumor (T): Lip and Oral Cavity

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor 2 cm or less in greatest dimension
- T2 Tumor more than 2 cm but not more than 4 cm in greatest dimension
- T3 Tumor more than 4 cm in greatest dimension
- T4a Lip: Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (chin or nose)
- T4a Oral cavity: Tumor invades through cortical bone, into deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus or skin of face
- T4b Lip and oral cavity: Tumor invades masticator space, pterygoid plate, or skull base, or encases internal carotid artery

Note: Superficial erosion alone of bone/tooth socket by primary gingival tumor is not sufficient to classify a tumor as T4.

PharynxAnatomical Sites and Subsites for Pharynx*Oropharynx*

- Anterior wall (glosso-epiglottic area)
 - Base of tongue (posterior to the vallate papillae or posterior third)
 - Vallecula
- Lateral wall
 - Tonsil
 - Tonsillar fossa and tonsillar (faucial) pillars
 - Glossotonsillar sulci
- Posterior wall
- Superior wall
 - Inferior surface of soft palate
 - Uvula

Nasopharynx

- Postero-superior wall: junction of the hard and soft palates to the base of the skull
- Lateral wall: includes fossa of Rosenmuller
- Inferior wall: superior surface of the soft palate

Note: The margin of the choanal orifices, including the posterior margin of the nasal septum, is included with the nasal fossa.

Hypopharynx

- Pharyngo-esophageal junction (postcricoid area): level of arytenoid cartilages and connecting folds to inferior border of cricoid cartilage (forming anterior wall of hypopharynx)
- Pyramidal sinus: pharyngoepiglottic fold to the upper end of the esophagus, bounded laterally by the thyroid cartilage and medially by the

hypopharyngeal surface of the aryepiglottic fold and the arytenoid and cricoid cartilages
 Posterior pharyngeal wall: superior level of the hyoid bone (floor of the vallecula) to the inferior border of the cricoid cartilage and the apex of one pyriform sinus to the other

Primary Tumor (T): Oropharynx

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor 2 cm or less in greatest dimension
- T2 Tumor more than 2 cm but not more than 4 cm in greatest dimension
- T3 Tumor more than 4 cm in greatest dimension
- T4a Tumor invades any of the following: larynx, deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), medial pterygoid muscle, hard palate, and mandible
- T4b Tumor invades any of the following: lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base; or encases the carotid artery

Primary Tumor (T): Nasopharynx

- T1 Tumor confined to nasopharynx
- T2 Tumor extends to soft tissue of oropharynx and/or nasal fossa
- T2a T2 without parapharyngeal extension[#]
- T2b T2 with parapharyngeal extension[#]
- T3 Tumor invades bony structures and/or paranasal sinuses
- T4 Tumor with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx or orbit or masticator space

[#] Parapharyngeal extension denotes postero-lateral infiltration of tumor beyond the pharyngo-basilar fascia.

Primary Tumor (T): Hypopharynx

- T1 Tumor limited to 1 subsite of hypopharynx (ie, pyriform sinus, post-cricoid region, or posterior wall) and 2 cm or less in greatest dimension
- T2 Tumor invades more than 1 subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest dimension, *without fixation of hemilarynx*[#]
- T3 Tumor measures more than 4 cm in greatest dimension, *or with fixation of hemilarynx*[#]
- T4a Tumor invades adjacent structures, eg, thyroid/cricoid cartilage, hyoid bone, thyroid gland, esophagus, or central compartment soft tissue^{##}
- T4b Tumor invades prevertebral fascia, encases carotid artery, or invades mediastinal structures

[#] May only be determined clinically.

^{##} Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

Regional Lymph Nodes (N): Lip and Oral Cavity, Oropharynx, and Hypopharynx

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
- N2 Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
- N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
- N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N3 Metastasis in a lymph node more than 6 cm in greatest dimension

Note: Midline nodes are considered ipsilateral nodes.

Regional Lymph Nodes (N): Nasopharynx

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Unilateral metastasis in lymph node(s),[#] 6 cm or less in greatest dimension, above supraclavicular fossa
- N2 Bilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above supraclavicular fossa
- N3 Metastasis in lymph node(s) more than 6 cm in greatest dimension and/or to supraclavicular fossa
- N3a Metastasis in lymph node(s) more than 6 cm in dimension
- N3b Metastasis in lymph node(s) residing wholly or in part in the supraclavicular fossa

[#] Midline nodes are considered ipsilateral nodes.

Distant Metastasis (M): Lip and Oral Cavity, Oropharynx, Nasopharynx, and Hypopharynx

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

Stage Groupings: Lip and Oral Cavity, Oropharynx, and Hypopharynx

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1,T2	N1	M0
	T3	N0,N1	M0
Stage IVA	T1,T2,T3	N2	M0
	T4a	N0,N1,N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0

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Stage IVC Any T Any N M1

Stage Groupings: Nasopharynx

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2a	N0	M0
Stage IIB	T1	N1	M0
	T2a	N1	M0
	T2b	N0,N1	M0
Stage III	T1	N2	M0
	T2a,T2b	N2	M0
	T3	N0,N1,N2	M0
Stage IVA	T4	N0,N1,N2	M0
Stage IVB	Any T	N3	M0
Stage IVC	Any T	Any N	M1

LarynxAnatomical Sites and Subsites for Larynx*Supraglottis*

Epilarynx, including marginal zone

Suprahoid epiglottis, including tip, lingual (anterior) and laryngeal surfaces

Aryepiglottic fold, laryngeal aspect

Arytenoid

Supraglottis, excluding epilarynx

Infrahyoid epiglottis

Ventricular bands (false cords)

Glottis

Vocal cords

Anterior commissure

Posterior commissure

*Subglottis***Primary Tumor (T): Supraglottis**

TX Primary tumor cannot be assessed

T0 No evidence of primary tumor

Tis Carcinoma in situ

T1 Tumor limited to 1 subsite of supraglottis (with normal vocal cord mobility)[#]

T2 Tumor invades mucosa of more than 1 adjacent subsite of supraglottis or glottis or region outside the supraglottis (eg, mucosa of base of tongue, vallecula, medial wall of pyriform sinus) (without fixation of the larynx)[#]

T3 Tumor limited to larynx (with vocal cord fixation)[#] and/or invades any of the following: postcricoid area, pre-epiglottic tissues paraglottic space, and/or minor thyroid cartilage erosion (eg, inner cortex)

T4a Tumor invades through the thyroid cartilage, and/or invades tissues beyond the larynx, eg, trachea, soft tissues of neck including deep/ extrinsic muscle of the tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid and esophagus

T4b Tumor invades prevertebral space, mediastinal structures, or encases carotid artery

May only be determined clinically.

Primary Tumor (T): Glottis

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor limited to vocal cord(s) (may involve anterior or posterior commissure) (with normal mobility)[#]
- T1a Tumor limited to 1 vocal cord
- T1b Tumor involves both vocal cords
- T2 Tumor extends to supraglottis and/or subglottis (and/or with impaired vocal cord mobility[#])
- T3 Tumor limited to larynx (with vocal cord fixation)[#] and/or invades paraglottic space, and/or minor thyroid cartilage erosion (eg, inner cortex)
- T4a Tumor invades through the thyroid cartilage, and/or invades tissues beyond the larynx, eg, trachea, soft tissues of neck including deep/extrinsic muscle of the tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid and esophagus
- T4b Tumor invades prevertebral space, mediastinal structures, or encases carotid artery

May only be determined clinically.

Primary Tumor (T): Subglottis

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor limited to subglottis
- T2 Tumor extends to vocal cord(s) (with normal or impaired mobility)[#]
- T3 Tumor limited to larynx (with vocal cord fixation)[#]
- T4a Tumor invades through the thyroid cartilage, and/or invades tissues beyond the larynx, eg, trachea, soft tissues of neck including deep/extrinsic muscle of the tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid and esophagus
- T4b Tumor invades prevertebral space, mediastinal structures, or encases carotid artery

May only be determined clinically.

Regional Lymph Nodes (N): Supraglottis, Glottis, and Subglottis

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in a single ipsilateral lymph node 3 cm or less in greatest dimension
- N2 Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension

- N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
- N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
- N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N3 Metastasis in a lymph node more than 6 cm in greatest dimension

Distant Metastasis (M): Supraglottis, Glottis, and Subglottis

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

Stage Groupings: Supraglottis, Glottis, and Subglottis

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0,N1	M0
Stage IVA	T1,T2,T3	N2	M0
	T4a	N0,N1,N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Paranasal SinusesAnatomical Subsites of Paranasal Sinuses*Nasal Cavity*

- Septum
- Floor
- Lateral wall
- Vestibule

*Maxillary sinus**Ethmoid sinus*

- Left
- Right

Primary Tumor (T): Maxillary Sinus

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor limited to the antral mucosa with no erosion or destruction of bone
- T2 Tumor causing bone erosion or destruction, except for the posterior antral wall, including extension into hard palate and/or middle nasal meatus
- T3 Tumor invades any of the following: bone of posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, ethmoid sinuses

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- T4a Tumor invades any of the following: anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinuses
- T4b Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve V2, nasopharynx, clivus

Primary Tumor (T): Nasal Cavity and Ethmoid Sinus

- TX Primary tumor cannot be assessed
 T0 No evidence of primary tumor
 Tis Carcinoma in situ
 T1 Tumor restricted to 1 subsite of nasal cavity or ethmoid sinus, with or without bony invasion
 T2 Tumor involves 2 subsites in a single site or extends to involve an adjacent site within the nasoethmoidal complex, with or without bony invasion
 T3 Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate
 T4a Tumor invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses
 T4b Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx, clivus

Regional Lymph Nodes (N): Nasal Cavity, Maxillary Sinus, and Ethmoid Sinus

- NX Regional lymph nodes cannot be assessed
 N0 No regional lymph node metastasis
 N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
 N2 Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
 N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
 N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
 N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
 N3 Metastasis in a lymph node more than 6 cm in greatest dimension

Distant Metastasis (M): Nasal Cavity, Maxillary Sinus, and Ethmoid Sinus

- MX Distant metastasis cannot be assessed
 M0 No distant metastasis
 M1 Distant metastasis

Stage Groupings: Nasal Cavity, Maxillary Sinus, and Ethmoid Sinus

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0,N1	M0
Stage IVA	T1,T2,T3	N2	M0
	T4a	N0,N1,N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Salivary Glands

Rules for Classification

The classification applies only to carcinomas of the major salivary glands: parotid, submandibular (submaxillary), and sublingual glands. 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, lip.

Primary Tumor (T): Salivary Glands

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- T1 Tumor 2 cm or less in greatest dimension without extraparenchymal extension[#]
- T2 Tumor more than 2 cm but not more than 4 cm in greatest dimension without extraparenchymal extension[#]
- T3 Tumor more than 4 cm and/or tumor with extraparenchymal extension
- T4a Tumor invades skin, mandible, ear canal, or facial nerve
- T4b Tumor invades base of skull, pterygoid plates, or encases carotid artery

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

Regional Lymph Nodes (N): Salivary Glands

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
- N2 Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension
- N2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
- N2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N3 Metastasis in a lymph node more than 6 cm in greatest dimension

Distant Metastasis (M): Salivary Glands

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

Stage Groupings: Salivary Glands

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1,T2,T3	N1	M0
Stage IVA	T1,T2,T3	N2	M0
	T4a	N0,N1,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).

Vessel Invasion

By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category. In all other cases, lymphatic and venous invasion by tumor are coded separately as follows.

Lymphatic Vessel Invasion (L)

LX	Lymphatic vessel invasion cannot be assessed
L0	No lymphatic vessel invasion
L1	Lymphatic vessel invasion

Venous Invasion (V)

VX	Venous invasion cannot be assessed
V0	No venous invasion
V1	Microscopic venous invasion
V2	Macroscopic venous invasion

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. Lymph nodes or distant sites with ITCs found by either histologic examination, immunohistochemistry, or nonmorphologic techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be classified as N0 or M0, respectively. Specific denotation of the assigned N category is suggested as follows for cases in which ITCs are the only evidence of possible metastatic disease.^{3,4}

pN0	No regional lymph node metastasis histologically, no examination for isolated tumor cells (ITCs)
pN0(i-)	No regional lymph node metastasis histologically, negative morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs
pN0(i+)	No regional lymph node metastasis histologically, positive morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs
pN0(mol-)	No regional lymph node metastasis histologically, negative nonmorphologic (molecular) findings for ITCs
pN0(mol+)	No regional lymph node metastasis histologically, positive nonmorphologic (molecular) findings for ITCs

F. Lymph Nodes

The status of cervical lymph nodes is the single most important prognostic factor in aerodigestive cancer. For purposes of pathologic evaluation, lymph nodes are organized by levels as shown in Figure 2.^{5,6}

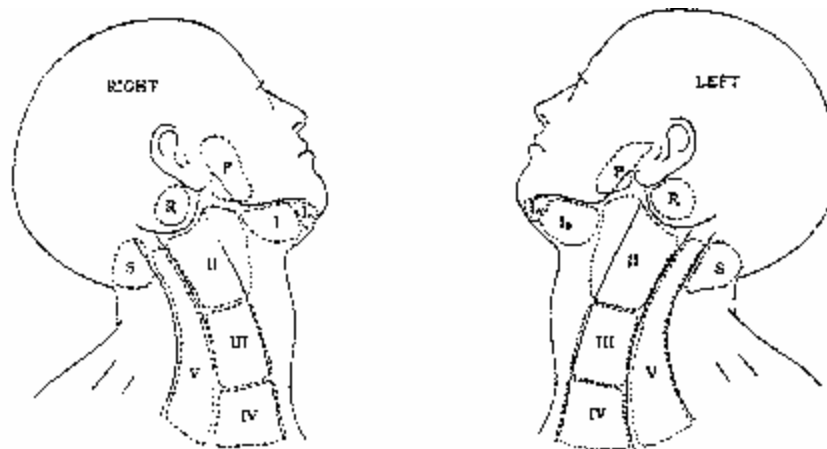


Figure 2. The lymph node groups included in the node dissection specimens should be designated as shown in the figure and identified with the assistance of the surgeon in charge, whenever possible.

P: Parotid-Preauricular.

R: Retroauricular.

S: Suboccipital.

From: Cummings CW, ed. *Otolaryngology Head and Neck Surgery*. 2nd ed. St. Louis: Mosby, Inc; 1992:1652. Reprinted with permission.

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

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

Level I. Submental Group

Lymph nodes within the triangular boundary of the anterior belly of the digastric muscles and the hyoid bone.

Submandibular Group

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

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

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.

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. When staging lymph node involvement by metastases from nasopharyngeal carcinoma, the supraclavicular fossa refers to a triangular region, the base of which is the superior margin of the clavicle between its sternal and lateral ends, and the apex of which is the point where the neck meets the shoulder. This includes caudal portions of Levels IV and V (see above). All cancers metastatic to the posterior nodes in the supraclavicular fossa are designated as N3b.

G. Lymph Node Number

Histological examination of a selective neck dissection specimen will ordinarily include 6 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen will ordinarily include 10 or more lymph nodes in the untreated neck.

H. Measurement of Tumor Metastasis

The cross-sectional diameter of the largest metastasis in a lymph node containing metastatic tumor 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. The prognostic impact of regional lymph node metastases from nasopharyngeal cancer, particularly undifferentiated nasopharyngeal carcinoma (lymphoepithelioma), differs from and is not necessarily comparable to the prognoses of other head and neck mucosal carcinomas. Therefore, a different N classification scheme is used for nasopharyngeal carcinoma.

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Thyroid Gland

Protocol applies to all malignant tumors of the thyroid gland, except lymphomas.

*Based on AJCC/UICC TNM, 6th edition
January 2004*

Procedures

- **Cytology** (No Accompanying Checklist)
- **Partial Thyroidectomy**
- **Total Thyroidectomy With/Without Lymph Node Dissection**

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Surgical Pathology Cancer Case Summary (Checklist)

*Applies to invasive carcinomas only
Based on AJCC/UICC TNM, 6th edition
January 2004*

THYROID: Resection

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC**Specimen Type**

- Total thyroidectomy
 Lobectomy
 Right lobe
 Left lobe
 Isthmectomy
 Other (specify): _____
 Not specified

Tumor Site (check all that apply)

- Right lobe
 Left lobe
 Isthmus
 Not specified

Tumor Focality

- Unifocal
 Multifocal

Tumor Size (largest nodule)

Greatest dimension: ___ cm

*Additional dimensions: ___ x ___ cm

___ Cannot be determined (see Comment)

2

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

MICROSCOPIC**Histologic Type**

- Follicular carcinoma (minimally invasive, widely invasive)
- Oncocytic (Hürthle cell) carcinoma
- Papillary carcinoma
- Papillary carcinoma, follicular variant
- Papillary carcinoma, tall cell variant
- Papillary carcinoma, diffuse sclerosing variant
- Papillary carcinoma, other variant
- Insular carcinoma (and other poorly differentiated carcinoma)
- Medullary carcinoma
- Undifferentiated (anaplastic) carcinoma
- Other (specify): _____
- Carcinoma, type cannot be determined

Pathologic Staging (pTNM)Primary Tumor (pT)

- pTX: Cannot be assessed
- pT0: No evidence of primary tumor
- pT1: Tumor size 2 cm or less, limited to thyroid
- pT2: Tumor more than 2 cm, but not more than 4 cm, limited to thyroid
- pT3: Tumor more than 4 cm, limited to thyroid or with minimal extrathyroidal extension (eg, extension to sternothyroid muscle or perithyroid soft tissues)
- pT4a: Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus or recurrent laryngeal nerve
- pT4b: Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels.

Anaplastic Carcinoma

- pT4a: Intrathyroidal anaplastic carcinoma—surgically resectable
- pT4b: Extrathyroidal anaplastic carcinoma—surgically unresectable

Regional Lymph Nodes (pN)

- pNX: Cannot be assessed
- pN0: No regional lymph node metastasis
- pN1a: Nodal metastases to Level VI (pretracheal, paratracheal and prelaryngeal/Delphian) lymph nodes
- pN1b: Metastases to unilateral, bilateral or contralateral cervical or superior mediastinal lymph nodes.

Specify: Number examined: ____
Number involved: ____

Distant Metastasis (pM)

- pMX: Cannot be assessed
- pM1: Distant metastasis

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

*Specify site(s), if known: _____

Margins

___ Cannot be assessed

___ Margins uninvolved by carcinoma

*Distance of invasive carcinoma to closest margin: ___ mm

___ Margin(s) involved by carcinoma

Site(s) of involvement: _____

***Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)**

(Venous vessels outside tumor or in capsule)

* ___ Cannot be assessed

* ___ Absent

* ___ Present

* ___ Indeterminate

***Additional Pathologic Findings (check all that apply)**

* ___ None identified

* ___ Nodular goiter

* ___ Adenoma

* ___ Thyroiditis

* ___ Other (specify): _____

***Comment(s)**

4 * Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Background Documentation

I. Cytologic Material

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information, if known
 - a. Relevant history
 - (1) previous treatment
 - (2) previous head and neck radiation
 - (3) family history of thyroid disease or multiple endocrine neoplasia (MEN) syndromes
 - b. Relevant findings
 - (1) single or multiple nodules
 - (2) euthyroid, hypothyroid or hyperthyroid, compensated euthyroid
 - (3) radiologic studies (eg, thyroid scan, ultrasound results)
 - (4) laboratory findings (eg, thyroid studies, antibodies)
 - (5) relevant molecular studies (eg, RET proto-oncogene mutational analysis)
 - c. Clinical diagnosis
 - d. Procedure (eg, intraoperative specimen cytology, fine-needle aspiration [FNA])
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
 - a. Type (eg, slides, fluid specimen, fine-needle biopsy)
 - b. Number of passes
 - c. Unfixed/fixed (specify fixative)
 - d. Number of slides received, if appropriate
 - e. Results of intraprocedural/preliminary on site consultation
2. Material prepared for microscopic evaluation (eg, smears, cytopins, filters, cell block)
3. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry)

C. Microscopic Evaluation

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason) (Note **A**)
2. Diagnostic category (Note **B**)
3. Additional pathologic findings, if present
 - a. Nodular goiter
 - b. Thyroiditis
 - c. Other(s)
4. Results/status of special studies (specify)
5. Comments

- a. Correlation with intraoperative consultation/on-site evaluation, as appropriate
- b. Correlation with other specimens, as appropriate
- c. Correlation with clinical information, as appropriate

II. Partial Thyroidectomy

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous treatment
 - (2) previous FNA results
 - (3) previous head and neck radiation
 - (4) family history of thyroid disease or multiple endocrine neoplasia (MEN) syndromes
 - b. Relevant findings
 - (1) euthyroid, hypothyroid or hyperthyroid, compensated euthyroid
 - (2) single or multiple nodules
 - (3) radiologic studies (eg, thyroid scan, ultrasound results)
 - (4) laboratory findings (eg, thyroid studies, antibodies)
 - c. Procedure (eg, lobectomy, isthmectomy)
 - d. Operative findings
 - e. Anatomic site(s) of specimen(s)
 - f. Availability of pertinent slides for review, if necessary

B. Macroscopic Examination

1. Specimen
 - a. Organ(s)/tissue(s) included
 - b. Unfixed/fixed (specify fixative)
 - c. Weight
 - d. Size (3 dimensions)
 - e. Descriptive characteristics, external surface
 - f. Descriptive characteristics, cut surface (eg, color, consistency)
 - g. Orientation, if indicated by surgeon
 - h. Nonneoplastic thyroid
 - i. Parathyroid gland(s) (if identified; give laterality and/or location, if known)
 - j. Results of intraoperative consultation
2. Tumor
 - a. Location
 - b. Encapsulated/nonencapsulated
 - c. Size(s) (Note **D**)
 - d. Extracapsular thyroid extension (Note **D**)
 - e. Descriptive characteristics (hemorrhage/necrosis)
 - f. Distance to margin of resection

3. Margins, as appropriate
4. Regional lymph nodes, if submitted
5. Tissue submitted for microscopic evaluation
 - a. Tumor(s)
 - b. Tumor in relation to capsule in toto, as appropriate
 - c. Nonnodular thyroid
 - d. Other mass(es)/nodule(s)
 - e. Margins, as appropriate
 - f. All lymph nodes, if submitted
 - g. Parathyroid glands, if identified
 - h. Frozen section tissue fragment(s) (unless saved for special studies)
 - i. Other tissue(s), as appropriate
6. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, DNA analysis [specify type])

C. Microscopic Evaluation

1. Tumor
 - a. Histologic type(s) (Note **C**)
 - b. Multicentricity, if present
 - c. Extent of invasion (Note **D**)
 - (1) capsular invasion - location and extent (minimally vs widely) (Note **C**)
 - (2) venous/lymphatic vessel invasion, if present (note extent: minimally vs widely) (Note **C**)
 - (3) extrathyroid capsular extension (Note **D**)
2. Additional pathologic findings, if present
 - a. Nodular goiter
 - b. Thyroiditis
 - c. Therapy-related changes
 - d. Other(s)
3. Margins, as appropriate (Note **E**)
4. Regional lymph nodes, if submitted
 - a. Number
 - b. Number with metastasis
 - c. Extranodal extension
5. Other tissues/organs (eg, parathyroid tissue) (give laterality and/or location of parathyroid, if known)
6. Metastasis to other organs/structures (specify sites)
7. Result/status of special studies (specify)
8. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

III. Total Thyroidectomy With/Without Lymph Node Dissection

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification number
 - c. Age (birth date)
 - d. Sex

2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Relevant history
 - (1) previous treatment
 - (2) previous FNA results
 - (3) previous head and neck radiation
 - (4) family history of thyroid disease or multiple endocrine neoplasia (MEN) syndromes
 - b. Relevant findings
 - (1) euthyroid, hypothyroid or hyperthyroid, compensated euthyroid
 - (2) single or multiple nodules
 - (3) radiologic studies (eg, thyroid scan, ultrasound results)
 - (4) laboratory findings (eg, thyroid studies, antibodies)
 - c. Clinical diagnosis
 - d. Procedure (eg, thyroidectomy with node dissection)
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
 - a. Organ(s)/tissue(s) included
 - b. Unfixed/fixed (specify fixative)
 - c. Thyroid gland
 - (1) weight
 - (2) size (3 dimensions)
 - (3) symmetry
 - (4) descriptive characteristics (eg, color, consistency)
 - (5) external surface
 - (6) cut surface
 - (7) nodule(s)/mass(es)
 - i. location
 - ii. character
 - iii. calcification
 - iv. cysts
 - d. Orientation, if indicated by surgeon
 - e. Parathyroid glands, if identified (give laterality and/or location, if known)
 - f. Description of other tissues
 - g. Results of intraoperative consultation
2. Tumor
 - a. Location
 - b. Descriptive features
 - c. Size(s) (Note **D**)
 - d. Extracapsular thyroid extension (Note **D**)
3. Margins, as appropriate
4. Regional lymph nodes
 - a. Number
 - b. Location, if possible
5. Tissue submitted for microscopic evaluation
 - a. Tumor(s)

- b. Mass(es)/nodule(s)
 - c. Tumor capsule in toto, as appropriate
 - d. Noninvolved thyroid
 - e. Margins
 - f. All lymph nodes, if submitted
 - g. Other lesions
 - h. Parathyroid tissue, if identified
 - i. Frozen section tissue fragment(s) (unless saved for special studies)
 - j. Other tissue(s) (specify)
 - k. Special circumstance: prophylactic thyroidectomy (familial medullary carcinoma or MEN syndrome) (Note **F**)
6. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, DNA analysis [specify type])

C. Microscopic Evaluation

1. Tumor
 - a. Histologic type(s) (Note **C**)
 - b. Multicentricity, if present
 - c. Location(s)
 - d. Extent of invasion (Note **D**)
 - (1) capsular invasion: location and extent (minimally vs widely) (Note **C**)
 - (2) venous/lymphatic vessel invasion, if present (note extent: minimally vs widely) (Note **C**)
 - (3) extrathyroid capsular extension (Note **D**)
 - (4) Invasion of tissue(s) adjacent to thyroid (specify)
2. Margin(s), as appropriate (Note **E**)
3. Lymph nodes
 - a. Number
 - b. Number involved by tumor
 - (1) location, if possible
 - (2) extranodal extension, if present
4. Additional pathologic findings, if present
 - a. Nodular goiter
 - b. Thyroiditis
 - c. Therapy-related changes
 - d. Adenomatous (hyperplastic, adenomatoid) nodules/adenoma
 - e. Other(s)
5. Other tissues/organs (eg, parathyroid tissue; give laterality and/or location, if known)
6. Results/status of special studies (specify)
7. Distant metastasis (specify site)
8. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Specimen Adequacy

The specimen adequacy criteria should be followed regardless of radiologic and clinical findings. A widely used criterion for specimen adequacy requires 6 or more groups of follicular cells with 10 to 20 cells per group on 2 different slides. Paucicellular specimens with abundant colloid almost always correspond to colloid nodules, but rarely papillary cancers may have these findings. Specimens with inadequate numbers of follicular cells and scant (or no) colloid should be interpreted as nondiagnostic. Paucicellular specimens having limited numbers of follicular cells showing some features of malignancy should be interpreted as suspicious. Although specimens showing only abundant proteinaceous material, histiocytes, and/or hemosiderin can be interpreted as cyst contents such specimens have a low risk of representing a malignancy, but a higher risk than otherwise benign adequate specimens. It should be recognized that cystic malignancies may rarely present with cytologic findings that are similar to those of benign cysts. Guidelines for fine-needle aspiration (FNA) of the thyroid have been published.¹

Guidelines for the Microscopic Evaluation of Specimen Adequacy¹

Number of Follicular Cells	Amount of Colloid	Interpretation
Numerous	Variable	Adequate for interpretation, diagnosis depends on cellular features
Few	Scanty or Absent	Unsatisfactory [#]
Few follicular, numerous histocytes	Variable	Nondiagnostic. Recommend repeat after 3 months, possible under ultrasound guidance. ^{##,###}

[#] One should be cautious in rendering a diagnosis of colloid nodule in a specimen which shows watery colloid, macrophages, and few follicular cells, because aspirates of papillary carcinoma with extensive cystic degeneration may also give rise to specimens with abundant colloid-like material, macrophages, and few follicular cells. If malignant cells, irrespective of the number, are positively identified in an aspirate, a malignant diagnosis should be made. However, if small numbers of follicular cells show atypical features short of overt malignancy, a “suspicious” diagnosis or a repeat aspiration may be suggested. The pathologist should discuss these findings with the clinician before rendering a “suspicious” diagnosis on a paucicellular specimen. In the majority of cases, a definite diagnosis of malignancy can be reached in an ultrasound guided repeat FNA.

^{##} The report should contain a qualifier stating that the interpretation is limited by the paucity of follicular cells.

Occasionally, a cystic papillary carcinoma may present a similar pattern. Check for residual solid areas, and re-aspirate if palpable. The risk of malignancy is higher in large (greater than 4 cm) lesions and those that increase in size despite therapy.

B. Fine-Needle Aspiration (FNA) Diagnostic Categories

Benign

Nodular goiter, Hyperplastic nodule, Thyroiditis

Suspicious

Follicular neoplasm, Hürthle cell neoplasm

Rule out / Suggestive of neoplasm

Malignant

Non-diagnostic

See Note C; Follicular and Hürthle cell carcinoma cannot be reliably diagnosed with FNA.

C. Histologic Type

The histologic classification published by the World Health Organization (WHO) is recommended by the protocol and shown below.²⁻⁴

WHO Classification of Carcinoma of the Thyroid

Follicular carcinoma (minimally invasive, widely invasive)

Oncocytic (Hürthle cell) carcinoma

Papillary carcinoma

Follicular variant

Tall cell variant

Diffuse sclerosing variant

Other variant

Poorly differentiated carcinoma (including insular carcinoma)

Medullary carcinoma

Undifferentiated (anaplastic) carcinoma

Other (specify)

The diagnosis of follicular carcinoma or Hürthle cell carcinoma depends on the identification of capsular and/or blood vessel invasion. Blood vessels should be of venous caliber and be located outside the tumor, within, or immediately outside the capsule. Encapsulated follicular tumors with vascular invasion have potential for metastasis.⁵ Tumor cells should be attached to the vessel wall and protrude into the lumen. Encapsulated follicular tumors with invasion of the capsule may have potential for metastasis, although this is still controversial.

“Minimally invasive” follicular carcinoma refers to lesions with no vascular invasion.

“Angioaggressive” follicular carcinoma refers to those tumors in which vascular invasion is identified. “Widely invasive” follicular and Hürthle cell carcinomas are those tumors with grossly apparent invasion of thyroid and/or soft tissue.

D. TNM and Stage Groupings

According to the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC), staging of thyroid cancer depends primarily on the histologic type.^{6,7} Thus, there are specific TNM stage groupings for papillary and follicular carcinomas that are stratified by age, and separate stage groupings not stratified by age for medullary carcinomas and undifferentiated carcinomas. Hürthle cell tumors are staged the same as follicular carcinomas. Undifferentiated or anaplastic carcinomas are always assigned stage IV. Age is not a prognostically important consideration for medullary or undifferentiated carcinomas. Tumor size and lymph node status are also considered in the TNM classification.

All categories may be subdivided: (a) solitary tumor, (b) multifocal tumor. With multifocal tumors, the largest one is used for classification. The lymph nodes must be specifically identified to classify regional node involvement.

Primary Tumor (T)

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- T1 Tumor 2 cm or less in greatest dimension limited to the thyroid
- T2 Tumor more than 2 cm but not more than 4 cm in greatest dimension limited to the thyroid
- T3 Tumor more than 4 cm in greatest dimension limited to the thyroid or any tumor with minimal extrathyroidal extension (eg, extension to sternothyroid muscle or perithyroid soft tissues)
- T4a Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus or recurrent laryngeal nerve
- T4b Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels.

All anaplastic carcinomas are considered T4 tumors

- T4a Intrathyroidal anaplastic carcinoma—surgically resectable
- T4b Extrathyroidal anaplastic carcinoma—surgically unresectable

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 is based on gross and microscopic examination. 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.

Regional Lymph Nodes (N) (see Note G)

- NX Regional nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1a Nodal metastases to Level VI (pretracheal, paratracheal and prelaryngeal/Delphian) lymph nodes
- N1b Metastases to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes

Distant Metastasis (M)

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

Stage Groupings

Papillary or Follicular Carcinoma

	<i>Under 45 Years of Age</i>			<i>45 Years or Older</i>		
Stage I	Any T	Any N	M0	T1	N0	M0
Stage II	Any T	Any N	M1	T2	N0	M0
Stage III				T3	N0	M0
				T1	N1a	M0
				T2	N1a	M0
			T3	N1a	M0	
Stage IVA				Any T [#]	Any N	M0
Stage IVB				T4b	Any N	M0
Stage IVC				Any T	Any N	M1

[#] Except T4b.

Medullary Carcinoma (Any Age)

Stage I	T1	N0	M0	
Stage II	T2	N0	M0	
	T3	N0	M0	
	T1	N1a	M0	
Stage III	T2	N1a	M0	
	T3	N1a	M0	
	T4a	N0	M0	
Stage IVA	T4a	N1a	M0	
	T1	N1b	M0	
	T2	N1b	M0	
	T3	N1b	M0	
	T4a	N1b	M0	
	Stage IVB	T4b	Any N	M0
	Stage IVC	Any T	Any N	M1

Undifferentiated Carcinoma (All Cases - Stage IV)

Stage IVA	T4a	Any N	M0
Stage IVB	T4b	Any N	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 DescriptorsResidual 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).

Vessel Invasion

By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category. In all other cases, lymphatic and venous invasion by tumor are coded separately as follows:

Lymphatic Vessel Invasion (L)

- LX Lymphatic vessel invasion cannot be assessed
L0 No lymphatic vessel invasion
L1 Lymphatic vessel invasion

Venous Invasion (V)

- VX Venous invasion cannot be assessed
V0 No venous invasion
V1 Microscopic venous invasion
V2 Macroscopic venous invasion

E. Margins

Few published studies have addressed the influence of margin status and patient outcome. Most surgeons, endocrinologists, and nuclear medicine specialists require knowledge of positive margins, ie, tumor extending to surgical resection edge. While this makes intuitive sense and it is recommended that a positive margin be mentioned in the final pathology report, data on the effect of positive margins and outcome in large series of patients with long-term follow-up is not available.

Similarly, a few authors refer to the value of measuring distance of tumor to closest resection margin since some therapists modify dose of postoperative radioiodine depending on closeness of margins.⁸ Since data on the prognostic import of close margins as an independent variable or even co-variable is lacking, assessment and reporting of this information is not currently recommended.

F. Prophylactic Total Thyroidectomy

In patients with familial medullary carcinoma (familial MTC, MEN 2 or variants) and in whom germline mutations in RET proto-oncogene are present, prophylactic total thyroidectomy is performed based on positive mutational analysis.⁹ Many of the thyroidectomy specimens appear grossly normal. In such cases, serial blocking of the gland is required to document the extent of C-cell hyperplasia and to assess for micromedullary carcinoma.¹⁰ These blocks should be taken in a superior to inferior direction for each lobe, and the isthmus should be submitted separately. This serial sectioning of the thyroid is performed because C-cells are restricted to a zone deep within the middle to upper thirds of the lateral lobes. The extreme upper and lower poles of each lobe and the isthmic regions are generally devoid of C-cells. Immunostains for calcitonin and CEA may be required to assess extent of C-cell disease.

G. 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.

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