Uveal Melanoma

Protocol applies to malignant melanoma of the uvea.

Protocol revision date: January 2005
Based on AJCC/UICC TNM, 6th edition

Procedures
• Cytology (No Accompanying Checklist)
• Biopsy (No Accompanying Checklist)
• Resection Specimen (Enucleation, Limited or Complete Exenteration)

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

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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 revision date: January 2005

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.
Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2005
Applies to melanomas of the uvea only
Based on AJCC/UICC TNM, 6th edition

Uveal Melanoma: Resection

Patient name:  
Surgical pathology number:  

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type

___ Enucleation
___ Limited exenteration
___ Complete exenteration
___ Other (specify): ____________________________
___ Not specified

Laterality

___ Right
___ Left
___ Unspecified

Specimen Size

For Enucleation
Anteroposterior diameter ___ mm
Horizontal diameter ___ mm
Vertical diameter ___ mm
Length of optic nerve ___ mm
Diameter of optic nerve ___ mm
___ Cannot be determined (see Comment)

For Exenteration
Greatest dimension: ___ mm
*Additional dimensions: ___ x ___ mm
___ 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.
**Tumor Site and Extent** (macroscopic examination/transillumination) (check all that apply)
___ Cannot be determined
___ Superotemporal quadrant of globe
___ Superonasal quadrant of globe
___ Inferotemporal quadrant of globe
___ Inferonasal quadrant of globe
___ Anterior chamber
___ Extrascleral extension
___ Optic nerve

* **Tumor Basal Dimensions on Transillumination**
* ___ Cannot be determined
* Specify: ___ x ___ mm

**Tumor Dimensions After Sectioning**
___ Cannot be determined
___ Base at cut edge: ___ mm
* ___ Height at cut edge: ___ mm
___ Maximal tumor height: ___ mm

* **Tumor Location After Sectioning**
* ___ Cannot be determined
* ___ Distance from anterior edge of tumor to limbus at cut edge: ___ mm
* ___ Distance of posterior margin of tumor base from edge of optic disc: ___ mm

**Tumor Involvement or Gross Pathology of Other Ocular Structures** (check all that apply)
___ Cannot be determined
___ Sclera
___ Vortex vein(s)
___ Optic disc
___ Vitreous
___ Choroid
___ Ciliary body
___ Iris
___ Lens
___ Anterior chamber
___ Extrascleral extension
___ Angle/Schlemm's canal
* ___ Cornea
* ___ Retinal detachment

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**Growth Pattern**
- Cannot be determined
- Solid mass
- Ciliary body ring
- Diffuse

**MICROSCOPIC**

**Histologic Type**
- Cannot be determined
- Spindle cell type
* - Spindle cell type, spindle A
* - Spindle cell type, spindle B
- Epithelioid cell type
- Mixed cell type
- Necrotic
* - Balloon cell

*Tumor Location*
* - Cannot be determined
* - Anterior margin located anterior to equator of globe
* - Within 1 mm of optic disc
* - None of above

**Scleral Involvement**
- Cannot be determined
- None
- Extrascleral
- Intrasceral

**Involvement of Other Structures (check all that apply)**
- Cannot be determined
- Vortex vein
- Optic Nerve
- Vitreous
- Retina
- Angle/Schlemm’s canal
- Other(s) (specify): _________________________

* 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): Iris
- **pTX:** Primary tumor cannot be assessed
- **pT0:** No evidence of primary tumor
- **pT1:** Tumor limited to the iris
  - **pT1a:** Tumor limited to the iris not more than 3 clock hours in size
  - **pT1b:** Tumor limited to the iris more than 3 clock hours in size
  - **pT1c:** Tumor limited to the iris with melanomalytic glaucoma
- **pT2:** Tumor confluent with or extending into the ciliary body and/or choroid
  - **pT2a:** Tumor confluent with or extending into the ciliary body and/or choroid with melanomalytic glaucoma
- **pT3:** Tumor confluent with or extending into the ciliary body and/or choroid with extrascleral extension
  - **pT3a:** Tumor confluent with or extending into the ciliary body with extrascleral extension and melanomalytic glaucoma
  - **pT4:** Tumor with extraocular extension

#### Primary Tumor (pT): Ciliary Body and Choroid
- **pTX:** Primary tumor cannot be assessed
- **pT0:** No evidence of primary tumor
- **pT1:** Tumor 10 mm or less in greatest diameter and 2.5 mm or less in greatest height (thickness)
  - **pT1a:** Tumor 10 mm or less in greatest diameter and 2.5 mm or less in greatest height (thickness) without microscopic extraocular extension
  - **pT1b:** Tumor 10 mm or less in greatest diameter and 2.5 mm or less in greatest height (thickness) with microscopic extension
  - **pT1c:** Tumor 10 mm or less in greatest diameter and 2.5 mm or less in greatest height (thickness) with macroscopic extraocular extension
- **pT2:** Tumor greater than 10 mm but not more than 16 mm in greatest basal diameter and between 2.5 and 10 mm in maximum height (thickness)
  - **pT2a:** Tumor 10 mm to 16 mm in greatest basal diameter and between 2.5 and 10 mm in maximum height (thickness) without microscopic extraocular extension
  - **pT2b:** Tumor 10 mm to 16 mm in greatest basal diameter and between 2.5 and 10 mm in maximum height (thickness) with microscopic extraocular extension
  - **pT2c:** Tumor 10 mm to 16 mm in greatest basal diameter and between 2.5 and 10 mm in maximum height (thickness) with macroscopic extraocular extension
- **pT3:** Tumor more than 16 mm in greatest diameter and/or greater than 10 mm in maximum height (thickness) without extraocular extension
- **pT4:** Tumor more than 16 mm in greatest diameter and/or greater than 10 mm in maximum height (thickness) with extraocular extension

*Note: When dimension and elevation show a difference in classification, the highest category should be used for classification.*

* 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.
Regional Lymph Nodes (pN)
___ pNX: Regional lymph nodes cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Regional lymph node metastasis

Distant Metastasis (pM)
___ pMX: Cannot be assessed
___ pM1: Distant metastasis
  *Specify site(s), if known: __________________________

Margins
___ Cannot be assessed
___ No melanoma at margins
___ Extrascleral extension (for enucleation specimens)
___ Other margin involved (specify): __________________________

*Additional Pathologic Findings (check all that apply)
* ___ None identified
* ___ Mitotic rate (number of mitoses per 40X objective
  with a field area of 0.152 mm$^2$): _____
* ___ Necrosis
* ___ Microvascular patterns
* ___ Vascular invasion (tumor vessels or other vessels)
* ___ Degree of pigmentation
* ___ Inflammatory cells/tumor infiltrating lymphocytes
* ___ Drusen
* ___ Retinal detachment
* ___ Invasion of Bruch’s membrane
* ___ Nevus
* ___ Hemorrhage
* ___ Neovascularization
* ___ Other (specify): __________________________

*Comment(s)

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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.
Background Documentation

Protocol revision date: January 2005

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
         a. Relevant history
            (1) clinical findings
            (2) past ocular history
            (3) previous ocular surgery
            (4) previous treatment
         b. Relevant findings (eg, liver function tests, ultrasound)
         c. Clinical diagnosis
         d. Procedure (eg, fine-needle aspiration [FNA], anterior chamber paracentesis)
         e. Operative findings
         f. Anatomic site (right or left eye; part of eye sampled)
   B. Macroscopic Examination
      1. Specimen
         a. Unfixed/fixed (specify fixative)
         b. Number of slides received
         c. Quantity and appearance of fluid specimen
         d. Other (eg, core of tissue in needle shaft)
         e. Intraoperative/intraprocedure consultation
      2. Material submitted for microscopic evaluation (eg, cytocentrifuge, smear, filter preparation)
      3. Material submitted for special studies (specify) (eg, immunocytochemistry)
   C. Microscopic Examination
      1. Adequacy of specimen for evaluation (if unsatisfactory for evaluation, specify reason)
      2. Tumor, if present
         a. Histologic type, if possible (Note A)
         b. Other characteristics (Note B)
            (1) presence of pigment
            (2) cytoplasmic indentation of nucleus
            (3) cytoplasmic vacuolization
      3. Additional pathologic findings, if present (eg, presence of retinal tissue, inflammatory cells)
      4. Retinal tissue
      5. Results/status of special studies (specify)
      6. Comments
         a. Correlation with intraprocedural consultation
         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)
   3. Date of procedure
   4. Other clinical information
      a. Relevant history
         (1) clinical findings
         (2) past ocular history
         (3) previous ocular surgery
         (4) previous treatment
      b. Relevant findings (eg, liver function tests, ultrasound)
      c. Procedure (eg, peripheral iridectomy, iridocyclectomy, sclerouveectomy)
      d. Operative findings
      e. Anatomic site of specimen (right or left eye)
B. Macroscopic Examination
   1. Specimen
      a. Unfixed/fixed (specify fixative)
      b. Orientation (if indicated by surgeon by written instruction, diagram, or suture); ink margins of excisional biopsy specimens
      c. Previously opened
      d. Number of pieces
      e. Size(s) (3 dimensions, if possible)
      f. Tumor
         (1) size (3 dimensions, if possible)
         (2) Presence of necrotic tissue
         (3) descriptive features
      g. Other tissues, as appropriate
      h. Results or intraoperative consultation
   2. Tissue submitted for microscopic evaluation (specify)
   3. Special studies (specify) (eg, special histochemical stains, immunohistochemical stains)
C. Microscopic Evaluation
   1. Tumor
      a. Histologic type (Note A)
      b. Histologic grade
      c. Extent
         (1) involvement of adjacent structures such as ciliary body
         (2) extraocular extension
         (3) invasion of normal vessels or tumor vessels
      d. Other prognostic features (Note B)
   2. Additional pathologic findings, if present
      a. Drusen
      b. Neovascularization
      c. Nevus
      d. Ectropion uveae
      e. Other(s)
3. Results/status of special studies (specify)
4. Comments
   a. Correlation with intraoperative consultation
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

III. Resection Specimen
     (Enucleation, Limited or Complete Exenteration)

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) clinical findings
         (2) past ocular history
         (3) previous ocular surgery
         (4) previous treatment
      b. Relevant findings (eg, liver function tests, ultrasound)
      c. Clinical diagnosis
      d. Procedure (usually enucleation)
      e. Operative findings
      f. Anatomic site of specimen (right or left eye)
   5. Documentation of areas marked by surgeon for orientation (eg, suture, diagram)

B. Macroscopic Examination
   1. Specimen
      a. Organ(s)/tissue(s) included
      b. Unfixed/fixed (specify fixative) (Note C)
      c. Orientation (Note D)
      d. Description of other tissues, as appropriate
      e. Results of intraoperative consultation
   2. Globe
      a. Evidence of previous excision or treatment
      b. Note if previously opened/sectioned and in what fashion (Note E)
      c. Size
         (1) anteroposterior, horizontal, vertical dimensions of globe
         (2) length and diameter of attached optic nerve
         (3) corneal horizontal and vertical diameter
         (4) diameter of pupil (if visible)
      d. Transillumination (helpful to identify location of tumor and measure basal dimension prior to sectioning globe)
         (1) quality of transillumination (eg, poor light transillumination, transilluminates light well)
         (2) transillumination defect
            i. location
            ii. quadrant/relationship to equator of globe
            iii. relationship to limbus
            iv. clock-hour(s) of iris/globe
            v. size (2 dimensions)
e. Mark outline with marking implement
f. Extrascleral extension, if present
g. Sectioning of specimen (globe) (Note E)
h. Mass/tumor, if present
   (1) location
   (2) size (Notes F and G)
      i. base at cut edge (ie, portion of tumor closest to sclera)
      ii. height at cut edge
   (3) distance of anterior margin of tumor base from limbus at cut edge
   (4) distance of posterior margin of tumor base from edge of optic disc
   (5) other descriptive features (color, consistency, shape)
   (6) structures involved and extent (Note G)
      i. retinal involvement
      ii. optic nerve involvement
      iii. macroscopic involvement of vitreous
      iv. involvement of ciliary body
      v. macroscopic involvement of anterior chamber angle
   i. Features of other (uninvolved) ocular tissues
      (1) cornea (eg, clear, cloudy, opaque)
      (2) anterior chamber (eg, deep, shallow, flat)
      (3) angle (eg, open, narrow, closed)
      (4) iris (eg, color, any abnormalities)
      (5) ciliary body
      (6) lens (eg, clear, cataractous, presence of lens implant, absence)
      (7) vitreous (eg, color, consistency, hemorrhage)
      (8) retina (eg, detachment, total or partial; hemorrhages)
      (9) choroid
      (10) sclera (eg, thinning, defects)
      (11) optic disc (eg, pallor, increased cup/disc ratio)
3. Tissues submitted for microscopic examination (specify) (Note F)
4. Special studies (specify) (eg, immunohistochemistry)
C. Microscopic Evaluation
1. Tumor
   a. Site (choroid/ciliary body/iris) (Note G)
   b. Histologic type (Note A)
   c. Histologic grade
   d. Extent of invasion (Note G)
   e. Size (Note F)
   f. Anatomic extent (Notes B and G)
      (1) anterior margin of tumor
      (2) retinal or scleral involvement
      (3) angle involvement
      (4) vitreal involvement
      (5) optic nerve involvement
2. Margins
   a. Extrascleral extension (Notes B and G)
   b. Surgical margin of optic nerve (Note B)
3. Other prognostic features (Note B)
4. Additional pathologic findings, if present
   a. Cancer-related
      (1) cataract
      (2) vitreous hemorrhage
      (3) glaucomatous optic atrophy
(4) secondary angle closure
(5) secondary open-angle glaucoma
(6) iris neovascularization
(7) retinal atrophy
b. Other
(1) corneal disease
(2) diabetic retinopathy
5. Results/status of special studies (specify)
6. Comments
   a. Correlation with intraoperative consultation
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Histologic Type
The modified Callender classification shown below is used for determining cell type, but has prognostic significance only for tumors of the choroid and ciliary body, not those of the iris, which generally have a benign course.\textsuperscript{1-4}

Spindle cell nevus: slender cells with fusiform nuclei, delicate nuclear chromatin and inapparent nucleoli, no mitoses are found
Spindle cell melanoma\#:
   Spindle A: slender cells with a thin, oval nucleus, indistinct nucleoli and often a longitudinal fold in the nuclear membrane
   Spindle B: larger, plumper nuclei with sharply defined, round nucleoli
Mixed cell melanoma: both spindle and epithelioid cells present
Epithelioid cell melanoma\#: larger, more pleomorphic, polygonal cells with large, sometimes multiple nucleoli

\# Spindle cell melanomas have the most favorable prognosis, and epithelioid cell melanomas the least favorable in terms of survival.

B. Other Pathologic Features of Prognostic Significance
Other histologic features with prognostic significance in choroidal and ciliary body melanoma include the number of mitoses in 40 high-powered fields, pigmentation, degree of inflammation, growth pattern (diffuse choroidal melanomas and ring melanomas of the ciliary body have a much less favorable prognosis), location of anterior margin of tumor, degree and patterns of vascularity, blood vessel invasion (both tumor vessels and normal vessels), tumor necrosis, extraocular extension and optic nerve involvement.\textsuperscript{4-15}

C. Fixative
The minimum recommended fixation time for whole globes with intraocular tumors is 48 hours. The globe should be fixed in an adequate volume of fixative with a 10:1 ratio of fixative volume to specimen volume recommended. Incisions or windows in the globe are not necessary for adequate penetration of fixative and are not recommended. Injection of fixative into the globe is also not recommended.
D. Orientation
The orientation of a globe may be determined by identification of extraocular muscle insertions, the optic nerve, and other landmarks, as illustrated in Figure 1. The terms *temporal* and *nasal* are generally used in place of *lateral* and *medial* with reference to ocular anatomy.

**Figure 1.** Anatomic landmarks of the posterior aspect of the globe (right eye). The position of the inferior oblique muscle relative to the optic nerve is most helpful in orienting the globe. The inferior oblique muscle insertion is located temporal (lateral) to the optic nerve on the sclera, and its fibers travel inferonasally from its insertion. The long posterior ciliary artery is often seen as a blue-gray line in the sclera on either side of the optic nerve and marks the horizontal meridian of the globe. *Reprinted with permission from WB Saunders Company.*
E. Sectioning the Globe

The globe is generally sectioned in the horizontal or vertical plane with care to include the pupil and optic nerve in the section to be submitted for microscopic examination. If the mass cannot be included with horizontal or vertical sectioning, the globe is sectioned obliquely to include the tumor, pupil and optic nerve, as illustrated in Figure 2. Alternative methods of sectioning have been described.16

![Diagram showing different sectioning methods](image)

**Figure 2.** The most common methods of sectioning a globe. After transillumination, the tumor base is marked, if possible, and included in the pupil-optic (p-o) nerve section and submitted for processing. If tumor is found in either of the calottes, these may also be submitted for sectioning. The meridian in which the globe was sectioned should be included in the gross description of the pathology report. It is not uncommon to induce an artifactitious retinal detachment while sectioning the globe. This can be minimized by gentle handling and by avoiding a sawing motion with the blade. *Reprinted with permission from WB Saunders Company.*
F. Tumor Size
Tumor size has prognostic significance. Many studies of choroidal and ciliary body melanoma have defined small tumors as being less than 10 mm in greatest diameter. More recently, an ongoing study started in 1986, the Collaborative Ocular Melanoma Study defined the following size classification based on clinical measurements.

Small tumors*: Smaller than medium or large tumors defined below
Medium tumors: Greater than or equal to 2.5 mm, less than or equal to 10 mm in height, and less than or equal to 16 mm in basal diameter
Large tumors: Greater than 10 mm in height or
Greater than 2 mm in height and greater than 16 mm in basal diameter or
Greater than 8 mm in height with optic nerve involvement

# Small tumors have a more favorable prognosis.

G. TNM Stage Groupings
The American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) TNM staging systems for uveal melanoma of the iris, ciliary body, and choroid are shown 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.

Primary Tumor (T): All Uveal Melanomas
TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Primary Tumor (T): Iris
T1  Tumor limited to the iris
T1a Tumor limited to the iris not more than 3 clock hours in size
T1b Tumor limited to the iris more than 3 clock hours in size
T1c Tumor limited to the iris with melanomalytic glaucoma
T2  Tumor confluent with or extending into the ciliary body and/or choroid
T2a Tumor confluent with or extending into the ciliary body and/or choroid with melanomalytic glaucoma
T3  Tumor confluent with or extending into the ciliary body and/or choroid with extrascleral extension
T3a Tumor confluent with or extending into the ciliary body with extrascleral extension and melanomalytic glaucoma
T4  Tumor with extraocular extension

Primary Tumor (T): Ciliary Body and Choroid
T1# Tumor 10 mm or less in greatest diameter and 2.5 mm or less in greatest height (thickness)
T1a Tumor 10 mm or less in greatest diameter and 2.5 mm or less in greatest height (thickness) without microscopic extraocular extension
T1b Tumor 10 mm or less in greatest diameter and 2.5 mm or less in greatest height (thickness) with microscopic extension
T1c Tumor 10 mm or less in greatest diameter and 2.5 mm or less in greatest height (thickness) with macroscopic extraocular extension
T2# Tumor greater than 10 mm but not more than 16 mm in greatest basal diameter and between 2.5 and 10 mm in maximum height (thickness)
T2a Tumor 10 mm to 16 mm in greatest basal diameter and between 2.5 and 10 mm in maximum height (thickness) without microscopic extraocular extension
T2b Tumor 10 mm to 16 mm in greatest basal diameter and between 2.5 and 10 mm in maximum height (thickness) with microscopic extraocular extension
T2c Tumor 10 mm to 16 mm in greatest basal diameter and between 2.5 and 10 mm in maximum height (thickness) with macroscopic extraocular extension
T3# Tumor more than 16 mm in greatest diameter and/or greater than 10 mm in maximum height (thickness) without extraocular extension
T4  Tumor more than 16 mm in greatest diameter and/or greater than 10 mm in maximum height (thickness) with extraocular extension

# When basal dimension and apical height do not fit this classification, the largest tumor diameter should be used for classification. In clinical practice, the tumor base may be estimated in optic disc diameters (dd) (average: 1 dd = 1.5 mm). The height may be estimated in diopters (average: 3 diopters = 1 mm). Techniques such as ultrasonography, visualization, and photography are frequently used to provide more accurate measurements.

Regional Lymph Nodes (N)
NX  Regional lymph nodes cannot be assessed
N0  No regional lymph node metastasis
N1  Regional lymph node metastasis

Distant Metastasis (M)
MX  Presence of distant metastasis cannot be assessed
M0  No distant metastasis
M1  Distant metastasis
TNM Stage Groupings

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It should be noted that regional lymph node involvement is rare in uveal melanoma, but metastasis to the liver and direct extension into the orbit are more common.\(^1\)

**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.

<table>
<thead>
<tr>
<th>RX</th>
<th>Presence of residual tumor cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0</td>
<td>No residual tumor</td>
</tr>
<tr>
<td>R1</td>
<td>Microscopic residual tumor</td>
</tr>
<tr>
<td>R2</td>
<td>Macroscopic residual tumor</td>
</tr>
</tbody>
</table>

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

**References**


**Bibliography**

