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**

Authors

Ben Z. Pilch, MD
Department of Pathology, Massachusetts General Hospital and Massachusetts Eye and Ear Infirmary, Boston, Massachusetts

Elizabeth Gillies, MD
Department of Pathology, VA Medical Center, Oklahoma City, Oklahoma

John R. Houck Jr, MD
Department of Otolaryngology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

Kyung-Whan Min, MD
Department of Pathology, Deaconess Hospital, Oklahoma City, Oklahoma

David Novis, MD
Department of Pathology, Wentworth-Douglass Hospital, Dover, New Hampshire

Jatin Shah, MD
Department of Head and Neck Surgery, Memorial Sloan-Kettering Cancer Center, New York

Richard J. Zarbo, MD, DMD
Department of Pathology, Henry Ford Hospital, Detroit, Michigan

For the Members of the Cancer Committee, College of American Pathologists

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
___ Adenocardinoma, 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): _____

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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

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

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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, paraglotic 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 extention into the hard palate and/or middle nasal meatus, except extention 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 (V_2), 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 (V_2), 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: Extention 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: _____

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)**

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to invasive cancers only
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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): _____

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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)**

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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.

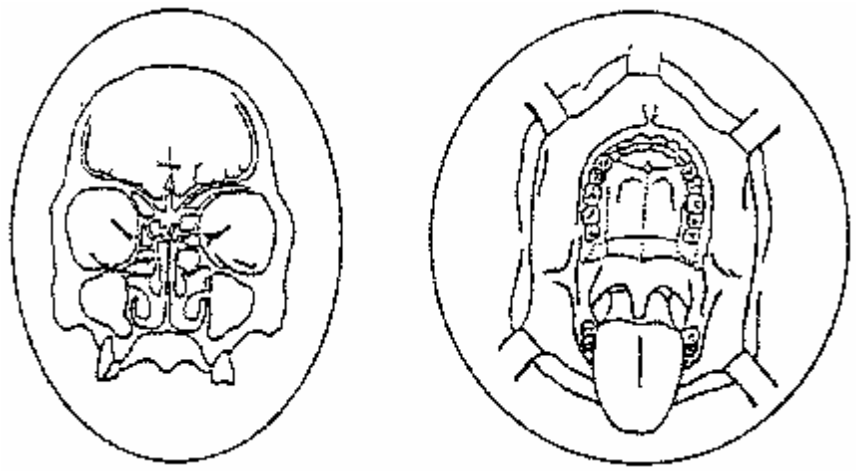

Figure 1. Whenever possible, the tissue examination request form should include a drawing of the resected specimen showing the extent of the tumor and its relation to the anatomic structures of the region. The lines and extent of the resection can be depicted on preprinted adhesive labels, as shown in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

<u>Anatomical Sites and Subsites for Lip and Oral Cavity</u>

Lip

- External upper lip (vermilion border)
- External lower lip (vermilion 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/extrinisic 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.

Pharynx

Anatomical 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)
- Pyriform 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

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

Larynx

Anatomical Sites and Subsites for Larynx

Supraglottis
- Epilarynx, including marginal zone
  - Suprahyoid 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 Sinuses

Anatomical 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

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]

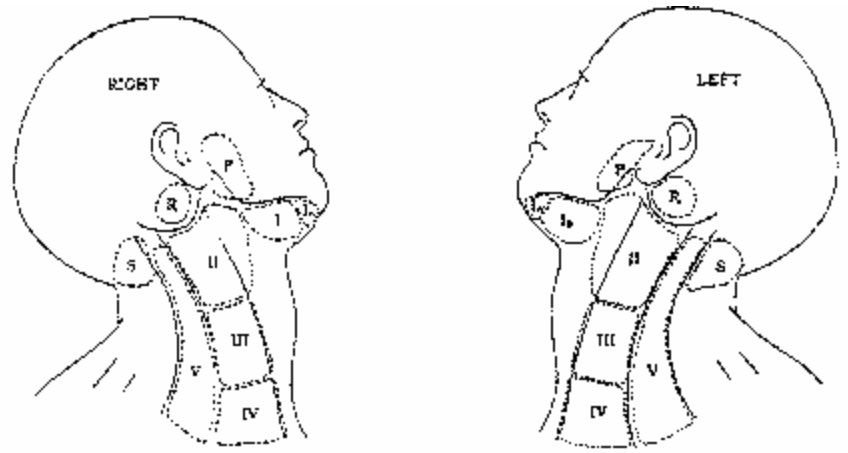

Figure 2. The lymph node groups included in the node dissection specimens should be designated as shown in the figure and identified with the assistance of the surgeon in charge, whenever possible.
P: Parotid-Preauricular.
R: Retroauricular.
S: Suboccipital.
From: Cummings CW, ed. *Otolaryngology Head 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.

<u>Submandibular Group</u>
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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Type of Margin

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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**

Authors

Virginia A. LiVolsi, MD
Department of Pathology, University of Pennsylvania Hospital, Philadelphia, Pennsylvania

Zubair W. Baloch, MD, PhD
Department of Pathology, University of Pennsylvania, Philadelphia, Pennsylvania

Michael Cibull, MD
Department of Pathology, University of Kentucky Hospital, Lexington, Kentucky

Susan Mandel, MD
Division of Endocrinology, Department of Internal Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

Robert Udelsman, MD
Chair, Department of Surgery, Yale University, New Haven, Connecticut

For the Members of the Cancer Committee, College of American Pathologists

Previous contributors: Diane Sneed, MD; Edward Paloyan, MD; Henry Travers, MD

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)

* 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
___p N1b: 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)**

* 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, cytospins, 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 intraprocedural 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 proteinacous 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 Adequacy[1]

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

	Under 45 Years of Age			*45 Years or Older*		
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
Stage III	T1	N1a	M0
	T2	N1a	M0
	T3	N1a	M0
Stage IVA	T4a	N0	M0
	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 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

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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