

**RECOMMENDATIONS FOR THE REPORTING OF TISSUES REMOVED AS  
PART OF THE SURGICAL TREATMENT OF COMMON MALIGNANCIES OF  
THE EYE AND ITS ADNEXA**

Robert Folberg M.D. (chairperson), Diva Salomao M.D., Hans E. Grossniklaus M.D.,  
Alan D. Proia M.D., Ph.D., Narsing A. Rao M.D., J. Douglas Cameron M.D.  
Departments of Pathology at the University of Illinois at Chicago, Mayo Clinic, Emory  
University, Duke University and Keck School of Medicine-University of Southern  
California

**THE ASSOCIATION OF DIRECTORS OF ANATOMIC AND SURGICAL PATHOLOGY**

Address correspondence to

Robert Folberg, MD  
University of Illinois at Chicago,  
Department of Pathology (MC 847),  
1819 West Polk Street, Room 446,  
Chicago, IL 60612-7335, U.S.A.

## **Introduction for ADASP reporting Guidelines**

It has been evident for decades that pathology reports are very variable even within a single institution. Standardization of reporting is the optimal way to insure that information necessary for patient management, prognostic and predictive factor assessment, grading, staging, analysis of outcomes and tumor registries is included in pathology reports. In recent years, two societies (first ADASP and then the CAP), have undertaken to publish guidelines for the reporting of common cancers. The CAP assigned multidisciplinary groups of pathologists, surgeons, radiation and medical oncologists to develop the protocols. They were then reviewed by other pathologists and clinicians. After those reviews the protocols were reviewed by multiple CAP committees and finally approved by the Board of Governors.

The ADASP, in contrast, chose a pathologist expert in each field to assemble a group from within the pathology community (with clinician input if desired ) to write specific cancer protocols. These were then approved by the ADASP council and subsequently by the membership. Even though both societies began the process at approximately the same time the streamlined approach adopted by the ADASP enabled them to publish years earlier in pathology journals frequented by anatomic pathologists. While the formats are somewhat different, the contents are essentially the same.

The American College of Surgery (ACS) Commission on Cancer (COC) accredits cancer centers in the USA. Recently, the COC decided to require elements, deemed as essential by the CAP, to be described in all pathology reports in their accredited cancer centers as of January 2004. Importantly they do not require that the specific CAP protocols or synoptic reports be utilized. ADASP has updated all of its protocols to comply with the COC requirements in the form of 37 uniform checklists. The checklists use the staging criteria cited in the American Joint Committee on Cancer (AJCC) 2002 staging manual (sixth edition) but include a variety of other references listed in each of the checklists. Moreover, the checklists are formatted for ease of use. They may be used as templates for uniform reporting and are designed to be compatible with voice activated transcription.

The different elements in these revised ADASP Diagnostic Checklists have been divided into *Required* and *Optional* . The term *Required* in this context only signifies compliance with the COC guidelines. ADASP realizes that specimens and practices vary and it will not be possible to report these elements in every case. However, ADASP hopes that pathologists will find these checklists to be useful in daily clinical practice, while facilitating compliance with the new COC requirements.

The checklists are in standard PDF file format, and may be easily downloaded from the ADASP website. They are not to be reproduced, altered or used for commercial purposes without consent from ADASP.

## **RECOMMENDATIONS FOR THE REPORTING OF COMMON MALIGNANCIES OF THE EYE AND ITS ADNEXA**

### **Introduction**

Before the public awareness of AIDS and Alzheimer's disease as health problems, the disease feared most by Americans was cancer; the second most feared condition was blindness (Gallup Organization, Inc. Public knowledge and attitudes concerning blindness: a survey sponsored by Research to Prevent Blindness, Inc., New York, October 1965 and April 1976, unpublished data). Patients who are confronted with a diagnosis of ocular cancer therefore face two of their most principal fears: shortening of their lifespan and loss of vision. Ophthalmologists who manage most patients with ocular malignancies often try to balance the patient's desire to preserve vision with the goal of eradicating the cancer. In general, the pathologist's report should catalog not only those features appropriate for estimating the natural history of the patient's disease (prognosis) but also those features that might compromise vision.

In general, it is recommended that pathologists report on malignancies of the orbit using formats either published or in development for the counterpart lesion elsewhere in the body. For example, lymphomas of the orbit should be reported according to generalized recommendations for reporting lymphomas. It is reasonable for the report for rhabdomyosarcoma (the most common primary malignancy of the orbit in childhood in the United States) to follow recommendations for reporting rhabdomyosarcomas in general. The lacrimal gland may be considered to be a minor salivary gland for the purposes of reporting malignancies in this region, and pathology reports dealing with lacrimal gland malignancies (principally adenoid cystic carcinoma) should follow recommendations for reporting this tumor as described for the salivary gland.

Recommendations are therefore offered for three classes of ocular malignancies:

conjunctival neoplasms (including those affecting the limbus, the junction between the cornea and sclera), sebaceous carcinoma (a common malignancy of the eyelid), and the two major intraocular neoplasms (retinoblastoma and malignant melanoma).

General-The Association recommends that the following features be included in the final report because they are generally accepted as being of prognostic importance, of visual importance, required for staging or therapy, and/or traditionally expected.

- A. How the specimen was received (eg, fresh or in fixative)
- B. How the specimen was identified (eg, labeled with the name, medical record number, and surgeon's name)
- C. Laterality of the lesion (eg, originating from the right or left eye)
- D. Exact anatomic location of the tumor
  - 1. Conjunctiva: bulbar (by quadrant: superior, inferior, nasal, temporal), palpebral (superior or inferior), fornix (superior or inferior)
  - 2. Limbus (by clock hour)
  - 3. Caruncle or plica semilunaris
  - 4. Eyelid (upper, lower, medial canthus, lateral canthus)
  - 5. Intraocular tissue (iris, ciliary body; by clock hour)

E. Type of surgical procedure

1. Incisional biopsy, excisional biopsy, shave biopsy (conjunctiva, eyelids)
2. Iridectomy (removal of iris tissue), iridocyclectomy (removal of iris and ciliary body tissue)
3. Enucleation (removal of eye)
4. Exenteration (removal of the eye and orbital contents, with or without eyelids, not covered in this report)

## **Gross description**

### **A. Conjunctival and eyelid biopsy**

1. Dimensions of the specimen (length, width, thickness)
2. Maximum diameter of any visible lesion
3. Measurement of minimum distance between edge of lesion and surgical margin (minimum clearance)
4. Presence or absence of ulceration
5. Color of the lesion and adjacent tissue
6. Description of attached tissue (episclera, cornea)
7. Orientation of the lesion if provided by the surgeon
  - a. Some surgeons will identify surgical margins of interest by applying a suture to an edge of the specimen, painting certain margins with dyes, or attaching the specimen to a piece of filter paper and making notations on the specimen mount.

### **B. Iridectomy/iridocyclectomy**

1. Dimensions of the specimen (length, width, thickness)
2. Description of tissue received (iris only, iris and ciliary body, iris, ciliary body, and peripheral cornea and/or sclera, including location by clock hour)
3. Dimensions of lesion (length, width, height)

4. Measurement of minimum distance between edge of lesion and surgical margin  
(minimum clearance)

a. Relevant surgical margins include the lateral margins and the posterior margin  
(the anterior margin is the pupillary border and is not a true surgical margin)

D. Enucleation

1. Dimensions of the eye (anterior-posterior, horizontal, vertical)
2. Length of optic nerve attached
3. Examination of the surface of the eye for gross evidence of extraocular extension of tumor
4. Dimensions of the cornea (horizontal and vertical)
5. Clarity of the cornea
6. Color of the iris (describe lesions, if present)
7. Shape and diameter of the pupil
8. Transillumination of the eye with dimensions of any shadows
  - a. Transillumination of the eye may be performed with a fiberoptic light source to locate a tumor within the eye by the shadow that it casts during this procedure.
  - b. Location of transillumination shadow(s) relative to the limbus and optic nerve  
(distance of shadow borders from limbus and optic nerve)

- c. Location of the shadow relative to clock hour
9. Describe the section plane used to open the eye.
  10. Obtain cross section of the optic nerve.
- E. Obtain a section from either the surgical margin of the optic nerve (the transected edge) or the cut surface of the optic nerve as it inserts in the eye.
1. If the cut section of the optic nerve adjacent to the eye is negative for tumor, then one may conclude that there is no involvement of the nerve posterior to the eye (tumor extends through the nerve without skip lesions).
  2. Frequently, the surgical margin of the optic nerve (the cut edge of the nerve) is crushed by enucleation scissors.
- F. Describe the cut surface of the eye.

### **Retinoblastoma**

1. Number and size of lesions
2. Location of the lesion(s)
3. Gross evidence of choroidal invasion or extraocular extension
4. Presence or absence of vitreous seeding
5. Presence or absence of retinal detachment

### **Uveal melanoma**

1. Tissues involved (choroid only, choroid and ciliary body, ciliary body only, iris and ciliary body, iris only)
2. Location of the melanoma relative to clock hour
3. Dimensions from cut surface (maximum zone of scleral contact, dimension perpendicular to maximum zone of scleral contact, elevation measured from top of lesion to interface with sclera)
4. Color of the surface lesion
  - a. Color of the lesion may provide important clinicopathologic correlations to the ophthalmologist.
5. A white plaque over the surface of the lesion may indicate fibrous metaplasia of the overlying retinal pigment epithelium.
6. Orange pigment over the surface of the tumor (lipofuscin) is considered by some ophthalmologists as clinical evidence of an aggressive tumor.
7. Color of the cut surface of the lesion (melanotic, amelanotic, variegated)
8. Presence or absence of retinal detachment or hemorrhage
9. Presence or absence of extraocular extension or involvement of intrascleral emissary channels

## **Microscopic description**

### **A. Conjunctival squamous cell carcinoma**

1. State presence or absence of invasion into underlying tissues (episclera, corneal stroma).
2. State presence or absence of tumor at resection margins, including the deep margin and all lateral margins.
3. State degree of differentiation (well differentiated, moderately differentiated, poorly differentiated).
4. State type (ordinary squamous cell carcinoma, spindle cell variant of squamous cell carcinoma, mucoepidermoid carcinoma).
5. State presence or absence of vascular, lymphatic, perineural, intraocular, or intraorbital invasion.

### **B. Conjunctival malignant melanoma**

1. State presence or absence of invasion into underlying tissues (episclera, corneal stroma).
2. State presence or absence of tumor at resection margins, including the deep margin and all lateral margins (description of margins should include presence or absence of intraepithelial primary acquired melanosis with atypia, see *Note*).

3. Thickness of the tumor in millimeters and tenths of millimeters as measured by the Jakobiec modification of the Breslow method using a calibrated ocular micrometer.

The tumor thickness is measured from the top of the epithelium (there is no granular layer in the normal conjunctival epithelium).

- a. Some pathologists consider a depth of invasion of 0.8 mm to be significant in separating patients at high risk for metastasis from those at low risk.

4. Intralymphatic invasion by tumor

5. Optional criteria

- a. Mitotic figures; proliferation indices using markers, such as MIB-1 or Ki-67

### **C. Sebaceous carcinoma of the eyelid**

1. Location of the tumor (upper eyelid versus lower eyelid)

2. Size (mm)

- a. Some pathologists consider this measurement to be optional.

3. Gland of origin (Meibomian vs. Zeis gland)

4. State presence or absence of infiltrative growth pattern.

5. Differentiation

- a. Some pathologists consider the differentiation of sebaceous carcinoma to be an optional feature of the report.

6. Multicentricity
7. Intraepithelial (intraepidermal) pagetoid involvement in conjunctiva, cornea, or eyelid skin
8. Tumor involvement of lymphatics or blood vessels or intraorbital invasion
9. State presence or absence of tumor at resection margins, including the deep margin and all lateral margins

#### **D. Retinoblastoma**

1. Growth pattern (diffuse, unifocal, multifocal)
2. Bilaterality and trilaterality (bilateral with involvement of the pineal gland)
3. Differentiation (presence of Flexner-Wintersteiner rosettes, Homer Wright rosettes, and fleurettes)
4. Invasion into the optic nerve by layer (prelaminar, laminar, retrolaminar, to optic nerve resection margin)
5. Extraocular extension
6. Some pathologists and oncologists consider choroidal invasion to be a significant risk factor for metastasis, although this feature is not universally accepted as prognostically significant.
7. Optional features of the tumor

- a. Endophytic versus exophytic, presence and degree of tumor necrosis, calcification, DNA deposition around blood vessels, vitreous seeding, anterior chamber seeding (pseudohypopyon)
8. Effects of the tumor on the eye
- a. Retinal detachment; iris neovascularization

#### **E. Uveal malignant melanoma**

1. Location (confined to the iris, involving the iris and ciliary body, confined to the ciliary body, involving the ciliary body and choroid, involving the iris, ciliary body and choroid, or confined to the choroid)
2. Extraocular extension
3. Growth pattern: diffuse melanoma, ring melanoma, focal melanoma
4. Cell type (McLean's modification of the Callender classification)
5. Mitotic figures per 40 high power fields
6. Presence or absence of 100 tumor infiltrating lymphocytes per 20 high power fields
7. Matrix-rich microcirculation-associated loops, networks or parallel with cross-linking structures (some pathologists have suggested that microvascular density is also a prognostic feature)
8. Optional features

- a. Pertaining to the tumor: presence of absence of nevus, necrosis, intrascleral invasion, invasion into the trabecular meshwork, or invasion into the vortex veins; cytomorphometric measurement of nucleolar diameter (mean of the largest nucleoli or standard deviation of nucleolar area), proliferation indices, cytogenetic abnormalities (especially chromosomes 3 and 8)
  
- b. Effects of the tumor on the eye: retinal detachment, Bruch's membrane rupture, retinal invasion, iris neovascularization, angle closure, cataract

**Note:**

Ophthalmic pathologists use the term "primary acquired melanosis with atypia" in place of the following terms: intraepithelial atypical melanocytic hyperplasia, malignant melanoma in situ, Level I malignant melanoma.

## REFERENCES

### Examination of Ocular Tissues

1. Folberg R, Verdick RE, Weingeist TA, et al. Gross examination of eyes removed for choroidal or ciliary body melanoma. *Ophthalmology* 1986; 93:1643-7.
2. Torczynski E. Preparation of ocular specimens for histopathologic examination. *Ophthalmology* 1981; 88:1367-71.

### Conjunctival Squamous Cell Carcinoma and Its Variants

3. Cohen BH, Green R, Iliff NT, et al. Spindle cell carcinoma of the conjunctiva. *Arch Ophthalmol* 1980; 98:1809-13.
4. Rao NA, Font RL. Mucoepidermoid carcinoma of the conjunctiva. *Cancer* 1976; 38:1699-709.
5. Zimmerman LE. The cancerous, precancerous, and pseudo-cancerous lesions of the cornea and conjunctiva. In: Rycroft PV, ed. *Corneoplastic Surgery: Proceedings of the Second International Corneoplastic Conference*. Oxford: Pergamon Press, 1969: 547.

### Conjunctival Malignant Melanoma

1. Folberg R, McLean IW, Zimmerman LE. Malignant melanoma of the conjunctiva. *Hum Pathol* 1985; 16:126-43.
2. Folberg R, Jakobiec FA, McLean IW, et al. Is primary acquired melanosis equivalent to melanoma in situ? *Mod Pathol* 1992; 5:2-5.
3. Jakobiec FA, Folberg R, Iwamoto T. Clinicopathologic characteristics of premalignant and malignant melanocytic lesions of the conjunctiva. *Ophthalmology* 1989; 96:147-66.
4. Seregard S. Conjunctival melanoma. *Surv Ophthalmol* 1998; 42:321-50.

### Sebaceous Carcinoma of the Eyelid

1. Rao NA, Hidayat AA, McLean IW, et al. Sebaceous gland carcinoma of the ocular adnexa: a clinicopathologic study of 104 cases with five year follow-up data. *Hum Pathol* 1982; 13:113-22.

### **Retinoblastoma**

1. Kopelman JE, McLean IW, Rosenberg SH. Multivariate analysis of risk factors for metastasis in retinoblastoma treated by enucleation. *Ophthalmology* 1987; 94:371-7.
2. Messmer EP, Heinrich T, Höpping W, et al. Risk factors for metastases in patients with retinoblastoma. *Ophthalmology* 1991; 98:136-41.
3. McLean IW, Rosenberg SH, Messmer EP, et al. Prognostic factors in cases of retinoblastoma: analysis of 974 patients from Germany and the United States treated by enucleation. In: Bornfeld N, Gragoudas ES, Höpping W, et al., eds. *Tumors of the Eye: Proceedings of the International Symposium on Tumors of the Eye*. Amsterdam: Kugler, 1991: 69-72.
4. McLean IW, Burnier MN, Zimmerman LE, et al. Tumors of the eye and ocular adnexa. In: *Atlas of Tumor Pathology*, 3rd series, fascicle 12. Washington, DC: Armed Forces Institute of Pathology, 1994:4

### **Uveal Malignant Melanoma**

1. de la Cruz Jr , PO Specht CS, McLean IW. Lymphocytic infiltration in uveal malignant melanoma. *Cancer* 1990; 65:112-5.
2. Folberg R, Rummelt V, Parys-van Ginderdeuren R, et al. The prognostic value of tumor blood vessel morphology in primary uveal melanoma. *Ophthalmology* 1993; 100:1389-98.
3. Grossniklaus HE, Oakman JH, Cohen C, et al. Histopathology, morphometry, and nuclear DNA content of iris melanocytic lesions. *Invest Ophthalmol Vis Sci* 1995; 1394:745-50.
4. Jakobiec FA, Silbert G. Are most iris "melanomas" nevi? *Arch Ophthalmol* 1981; 99:2117-32.
5. McLean IW, Foster WD, Zimmerman LE, et al. Modifications of Callender's classification of uveal melanoma at the Armed Forces Institute of Pathology. *Am J Ophthalmol* 1983; 96:502-9.
6. Mooy CM, De Jong PTVM. Prognostic parameters in uveal melanoma: a review. *Surv Ophthalmol* 1996; 41:215-28.
7. Seregard S, Oskarsson M, Spangberg B. PC-10 as a predictor of prognosis after antigen retrieval in posterior uveal melanoma. *Invest Ophthalmol Vis Sci* 1996; 37:1451-8.
8. Sorensen FB, Gamel JW, Jensen OA, et al. Prognostic value of nucleolar size and size pleomorphism in choroidal melanomas. *APMIS* 1993; 101:358-68.

1. Site (circle all affected)
  - Conjunctiva
  - Bulbar, palpebral, fornix
  - Caruncle
  - Plica semilunaris
  - Limbus
  - Cornea
2. Procedure
  - Excisional biopsy
  - Incisional biopsy
  - Debridement of corneal epithelium
3. Involvement of: (circle all that apply)
  - Corneal stroma
  - Episclera
  - Orbital fat
4. Type (circle one)
  - Squamous cell carcinoma, common type
  - Spindle cell variant, squamous cell carcinoma
  - Acantholytic variant, squamous cell carcinoma
  - Mucoepidermoid carcinoma
5. Excision (circle one)
  - Complete
  - Not complete laterally (indicate affected margins)  
but complete in depth
  - Not complete in depth but complete laterally
  - Not complete either laterally or in depth
6. Vascular invasion (circle one)
  - Absent
  - Blood vessels
  - Lymphatics
  - Blood vessels and lymphatics

FIG. 1. Checklist for conjunctival squamous cell carcinoma.

1. Site (circle all affected)
  - Conjunctiva
  - Bulbar, palpebral, fornix
  - Caruncle
  - Plica semilunaris
  - Limbus
  - Cornea
2. Procedure
  - Excisional biopsy
  - Incisional biopsy
  - Debridement of corneal epithelium
3. Involvement of the (circle all that apply)
  - Corneal stroma
  - Episclera
  - Orbital fat
4. Thickness (mm)
5. Mitoses
6. Vascular invasion (circle one)
  - Absent
  - Blood vessels
  - Lymphatics
  - Blood vessels and lymphatics

FIG. 2. Checklist for conjunctival melanoma.

1. Site
2. Procedure (circle one)
  - Excisional biopsy
  - Incisional biopsy
  - Shave biopsy
  - Map biopsy (conjunctiva)
3. Lesion (circle one)
  - Unifocal
  - Multifocal
4. Origin (circle one)
  - Zeis gland
  - Meibomian gland
  - Both Zeis and Meibomian glands
5. Size (mm)
6. Infiltrative growth pattern (circle one)
  - Absent
  - Present
7. Pagetoid spread (circle one)
  - Absent
  - Present
8. Excision (circle one)
  - Complete
  - Not complete laterally (indicate affected margins)  
but complete in depth
  - Not complete in depth but complete laterally
  - Not complete either laterally or in depth

FIG. 3. Checklist for sebaceous carcinoma, eyelid, and/or conjunctiva.

1. Site  
Right eye, left eye
2. Growth pattern (circle one)  
Diffuse  
Unifocal  
Multifocal
3. Extraocular extension (circle one)  
Absent  
Present
4. Invasion into the optic nerve (circle one)  
None  
Prelaminar  
To the lamina scleralis (cribrosa)  
Retrolaminar  
Posterior resection margin
5. Differentiation (circle all that apply)  
Poorly differentiated  
Flexner-Wintersteiner rosettes  
Home Wright rosettes  
Fleurettes

FIG. 4. Checklist for retinoblastoma.

1. Location (circle all involved)  
Iris  
Ciliary body  
Choroid
2. Extraocular extension  
Yes  
No
3. Growth pattern (circle one)  
Diffuse  
Ring  
Focal
4. Dimension of largest diameter in contact with the sclera (mm)
5. Cell type (Callender classification—circle one)  
Spindle cell type  
Mixed cell type  
Epithelioid cell type  
Necrotic
6. Number of mitotic figures per 40× field
7. Presence of >100 tumor infiltrating lymphocytes per 20 high power field (circle one)  
Present  
Absent
8. Matrix-rich microcirculation-associated patterns (circle all that apply)  
Nevus-like (normal, avascular, straight, parallel)  
Loops  
Networks  
Parallel vessels with cross-linking

FIG. 5. Checklist for uveal melanoma.