

# Thyroid Gland

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

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*Protocol web posting date: July 2006  
Protocol effective date: April 2007  
Based on AJCC/UICC TNM, 6<sup>th</sup> 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*

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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, 6<sup>th</sup> edition*

### THYROID: Resection

Patient name:

Surgical pathology number:

**Note: Check 1 response unless otherwise indicated.**

### 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 (eg, extension to sternothyroid muscle or perithyroid soft tissues)  
 pT4a: Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus or recurrent laryngeal nerve  
 pT4b: Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels.

Anaplastic Carcinoma

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

Regional Lymph Nodes (pN)

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

Distant Metastasis (pM)

- pMX: Cannot be assessed  
 pM1: Distant metastasis  
 \*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

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*Protocol web posting date: July 2006*

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### **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, cytopsins, 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 site)
8. Comments
  - a. Correlation with intraoperative consultation, as appropriate
  - b. Correlation with other specimens, as appropriate
  - c. Correlation with clinical information, as appropriate

## Explanatory Notes

### A. Specimen Adequacy

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

**Guidelines for the Microscopic Evaluation of Specimen Adequacy<sup>1</sup>**

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

<sup>#</sup> 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.

<sup>##</sup> The report should contain a qualifier stating that the interpretation is limited by the paucity of follicular cells.

<sup>###</sup> 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.<sup>2-4</sup>

**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.<sup>5</sup> 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).<sup>2</sup>

**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.<sup>6,7</sup> 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)

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

*All anaplastic carcinomas are considered T4 tumors*

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

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

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

### Regional Lymph Nodes (N) (see Note G)

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

**Distant Metastasis (M)**

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

**Stage Groupings**

Papillary or Follicular Carcinoma

	<i>Under 45 Years of Age</i>			<i>45 Years or Older</i>		
Stage I	Any T	Any N	M0	T1	N0	M0
Stage II	Any T	Any N	M1	T2	N0	M0
Stage III				T3	N0	M0
				T1	N1a	M0
				T2	N1a	M0
			T3	N1a	M0	
Stage IVA				Any T <sup>#</sup>	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
	T4b	Any N	M0
Stage IVB	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.<sup>8</sup> 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.<sup>9</sup> 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.<sup>10</sup> 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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