Protocol for the Examination of Specimens from Patients with Uveal Melanoma

Version: 4.2.0.0
Protocol Posting Date: September 2025
CAP Laboratory Accreditation Program Protocol Required Use Date: June 2026
The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes local resection, enucleation, and partial or complete exenteration
Tumor Type	**Description**
Uveal melanoma	Limited to melanoma of the iris, ciliary body, and choroid

The following tumor types should NOT be reported using this protocol:

Tumor Type
Cutaneous melanoma (consider Skin Melanoma protocol)

Version Contributors

Authors: Tatyana Milman, MD*, Patricia Chevez-Barrios, MD*, Hans Grossniklaus, MD, MBA*, Ralph Eagle, Jr., MD*, Dan Gombos, MD, FACS*
* Denotes primary author.

For any questions or comments, contact: cancerprotocols@cap.org.

Glossary:
Author: Expert who is a current member of the Cancer Committee, or an expert designated by the chair of the Cancer Committee.
Expert Contributors: Includes members of other CAP committees or external subject matter experts who contribute to the current version of the protocol.

Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is "not applicable" or "cannot be determined."
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with "+" and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (i.e., secondary consultation, second opinion, or review of outside case at second institution).

Synoptic Reporting
All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
    - Anatomic site or specimen, laterality, and procedure
    - Pathologic Stage Classification (pTNM) elements
    - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e., all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

v 4.1.0.1

- pTNM Classification update
- "Gene Expression Profile (GEP)" question update and addition of optional "Other Special Studies (specify)" question response in SPECIAL STUDIES section
- eCP only metadata and eCP only explanatory note electronic link updates

Reporting Template

Protocol Posting Date: September 2025
Select a single response unless otherwise indicated.
CASE SUMMARY: (UVEAL MELANOMA)
Standard(s): AJCC 8

CLINICAL

+Treatment History
___ No known preoperative therapy
___ Preoperative therapy given (specify, if known): _____
___ Not specified

SPECIMEN (Note A)

Procedure (select all that apply)
___ Local resection
___ Enucleation
___ Limited exenteration
___ Complete exenteration
___ Other (specify): _____
___ Not specified

Tumor Sampling for Molecular Studies
___ Yes
___ No
___ Not known

Specimen Laterality
___ Right
___ Left
___ Not specified

TUMOR

Tumor Site (macroscopic examination / transillumination) (Note B) (select all that apply)
___ Superotemporal quadrant of globe
___ Superonasal quadrant of globe
___ Inferotemporal quadrant of globe
___ Inferonasal quadrant of globe
___ Superior quadrant of globe
___ Inferior quadrant of globe
___ Nasal quadrant of globe
___ Temporal quadrant of globe

___ Anterior chamber
___ Other (specify): _____
___ Cannot be determined: _____

Tumor Site after Sectioning (Note C) (select all that apply)
___ Superonasal
___ Inferonasal
___ Superotemporal
___ Inferotemporal
___ Superior quadrant of globe
___ Inferior quadrant of globe
___ Nasal quadrant of globe
___ Temporal quadrant of globe
___ Anterior chamber
___ Other (specify): _____
___ Cannot be determined: _____

+Distance from Anterior Edge of Tumor to Limbus at Cut Edge
Specify in Millimeters (mm)
___ Exact distance: _____ mm
___ At least: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____

+Distance from Posterior Margin of Tumor Base to Edge of Optic Disc
Specify in Millimeters (mm)
___ Exact distance: _____ mm
___ At least: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____

Tumor Size after Sectioning (Note D)
___ Cannot be determined: _____
___ Size can be determined

Greatest Basal Diameter of Tumor
Specify in Millimeters (mm)
___ Exact measurement: _____ mm
___ At least: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____

+Basal Diameter at Cut Edge of Tumor
Specify in Millimeters (mm)
___ Exact measurement: _____ mm
___ At least: _____ mm

___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____

Greatest Thickness of Tumor
Specify in Millimeters (mm)
___ Exact measurement: _____ mm
___ At least: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____

+Thickness at Cut Edge of Tumor
Specify in Millimeters (mm)
___ Exact measurement: _____ mm
___ At least: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____

Tumor Growth Pattern (select all that apply)
___ Solid mass
___ Cavitary
___ Dome shape
___ Mushroom shape
___ Diffuse (ciliary body ring)
___ Diffuse (flat)
___ Other (specify): _____
___ Cannot be determined: _____

Tumor Size in Microscopic Sections (Note D)
___ Cannot be determined: _____
___ Size can be determined

Greatest Basal Diameter of Tumor (microscopic)
Specify in Millimeters (mm)
___ Exact measurement: _____ mm
___ At least: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____

Greatest Thickness of Tumor (microscopic)
Specify in Millimeters (mm)
___ Exact measurement: _____ mm
___ At least: _____ mm
___ Less than 1 mm
___ Other (specify): _____
___ Cannot be determined: _____

Histologic Type (Note E)
___ Spindle cell melanoma (greater than 90% spindle cells)
___ Mixed cell melanoma (greater than 10% epithelioid cells and less than 90% spindle cells)
___ Epithelioid cell melanoma (greater than 90% epithelioid cells)
___ Other histologic type not listed (specify): _____
___ Cannot be determined: _____
+Histologic Type Comment: _____

Other Ocular Structures Involved by Tumor (select all that apply)
___ Sclera (direct invasion)
___ Sclera (within intrascleral emissarial canals)
___ Vortex vein(s)
___ Optic nerve head
___ Vitreous
___ Choroid
___ Ciliary body
___ Iris
___ Lens
___ Anterior chamber
___ Extrascleral extension (anterior)
___ Extrascleral extension (posterior)
___ Angle / Schlemm's canal
___ Optic nerve
___ Retina
___ Other (specify): _____
___ Cannot be determined: _____

+Tumor Location (select all that apply)
___ Anterior margin between ciliary body and iris (sulcus)
___ Anterior margin between equator and ciliary body
___ Anterior margin between disc and equator
___ Posterior margin between ciliary body and iris (sulcus)
___ Posterior margin between equator and ciliary body
___ Posterior margin between disc and equator
___ Other (specify): _____
___ Cannot be determined: _____

Scleral Involvement
___ Not identified
___ Intrascleral, within intrascleral emissarial canals
___ Intrascleral, direct invasion
___ Extrascleral, less than or equal to 5mm in largest diameter
___ Extrascleral, greater than 5mm in largest diameter
___ Cannot be determined: _____

+Tumor Comment: _____

MARGINS

Margin Status
___ All margins negative for melanoma
___ Extrascleral extension of melanoma present (for enucleation specimens)
___ Other (specify): _____
___ Cannot be determined: _____
+Margin Comment: _____

REGIONAL LYMPH NODES

Regional Lymph Node Status
___ Not applicable (no regional lymph nodes submitted or found)
___ Regional lymph nodes present
___ All regional lymph nodes negative for tumor
Discrete Tumor Deposits in Orbit
___ Not identified
___ Present
___ Cannot be determined: _____
___ Tumor present in regional lymph node(s)
Number of Lymph Nodes with Tumor
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
Number of Lymph Nodes Examined
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Regional Lymph Node Comment: _____

DISTANT METASTASIS

Distant Site(s) Involved, if applicable
___ Not applicable
___ Specify site(s): _____
Largest Diameter of Largest Distant Metastasis in Centimeters (cm)

___ Specify in Centimeters (cm): _____ cm
___ Less than or equal to 3 cm
___ 3.1 to 8.0 cm
___ Greater than or equal to 8.1 cm
___ Cannot be determined: _____
___ Cannot be determined: _____

pTNM CLASSIFICATION (AJCC 8th Edition) (Note F)
Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.

Modified Classification (required only if applicable) (select all that apply)
___ Not applicable
___ y (post-neoadjuvant therapy)
___ r (recurrence)

pT Category
___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
Iris
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 secondary glaucoma
___ pT1 (subcategory cannot be determined)
pT2: Tumor confluent with or extending into the ciliary body, choroid, or both
___ pT2a: Tumor confluent with or extending into the ciliary body, without secondary glaucoma
___ pT2b: Tumor confluent with or extending into the ciliary body and choroid, without secondary glaucoma
___ pT2c: Tumor confluent with or extending into the ciliary body, choroid, or both, with secondary glaucoma
___ pT2 (subcategory cannot be determined)
___ pT3: Tumor confluent with or extending into the ciliary body, choroid, or both, with scleral extension
pT4: Tumor with extrascleral extension
___ pT4a: Tumor with extrascleral extension less than or equal to 5 mm in largest diameter
___ pT4b: Tumor with extrascleral extension greater than 5 mm in largest diameter
___ pT4 (subcategory cannot be determined)
Iris melanomas originate from, and are predominantly located in, this region of the uvea. If less than half the tumor volume is located within the iris, the tumor may have originated in the ciliary body, and consideration should be given to classifying it accordingly.
Ciliary Body and Choroid
pT1: Tumor size category 1
___ pT1a: Tumor size category 1 without ciliary body involvement and extraocular extension
___ pT1b: Tumor size category 1 with ciliary body involvement
___ pT1c: Tumor size category 1 without ciliary body involvement but with extraocular extension less than or equal to 5 mm in largest diameter
___ pT1d: Tumor size category 1 with ciliary body involvement and extraocular extension less than or equal to 5 mm in largest diameter

___ pT1 (subcategory cannot be determined)
pT2: Tumor size category 2
___ pT2a: Tumor size category 2 without ciliary body involvement and extraocular extension
___ pT2b: Tumor size category 2 with ciliary body involvement
___ pT2c: Tumor size category 2 without ciliary body involvement but with extraocular extension less than or equal to 5 mm in largest diameter
___ pT2d: Tumor size category 2 with ciliary body involvement and extraocular extension less than or equal to 5 mm in largest diameter
___ pT2 (subcategory cannot be determined)
pT3: Tumor size category 3
___ pT3a: Tumor size category 3 without ciliary body involvement and extraocular extension
___ pT3b: Tumor size category 3 with ciliary body involvement
___ pT3c: Tumor size category 3 without ciliary body involvement but with extraocular extension less than or equal to 5 mm in largest diameter
___ pT3d: Tumor size category 3 with ciliary body involvement and extraocular extension less than or equal to 5 mm in largest diameter
___ pT3 (subcategory cannot be determined)
pT4: Tumor size category 4
___ pT4a: Tumor size category 4 without ciliary body involvement and extraocular extension
___ pT4b: Tumor size category 4 with ciliary body involvement
___ pT4c: Tumor size category 4 without ciliary body involvement but with extraocular extension less than or equal to 5 mm in largest diameter
___ pT4d: Tumor size category 4 with ciliary body involvement and extraocular extension less than or equal to 5 mm in largest diameter
___ pT4e: Any tumor size category with extraocular extension greater than 5 mm in largest diameter
___ pT4 (subcategory cannot be determined)
Primary ciliary body and choroidal melanomas are classified according to the four tumor size categories defined in Figure 3 (CAP Cancer Protocol Explanatory Notes).
In clinical practice, the largest tumor basal diameter may be estimated in optic disc diameters (DD; average: 1 DD = 1.5 mm), and tumor thickness may be estimated in diopters (average: 2.5 diopters = 1 mm). Ultrasonography and fundus photography are used to provide more accurate measurements.
When histopathologic measurements are recorded after fixation, tumor diameter and thickness may be underestimated because of tissue shrinkage.

T Suffix (required only if applicable)
___ Not applicable
___ (m) multiple primary synchronous tumors in a single organ

pN Category
___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)
___ pN0: No regional lymph node metastasis
pN1: Regional lymph node metastasis or discrete tumor deposits in the orbit
___ pN1a: Metastasis in one or more regional lymph node(s)
___ pN1b: No regional lymph nodes are positive, but there are discrete tumor deposits in the orbit that are not contiguous to the eye (choroidal and ciliary body)
___ pN1 (subcategory cannot be determined)

pM Category (required only if confirmed pathologically)
___ Not applicable - pM cannot be determined from the submitted specimen(s)
pM1: Distant metastasis
___ pM1a: Largest diameter of the largest metastasis less than or equal to 3 cm
___ pM1b: Largest diameter of the largest metastasis 3.1-8.0 cm
___ pM1c: Largest diameter of the largest metastasis greater than or equal to 8.1 cm
___ pM1 (subcategory cannot be determined)

ADDITIONAL FINDINGS (Note G)

+Additional Findings (select all that apply)
___ None identified
___ Mitotic rate (number of mitoses per 40 fields determined by using a 40X objective with a field area of 0.152 mm2) (specify): _____ mitoses per 40 high-power fields (HPF)
___ Vasculogenic mimicry patterns (extracellular closed loops and networks, the latter defined as at least 3 back-to-back closed loops, is associated with death from metastatic disease)
___ Vascular invasion (tumor vessels or other vessels)
___ Degree of pigmentation (specify): _____
___ Tumor infiltrating lymphocytes
___ Tumor infiltrating macrophages
___ Drusen
___ Retinal detachment
___ Rupture of Bruch's membrane
___ Nevus
___ Hemorrhage (specify site): _____
___ Neovascularization
___ Other (specify): _____

SPECIAL STUDIES

+Gene Expression Profile (GEP)
___ Class 1
___ Class 2
___ Other (specify): _____

+TCGA Classification
___ Group A
___ Group B
___ Group C
___ Group D

+BAP1 Result by Immunohistochemistry
___ Intact nuclear expression
___ Loss of nuclear expression
___ Cannot be determined (explain): _____

+BAP1 Mutational Analysis
___ No mutation detected
___ Mutation(s) identified: _____

+PRAME Expression Status
___ Positive
___ Negative

+Other Special Studies (specify): _____
COMMENTS

Comment(s): _____

Explanatory Notes

A. Fixative
The minimum recommended fixation time for whole globes with intraocular tumors is 24 to 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.

B. 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.

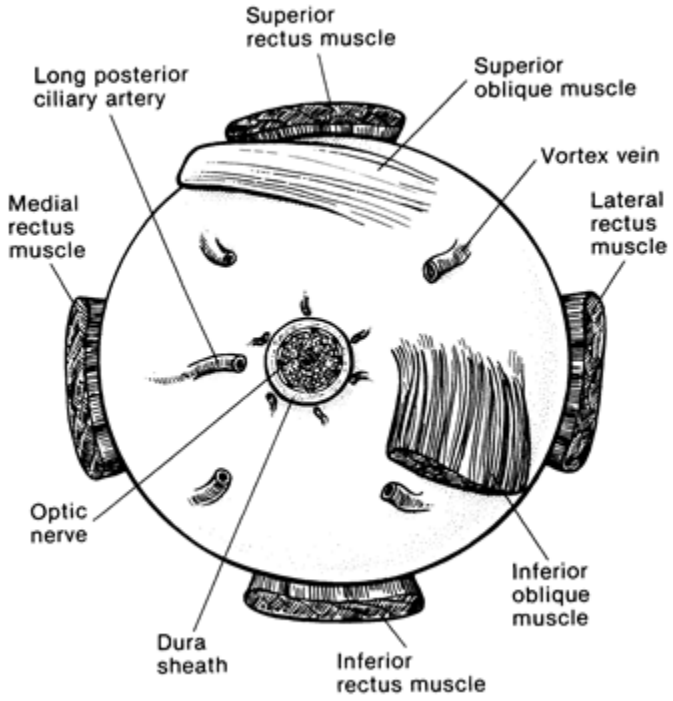

Figure 1. Anatomic landmarks of the posterior aspect of the globe (right eye). The position of the inferior oblique muscle relative to the optic nerve is most helpful in orienting the globe. The inferior oblique muscle insertion is located temporal (lateral) to the optic nerve on the sclera, and its 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.

C. Sectioning the Globe
The globe is generally sectioned in the meridian to include the largest (or the most informative) portion of the tumor, with care to include the pupil and optic nerve in the section to be submitted for microscopic examination, as illustrated in Figure 2. Alternative methods of sectioning have been described.[1,2,3]

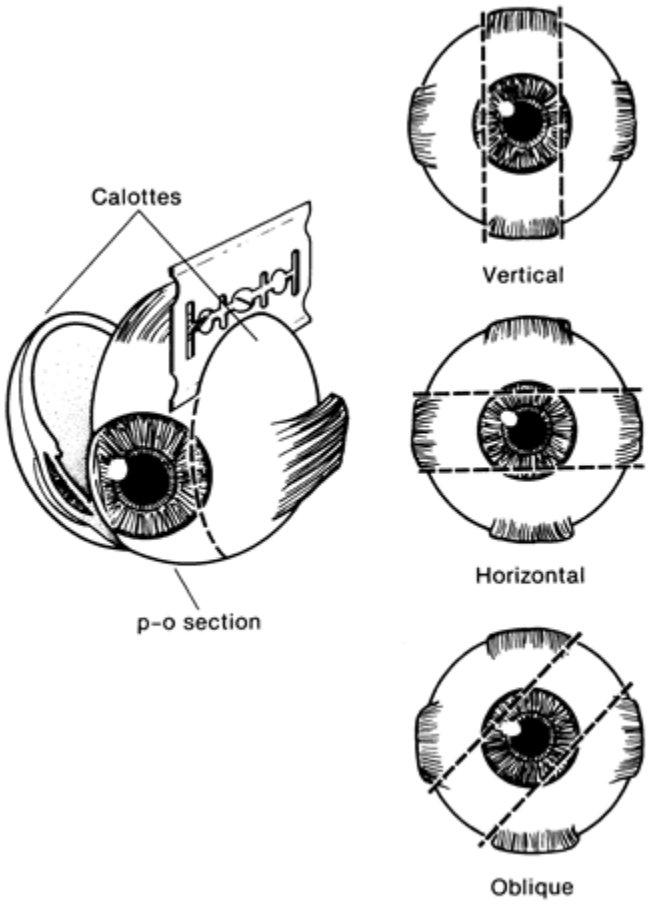

Figure 2. The most common methods of sectioning a globe. After transillumination, the tumor base is marked, if possible, and included in the pupil-optic (p-o) nerve section and submitted for processing. If tumor is found in either of the calottes, these may also be submitted for sectioning. The meridian 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. When a scleral window has been created to retrieve fresh tumor, this window should be included in one of the calottes to allow for an intact PO section. Reprinted with permission from WB Saunders Company.

References

1. Kujala E, Damato B, Coupland SE, et al. Staging of ciliary body and choroidal melanomas based on anatomic extent. *J Clin Oncol.* 2013; 31:2825-2831.
2. Folberg R, Chévez-Barrios P, Lin A Y, Millman T. Pathological examination of ocular specimens. In: *Tumors of the Eye and Ocular Adnexa, Fifth Series of the AFIP Atlases of Tumor and Non-tumor Pathology.* Arlington, Virginia: American Registry of Pathology; 2020. p. 1-9.

3. Folberg R, Chévez-Barrios P, Lin A Y, Millman T. Tumors of the Uvea. In: *Tumors of the Eye and Ocular Adnexa, Fifth Series of the AFIP Atlases of Tumor and Non-tumor Pathology.* Arlington, Virginia: American Registry of Pathology; 2020. p. 167-178.

D. Tumor Size

Tumor greatest basal diameter is measured as the greatest arc of contact of the tumor base with the sclera. The tumor height is measured perpendicular to the sclera from the base of the tumor to its apex. See Figure 3. Tumor size can be also measured on a microscopic slide in accordance with the same guidelines. In general, the largest dimensions (either gross or microscopic) are recorded for T category.[1]

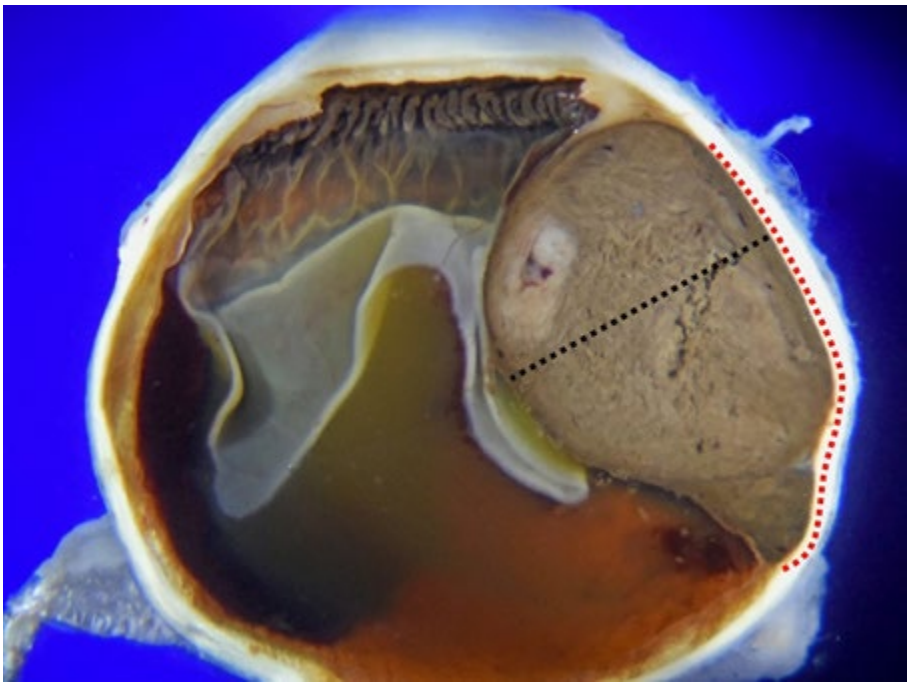

Figure 3. The dotted red line designates the measurement of largest basal diameter. The dotted black line designates the measurement of apical height. Courtesy of Ralph C. Eagle, Jr. M.D.

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.[2] More recently, an ongoing study started in 1986, the Collaborative Ocular Melanoma Study,[3,4] 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 than16 mm in basal diameter *or* Greater than 8 mm in height with optic nerve involvement

#Small tumors have a more favorable prognosis.[5,6]

Since then, the AJCC TNM system defined empirically 4 tumor sizes (Figure 3) – small (T1), medium (T2), large (T3), and very large (T4) – that differ significantly in survival prognosis.[7,8] This size classification was externally validated and is now recommended.

References

1. Folberg R, Chévez-Barrios P, Lin A Y, Millman T. Tumors of the Uvea. In: *Tumors of the Eye and Ocular Adnexa, Fifth Series of the AFIP Atlases of Tumor and Non-tumor Pathology.* Arlington, Virginia: American Registry of Pathology; 2020:167-178.
2. Zimmerman LE. Malignant melanoma of the uveal tract. In: *Spencer WH, ed. Ophthalmic Pathology: An Atlas and Textbook. 3rd ed. Philadelphia, PA*: WB Saunders Co; 1986:2072-2139.
3. Diener-West M, Hawkins BS, Fine SL, et al. The Collaborative Ocular Melanoma Study Group. Design and methods of a clinical trial for a rare condition: COMS report no. 3. *Control Clin Trials.* 1993; 14:362-391.
4. Diener-West M, Earle JD, Fine SL, et al. The Collaborative Ocular Melanoma Study Group. COMS Manual of Procedures. Springfield, VA: National Technical Information Service; 1989. NTIS Accession No. PB90-115536.
5. McLean IW, Foster WD, Zimmerman LE. Prognostic factors in small malignant melanomas of choroid and ciliary body. *Arch Ophthalmol.* 1977; 95:48-58.
6. Affeldt JC, Minckler DS, Azen SP, Yeh L. Prognosis in uveal melanoma with extraocular extension. *Arch Ophthalmol.* 1980; 98:1975-1979.
7. Kujala E, Damato B, Coupland SE, et al. Staging of ciliary body and choroidal melanomas based on anatomic extent. *J Clin Oncol.* 2013; 31:2825-2831.
8. Simpson ER, Gallie BL, Saakyan S, et al. AJCC Ophthalmic Oncology Task Force. International validation of the American Joint Committee on Cancer's 7th edition classification of uveal melanoma. *JAMA Ophthalmol.* 2015; 133:376-383.

E. 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 unless they invade the chamber angle.[1,2,3,4,5,6] The American Joint Committee on Cancer (AJCC) defined the histopathologic types# as follows:[4]

Spindle cell melanoma	(>90% spindle cells)
Mixed cell melanoma	(>10% epithelioid cells and <90% spindle cells)
Epithelioid cell melanoma	(>90% epithelioid cells)

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

Histologic Grade (G)

G	***G Definition***
GX	Grade cannot be assessed
G1	Spindle cell melanoma (>90% spindle cells)
G2	Mixed cell melanoma (>10% epithelioid cells and <90% spindle cells)
G3	Epithelioid cell melanoma (>90% epithelioid cells)
Note: Because of the lack of universal agreement regarding which proportion of epithelioid cells classifies a tumor as mixed or epithelioid, some ophthalmic pathologists currently combine grades 2 and 3 (nonspindle, i.e., epithelioid cells detected) and contrast them with grade 1 (spindle, i.e., no epithelioid cells detected) or even tumors that have no epithelioid cells with those that have any epithelioid cells.	

References

1. Zimmerman LE. Malignant melanoma of the uveal tract. In: *Spencer WH, ed. Ophthalmic Pathology: An Atlas and Textbook. 3rd ed. Philadelphia, PA:* WB Saunders Co; 1986:2072-2139.
2. Folberg R, Verdick R, Weingeist TA, Montague PR. The gross examination of eyes removed for choroidal and ciliary body melanomas. *Ophthalmology.* 1986; 93:1643-1647.
3. Callender GR. Malignant melanotic tumors of the eye: a study of histologic types in 111 cases. Trans Am *Acad Ophthalmol Otolaryngol.* 1931; 36:131-142.
4. McLean IW, Zimmerman LE, Evans RM. Reappraisal of Callender's spindle a type of malignant melanoma of choroid and ciliary body. *Am J Ophthalmol.* 1978; 86:557-564.
5. McLean IW, Foster WD, Zimmerman LE. Modifications of Callender's classification of uveal melanoma at the Armed Forces Institute of Pathology. *Am J Ophthalmol.* 1983; 96:502-509.
6. Folberg R, Chévez-Barrios P, Lin A Y, Millman T. Tumors of the Uvea. In: *Tumors of the Eye and Ocular Adnexa, Fifth Series of the AFIP Atlases of Tumor and Non-tumor Pathology.* Arlington, Virginia: American Registry of Pathology; 2020. p. 167-178.

F. pTNM Classification

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.[1]
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.

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 (i,e., 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 (i.e., 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 (e.g., 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).

T Category Considerations
Iris melanomas originate from, and are predominantly located in, this region of the uvea. If less than half of the tumor volume is located within the iris, the tumor may have originated in the ciliary body, and consideration should be given to classifying it accordingly.
Ciliary Body and Choroid
Primary ciliary body and choroidal melanomas are classified according to the 4 tumor size categories below[1]:

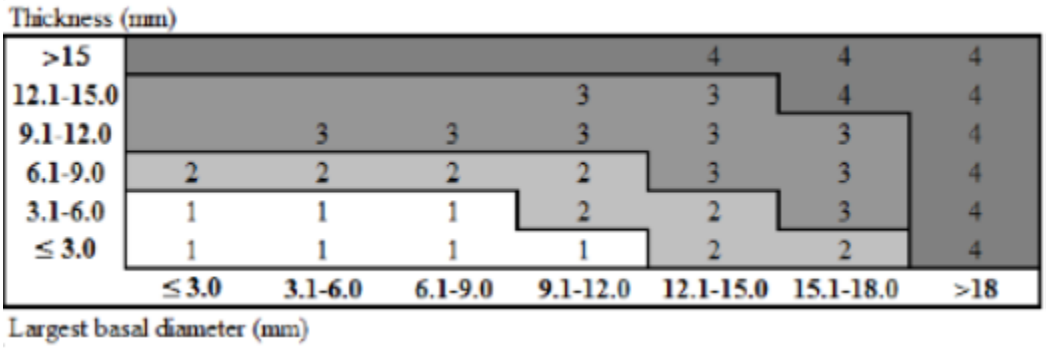

Figure 3. In clinical practice, the largest tumor basal diameter may be estimated in optic disc diameters (dd, average: 1 dd = 1.5 mm). Tumor thickness may be estimated in diopters (average: 2.5 diopters = 1 mm). However, techniques such as ultrasonography and fundus photography are used to provide more accurate measurements. Ciliary body involvement can be evaluated by the slit-lamp, ophthalmoscopy, gonioscopy, and transillumination. However, high-frequency ultrasonography (ultrasound biomicroscopy) is used for more accurate assessment. Extension through the sclera is evaluated visually before and during surgery, and with ultrasonography, computed tomography, or magnetic resonance imaging.

When histopathologic measurements are recorded after fixation, tumor diameter and thickness may be underestimated because of tissue shrinkage.

Lymph-Vascular Invasion (LVI)

LVI indicates whether microscopic lymph-vascular invasion is identified in the pathology report. LVI includes lymphatic invasion, vascular invasion, or lymph-vascular invasion. By AJCC/UICC convention, LVI does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category. 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]

Stage Grouping

Stage I	T1a	N0	M0
Stage IIA	T1b-d	N0	M0
	T2a	N0	M0
Stage IIB	T2b	N0	M0
	T3a	N0	M0
Stage IIIA	T2c-d	N0	M0
	T3b-c	N0	M0
	T4a	N0	M0
Stage IIIB	T3d	N0	M0
	T4b-c	N0	M0
Stage IIIC	T4d-e	N0	M0
Stage IV	Any T	N1	M0
	Any T	Any N	M1a-c

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G. 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, tumor infiltrating lymphocytes, tumor infiltrating macrophages, 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, optic nerve involvement, and lack of nuclear BAP1 immunostaining.[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19]

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