

Intraocular (Uveal) Melanoma Malignant intraocular (uveal) melanoma is the most common eye cancer in adults. The tumor affects the uveal tract, which is the middle layer of the wall of the eye.

The most common site for ocular melanoma is the choroid, followed by the ciliary body, and the iris.

In the United States, choroidal melanoma affects approximately 2500 people per year with an incidence of 6 per million. Ocular melanoma is more common in fair-skinned individuals. Smoking increases the risk for the condition, which typically affects people in their 60s. Unlike skin (cutaneous) melanoma, ocular melanoma is generally not associated with previous sun exposure.

In rare cases, a genetic condition may increase a person's chances of developing ocular melanoma, but it does not "run" in families. Children, brothers, sisters, and parents of ocular melanoma patients may be screened, but are almost universally free from the condition.

Unlike other severe eye diseases, ocular melanoma does not show signs or symptoms in the vast majority of patients. When symptoms are present, they are non-specific and include **floaters**, **flashes**, or loss of vision from the affected eye. Rarely is the eye red or painful. As such, uveal melanoma is most often recognized by the primary eye care specialist. In these instances, the patient is typically referred to a retina specialist and often an ocular oncologist (eye cancer specialist).

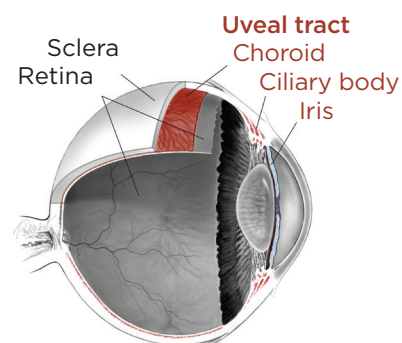
Diagnostic testing

During a targeted tumor examination, diagnostic testing typically includes a complete eye exam with dilation of the **fundus**, indirect **ophthalmoscopy**, tumor photography (**fundus photography**), tumor ultrasound, and vascular studies of the tumor (**fluorescein angiography**, **indocyanine green angiography**, **spectral-domain OCT angiography** (sd OCT)), along with laser studies of the **macula**. These imaging studies evaluate the tumor, allowing documentation of the clinical diagnosis. (See Clinical Terms section for other related screenings.) The ocular tumor is then *staged*—a process that defines the extent of tumor based on its length, width, and height.

Historically, tumors were sized using the Collaborative Ocular Melanoma Study (COMS) staging criteria, but recent advances in staging now incorporate multiple factors preoperatively and are often modified by inclusion of tumor genetics obtained during surgery. The *Eighth Edition American Joint Committee on Cancer (AJCC) Cancer Staging Manual* has updated the staging of ocular melanoma. A biopsy of the melanoma reveals tumor genetics that can give the patient and physician an understanding of the risk of the tumor spreading.

continued next page

RETINAL UVEAL TRACT



The eye has 3 layers:

- The *sclera*—the rigid, white wall of the eye
- The *uvea*—the pigmented blood supplying middle of the eye wall
- The *retina*—the clear tissue that functions like film in a camera

The uveal tract, where intraocular melanoma develops, has 3 main parts:

- The *choroid*—the tissue layer filled with blood vessels
- The *ciliary body*—the ring of muscle tissue that changes the size of the pupil and the shape of the lens
- The *iris*—the colored part of the eye

Intraocular (Uveal) Melanoma *continued from previous page*

Diagnosis

An ocular oncologist will typically make and discuss a diagnosis at the time of the completed examination. Unlike in other oncology specialties, a biopsy for diagnosis is rarely required. However, advances in genetic testing can only be utilized with the availability of a tumor tissue sample. These samples are taken after the clinical diagnosis of intraocular melanoma is made and are often gathered at the time of treatment. After diagnosis, treatment options that range from observation, laser, vitrectomy, radiation, or enucleation (removal) of the tumor-bearing eye are discussed.

For patients with high-risk tumors, or those requiring surgery, further testing is indicated to determine whether the eye tumor is present outside of the eye (metastatic screening) or to ensure the patient can be safely taken to the operating room for treatment.

In many cases, the patient is seen by a primary care eye specialist, followed by a vitreoretinal specialist, and finally by the ocular oncologist. Most patients do not need an additional evaluation after their diagnosis to be appropriately treated.

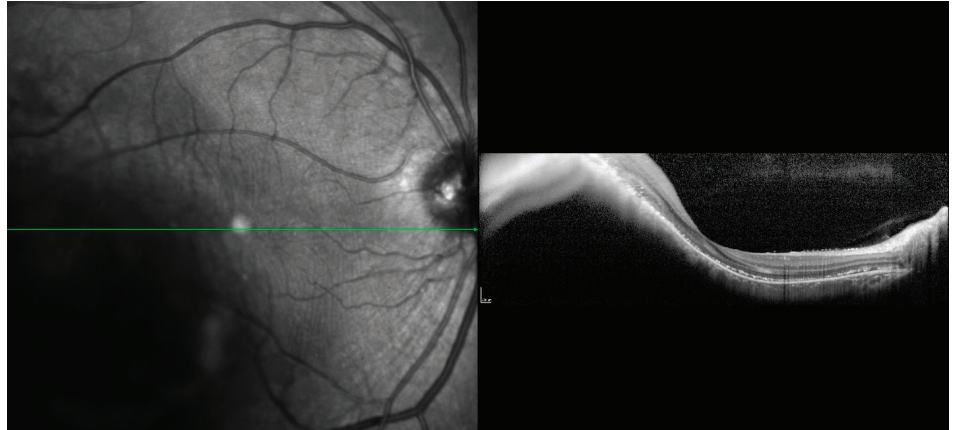


Figure 1. OCT analysis of macular choroidal melanoma medium. Photo credit: Timothy G. Murray, MD, MBA

Tumor sizing

Typically, ocular oncologists use 5 categories for tumor sizing: small, medium, large, extra-large, and a fifth category for borderline small tumors called *atypical nevi* (singular: *nevus*). Tumor sizing is important, as it has an impact on treatment options for the patient. Choroidal nevi (sometimes called eye freckles) occur in approximately 20% of the population and are benign. They are the potential precursor to choroidal melanoma, but there are certain clinical characteristics such as thickening that may give the nevus a higher risk for transformation into a melanoma. These atypical nevi should be photographed/ documented with baseline ultrasound and followed every 6 months.

continued next page

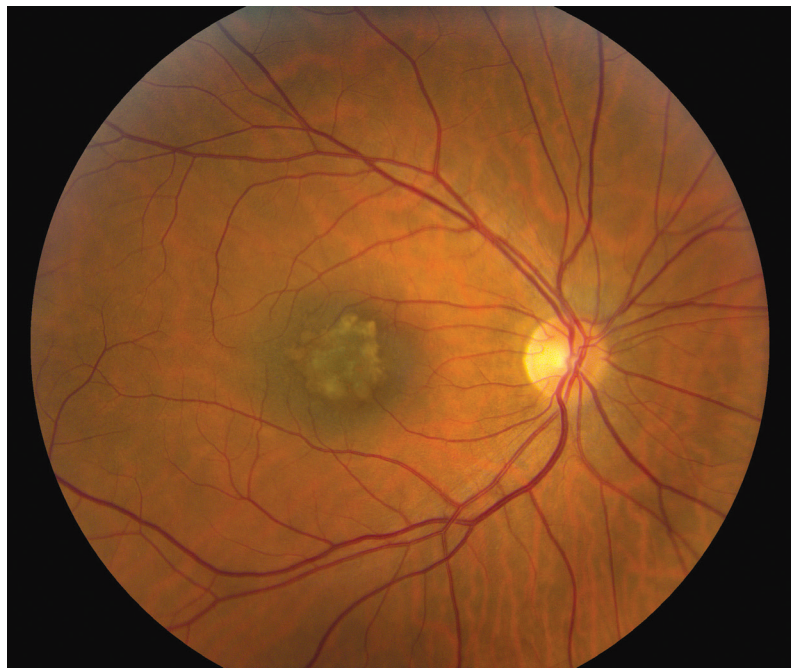


Figure 2. Small benign macular choroidal freckle/nevus. Photo credit: Timothy G. Murray, MD, MBA

Intraocular (Uveal) Melanoma *continued from previous page*

Treatment options

- **Observation:** This treatment includes ongoing clinical evaluation of the tumor, typically to determine change. Often, patients are seen at 3 months, every 4 months, and ultimately every 6 months. Comprehensive testing is performed on each visit to assess any change in tumor size or characteristics.

Observation is typically limited to atypical nevi to monitor for change to a small melanoma. This treatment has been shown to be extremely effective when the follow-up visits are carefully maintained.

- **Laser tumor ablation (LASER):** Laser destruction (ablation) of a tumor has been effective but limited in its application due to penetration and secondary retinal damage. Recent advances have shown excellent success (efficacy) when tumor treatment is performed during vitrectomy surgery. Laser surgical approaches are typically offered as primary treatments for small ocular melanomas. Laser surgical approaches may be used as a primary treatment in some small ocular melanomas.
- **Vitrectomy (micro-incision vitrectomy surgery, or MIVS):** This is surgery to remove the vitreous gel (jelly-like substance inside the back compartment of the eye), remove tissue traction and scarring (membrane peeling), laser destruction of the tumor, biopsy of the tumor (fine-needle biopsy or *FNAB*), and suppression of post-surgical inflammation. Additionally, MIVS surgery may be used to place silicone oil in the back compartment of the eye to stabilize the retina or potentially reduce radiation complications.
- **Radiotherapy:** Two major types of radiation treatment are routinely used for ocular melanoma— brachytherapy and charged-particle therapy.
 - **Brachytherapy** is the most common radiation treatment for ocular melanoma; it uses a patch approximately the size of a quarter that is attached directly to the eye in surgery. The “patch” typically remains on the eye for 3 to 5 days and is removed in a second, brief operation. During the brachytherapy surgery, the eye is often biopsied for tumor genetic testing. The patch is shielded to protect the non-tumor tissues during the procedure. In many studies, this treatment has achieved tumor control in almost 100% of eyes.
 - **Charged-particle radiotherapy** uses a beam of charged radiation particles to destroy the tumor. This treatment typically requires surgery to localize the tumor with small metallic clips sewn onto the eye to surround the tumor. These metallic clips help to localize the tumor so the charged particles can be directed precisely to the tumor. Charged-particle treatment is much less common for ocular melanoma, but has virtually identical success rates for tumor control.
- **Enucleation:** Removal of the *entire* eye to eliminate the tumor. This surgery is typically performed with reconstruction of the eye socket and placement of an implant. Enucleation is typically performed only for extra-large tumors, or for tumors that have failed initial treatment. No benefit has been shown for enucleation of smaller tumors compared with other treatments that preserve the eye.

continued next page



Figure 3.
Small/medium malignant choroidal melanoma.
Photo credit: Timothy G. Murray, MD, MBA



Figure 4.
Small/medium malignant choroidal melanoma after brachytherapy. Tumor size reduced by 40%. Notice small bleeding from the radiation. Photo credit: Timothy G. Murray, MD, MBA

Intraocular (Uveal) Melanoma *continued from previous page*

Genetic testing

A major advance in ocular oncology has been the use of tumor genetics to define the genetic risk of tumors spreading outside of the eye (metastasis). Two genetic testing approaches are now available: gene expression profiling (GEP) and cytogenetics (chromosomal analysis). GEP testing yields 2 classes of tumor—class 1 (1a and 1b) and class 2.

These classes are statistically associated with risk for metastatic disease. We have learned from cytogenetics that alterations in chromosomes 3, 6, and 8 greatly impact the risk of developing metastatic disease. These genetic tests require tumor tissue (biopsy) and are important for prognostication (risk assessment for metastatic disease) but do not influence the primary treatment of the tumor. Recent studies have shown that genetic testing may be performed after primary treatment without compromising test results.

Ocular melanoma is the most common primary eye cancer of adults but, fortunately, remains a rare cancer. Expert treatment is recommended for each patient. ●

Clinical Terms *(appearing green within fact sheet text)*

Dilated ophthalmoscopy: An exam of the inside of the eye with the pupil dilated (enlarged with medicated drops) to check the retina, optic nerve, and other parts of the eye using a small handheld magnifying lens and a bright light. This is the most important part of the clinical examination.

Flashes: Streaks of light, usually appearing at the side of vision.

Floater: Mobile blurry shadow that partially obscures vision. Floaters are most bothersome when near the center of vision and less annoying when they settle to the side of the vision. They may appear like cobwebs, dust, or a swarm of insects—or in the shape of a circle or oval, called a *Weiss ring*.

Fluorescein angiography (FA): An imaging technique where a yellow dye called *sodium fluorescein* is injected into a vein in the arm, allowing a special camera to record circulation in the retina and *choroid* in the back of the eye. This test can be very useful in diagnosing a number of retinal disorders.

Fundus: The back of the eye where the retina, macula, vitreous, choroid, and optic nerve are located.

Fundus photography: Imaging that uses specialized cameras equipped with lenses that capture images of the back of the eye where the retina, macula, vitreous, choroid and optic nerve are located.

Gonioscopy: An exam of the front part of the eye between the cornea and iris (called the angle) where fluid is normally drained from the eye. A special contact lens instrument is used to see if the tumor affects this portion of the eye, which may cause glaucoma.

Indocyanine green angiography (ICGA): A diagnostic procedure that uses a green dye to illuminate blood flow in the choroid, a layer of blood vessels located between the white of the eye (sclera) and the retina that supplies nutrients to the inner eye.

Macula: A small area at the center of the retina where light is sharply focused to produce the detailed color vision needed for tasks such as reading and driving.

Optical coherence tomography (OCT): A non-invasive imaging technique that uses light to create a 3-dimensional image of your eye for physician evaluation.

Slit-lamp biomicroscopy: An exam of the front structures of the eye (conjunctiva, cornea, anterior chamber, iris, lens, and anterior vitreous) using a strong beam of light and a table-mounted microscope.

Transillumination of the globe and iris: An exam of the iris, cornea, lens, and ciliary body with a light placed on either the upper or lower lid.

THANK YOU TO THE RETINA HEALTH SERIES AUTHORS

Sophie J. Bakri, MD, FASRS
Audina Berrocal, MD, FASRS
Antonio Capone, Jr., MD
Netan Choudhry, MD, FRCS-C, FASRS
Thomas Ciulla, MD, MBA, FASRS
Pravin U. Dugel, MD, FASRS
Geoffrey G. Emerson, MD, PhD, FASRS
K. Bailey Freund, MD
Roger A. Goldberg, MD, MBA, FASRS
Darin R. Goldman, MD
Dilraj Grewal, MD, FASRS
Larry Halperin, MD, FASRS
Vivienne S. Hau, MD, PhD, FASRS
Suber S. Huang, MD, MBA, FASRS
G. Baker Hubbard, MD, FASRS
Mark S. Humayun, MD, PhD
Talia R. Kaden, MD
Peter K. Kaiser, MD, FASRS
M. Ali Khan, MD, FASRS
Ivana K. Kim, MD, FASRS
Eleonora Lad, MD, PhD
Anat Loewenstein, MD
Mathew J. MacCumber, MD, PhD, FASRS
Maya Maloney, MD
Timothy G. Murray, MD, MBA, FASRS
Hossein Nazari, MD
Oded Ohana, MD, MBA
Jonathan L. Prenner, MD, FASRS
Gilad Rabina, MD
Carl D. Regillo, MD, FACS, FASRS
Naryan Sabherwal, MD
Sherveen Salek, MD
Andrew P. Schachat, MD
Adrienne W. Scott, MD, FASRS
Michael Seider, MD
Janet S. Sunness, MD
Eduardo Uchiyama, MD, FASRS
Allen Z. Verne, MD, FASRS
Christina Y. Weng, MD, MBA, FASRS
Yoshihiro Yonekawa, MD, FASRS

EDITOR

John T. Thompson, MD

MEDICAL ILLUSTRATOR

Tim Hengst