Thyroid Gland

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

Protocol web posting date: July 2006
Protocol effective date: April 2007
Based on AJCC/UICC TNM, 6th edition

Procedures
• Cytology (No Accompanying Checklist)
• Partial Thyroidectomy
• Total Thyroidectomy With/Without Lymph Node Dissection

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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the “Surgical Pathology Cancer Case Summary (Checklist)” portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The College developed these protocols as an educational tool to assist pathologists in the useful reporting of relevant information. It did not issue the protocols for use in litigation, reimbursement, or other contexts. Nevertheless, the College recognizes that the protocols might be used by hospitals, attorneys, payers, and others. Indeed, effective January 1, 2004, the Commission on Cancer of the American College of Surgeons mandated the use of the checklist elements of the protocols as part of its Cancer Program Standards for Approved Cancer Programs. Therefore, it becomes even more important for pathologists to familiarize themselves with the document. At the same time, the College cautions that use of the protocols other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.
Summary of Changes to Checklist(s)

Protocol web posting date: July 2006
Protocol effective date: April 2007

The following change has been made since the January 2005 revision:

Histologic Type has been updated, as shown below.

**Histologic Type (check all that apply; choose 1 histologic type and all applicable subtypes)**

___ Follicular carcinoma
   Invasiveness, specify
   ___ Minimally invasive
   ___ Grossly encapsulated with angioinvasion
   ___ Widely invasive
   * Variant, specify
     *___ Oncocytic (Hürthle cell) variant
     *___ Clear cell variant

___ Papillary carcinoma
  *Variant, specify
   *___ Microcarcinoma (occult, small or microscopic)
   *___ Encapsulated variant
   *___ Follicular variant
   *___ Macrofollicular variant
   *___ Oncocytic or oxyphilic variant
   *___ Clear cell variant
   *___ Solid variant or radiation-induced pediatric variant
   *___ Cribriform-morular variant
   *___ Warthin-like variant
   *___ Diffuse follicular variant
   *___ Diffuse sclerosing variant
   *___ Tall cell variant
   *___ Columnar cell variant

___ Insular carcinoma (and other poorly differentiated carcinoma)
___ Medullary carcinoma
___ Undifferentiated (anaplastic) carcinoma
___ Other (specify): ____________________________
___ Carcinoma, type cannot be determined
**Surgical Pathology Cancer Case Summary (Checklist)**

*Protocol web posting date: July 2006*

*Protocol effective date: April 2007*

*Applies to invasive carcinomas only*

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

**THYROID: Resection**

Patient name:  
Surgical pathology number:

<table>
<thead>
<tr>
<th>Note: Check 1 response unless otherwise indicated.</th>
</tr>
</thead>
</table>

**MACROSCOPIC**

**Specimen Type**
- ___ Total thyroidectomy
- ___ Lobectomy
- ___ Isthmusectomy
- ___ 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)
MICROSCOPIC

Histologic Type (check all that apply; choose 1 histologic type and all applicable subtypes)

___ Follicular carcinoma
   Invasiveness, specify:
   ___ Minimally invasive
   ___ Grossly encapsulated with angioinvasion
   ___ Widely invasive
   *Variant, specify:
   *___ Oncocytic (Hürthle cell) variant
   *___ Clear cell variant

___ Papillary carcinoma
   *Variant, specify:
   *___ Microcarcinoma (occult, small or microscopic)
   *___ Encapsulated variant
   *___ Follicular variant
   *___ Macrofollicular variant
   *___ Oncocytic or oxyphilic variant
   *___ Clear cell variant
   *___ Solid variant or radiation-induced pediatric variant
   *___ Cribriform-morular variant
   *___ Warthin-like variant
   *___ Diffuse follicular variant
   *___ Diffuse sclerosing variant
   *___ Tall cell variant
   *___ Columnar cell variant

___ Insular carcinoma (and other poorly differentiated carcinoma)

___ Medullary carcinoma

___ Undifferentiated (anaplastic) carcinoma

___ Other (specify): ____________________________

___ Carcinoma, type cannot be determined

* 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.
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 any tumor with minimal extrathyroid extension (e.g., 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
  *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**

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* 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.
*Additional Pathologic Findings (check all that apply)
*___ None identified
*___ Nodular goiter
*___ Adenoma
*___ Thyroiditis
*___ Other (specify): ____________________________

*Comment(s)
Background Documentation

Protocol web posting date: July 2006
Protocol effective date: April 2007

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, isthmusectomy)
   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 - extent (minimally vs widely) (Note C)
      (2) angioinvasion, , 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: extent (minimally vs widely) (Note C)
   (2) angioinvasion (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)

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 Adequacy

<table>
<thead>
<tr>
<th>Number of Follicular Cells</th>
<th>Amount of Colloid</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numerous</td>
<td>Variable</td>
<td>Adequate for interpretation, diagnosis depends on cellular features</td>
</tr>
<tr>
<td>Few</td>
<td>Scanty or Absent</td>
<td>Unsatisfactory#</td>
</tr>
<tr>
<td>Few follicular, numerous histocytes</td>
<td>Variable</td>
<td>Nondiagnostic. Recommend repeat after 3 months, possible under ultrasound guidance.##.###</td>
</tr>
</tbody>
</table>

# 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,
  - Rule out / Suggestive of neoplasm

Malignant
- Non-diagnostic

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

C. Histologic Type

The histologic classification recommended below is modified from the World Health Organization (WHO) published recommendations. 2-4
WHO Classification of Carcinoma of the Thyroid

Follicular carcinoma

Invasiveness
- Minimally invasive
- Grossly encapsulated with angioinvasion
- Widely invasive

Variant
- Oncocytic (Hürthle cell) variant
- Clear cell variant

Papillary carcinoma

Variant
- Microcarcinoma (occult, small or microscopic)
- Encapsulated variant
- Follicular variant
- Macrofollicular variant
- Oncocytic or oxyphilic variant
- Clear cell variant
- Solid variant or radiation-induced pediatric variant
- Cribriform-morular variant
- Warthin-like variant
- Diffuse follicular variant
- Diffuse sclerosing variant
- Tall cell variant
- Columnar cell variant

Insular carcinoma (and other poorly differentiated carcinoma)

Medullary carcinoma

Undifferentiated (anaplastic) carcinoma

Carcinoma, type cannot be determined

The diagnosis of follicular carcinoma, including histologic variants 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. 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.

The criteria defining “minimally invasive” follicular carcinoma is controversial and still evolving. In some schemes, this designation refers to lesions with capsular and/or small caliber sized angioinvasion. However, in other schemes this designation is limited to tumors with capsular invasion but no vascular invasion. Instead, the designation “grossly encapsulated angioinvasive follicular carcinoma” has been suggested. “Widely invasive” follicular carcinomas are those tumors with grossly apparent invasion of thyroid and/or soft tissue (ie, extrathyroidal invasion).

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. 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. Histologic variants of follicular carcinomas, including oncocytic (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)**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension limited to the thyroid</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor more than 2 cm but not more than 4 cm in greatest dimension limited to the thyroid</td>
</tr>
<tr>
<td>T3</td>
<td>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)</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus or recurrent laryngeal nerve</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels</td>
</tr>
</tbody>
</table>

*All anaplastic carcinomas are considered T4 tumors*

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4a</td>
<td>Intrathyroidal anaplastic carcinoma—surgically resectable</td>
</tr>
<tr>
<td>T4b</td>
<td>Extrathyroidal anaplastic carcinoma—surgically unresectable</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1a</td>
<td>Nodal metastases to Level VI (pretracheal, paratracheal and prelaryngeal/Delphian) lymph nodes</td>
</tr>
<tr>
<td>N1b</td>
<td>Metastases to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes</td>
</tr>
</tbody>
</table>
Distant Metastasis (M)
MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis

Stage Groupings

Papillary or Follicular Carcinoma

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IVA</th>
<th>Stage IVB</th>
<th>Stage IVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 45 Years of Age</td>
<td>Any T</td>
<td>Any N</td>
<td>M0</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
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<tr>
<td>45 Years or Older</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>T1</td>
<td>N1a</td>
<td>M0</td>
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<tr>
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<td>M0</td>
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<td>N1a</td>
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<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>T3</td>
<td>N1a</td>
<td>M0</td>
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<tr>
<td>Stage IVA</td>
<td>Any T#</td>
<td>Any N</td>
<td>M0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IVB</td>
<td>T4b</td>
<td>Any N</td>
<td>M0</td>
<td></td>
<td></td>
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<tr>
<td>Stage IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# Except T4b.

Medullary Carcinoma (Any Age)

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IVA</th>
<th>Stage IVB</th>
<th>Stage IVC</th>
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Undifferentiated Carcinoma (All Cases - Stage IV)

<table>
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<th>Stage IVA</th>
<th>Stage IVB</th>
<th>Stage IVC</th>
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<tbody>
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<tr>
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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. 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. 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. 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.

References

Bibliography


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Shin DH, Mark EJ, Suen HC, Grillo HC. Pathologic staging of papillary carcinoma of the thyroid with airway invasion based on the anatomic manner of extension to the trachea: a clinicopathologic study based on 22 patients who underwent thyroidectomy and airway resection. *Hum Pathol.* 1993;24:866-870.