



# A GUIDE TO **UVEAL MELANOMA**

## **MELANOMA OF THE EYE:**

An information guide for patients newly diagnosed with uveal melanoma

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## QUICK FACTS

- Uveal melanoma is the most common eye cancer in adults.
- Although it is called melanoma, it is much rarer than skin melanoma.
- Approximately 200 people are diagnosed in Canada each year.
- Treatment options include radiation therapy and surgery. There is no chemotherapy for uveal melanoma.
- At this time, there is no cure for metastatic uveal melanoma. However, there are treatment options.
- If you are diagnosed with uveal melanoma, you are not alone. Melanoma Network of Canada offers a number of free support programs to help you through your journey. Visit [www.melanomanetwork.ca](http://www.melanomanetwork.ca) or call 1-877-560-8035

# INTRODUCTION

There are several different types of eye cancer. This information guide focuses on uveal melanoma.

Melanoma is a malignant tumour of the melanocytes. Melanocytes are pigmented or colour-producing cells found in various locations in the body including the skin, hair and eyes. Melanoma of the skin (or cutaneous melanoma) is much more common and is very distinct from melanoma of the eye (or uveal melanoma).

An information booklet on skin melanoma entitled “Melanoma, What You Need to Know” is available from the Melanoma Network of Canada at <https://www.melanomanetwork.ca/mncpub/>

## The eye:

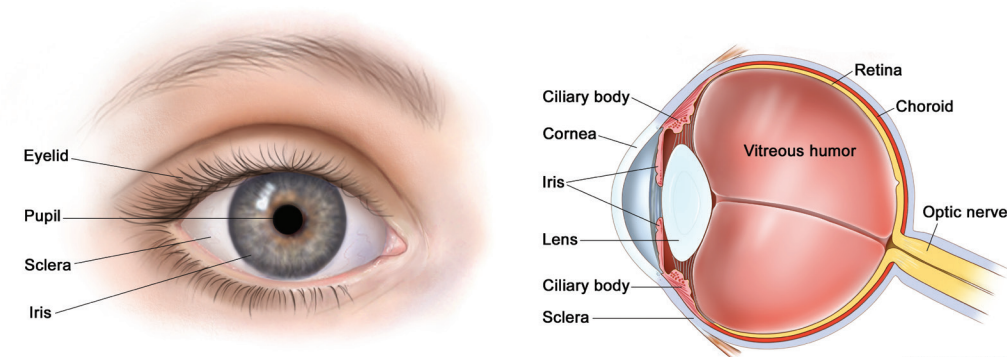
The eye is a ball with a wall made of three layers:

The outer layer is the white visible portion called the sclera and there is a clear portion that covers the front of the eye called the “cornea”.

The middle layer is called the uvea and is comprised of the iris, which is visible through the cornea, the ciliary body and the choroid, which are undercover of the sclera. A more detailed picture of the uvea is captured in the diagram directly below.

The inner layer is called the retina. It is comprised of cells that can sense light and transmit this information via the optic nerve to the brain for vision.

## The uvea:



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The uvea (or uveal tract) is the middle layer of the eye. As mentioned, the uvea has three parts: the iris, the ciliary body and the choroid.

1. The iris provides a person's eye colour that surrounds the pupil.
2. The ciliary body is a muscle that controls the size of the pupil and the shape of the lens to help the eye focus.
3. The choroid is a layer of blood vessels that provide the eye with nutrients and oxygen.

The previous structures contain plenty of melanocytes.

### **Uveal melanoma:**

Uveal melanoma refers to melanocytes of the uvea that become cancerous. This can occur in any part of the uvea: the iris, the ciliary body and/or the choroid. Uveal melanoma cases occur nearly 85% of the time in the choroid, another 10% in the ciliary body and approximately 5% in the iris.

Although uveal melanoma (eye) and cutaneous melanoma (skin) both affect melanocytes, they are distinct cancers. Uveal and cutaneous melanomas are distinct in that they have different genetic mutations, they behave differently, and cutaneous melanoma is much more common (nearly 40 times more common). Having uveal melanoma does not mean you will develop cutaneous melanoma or vice versa.

### **Risk factors and prevention:**

The cause of uveal melanoma is unclear. Therefore, we do not know how to prevent uveal melanoma. Unlike skin melanoma, which is often closely linked to UV radiation damage from the sun or other sources, there is no hard evidence to support causal relationship. However, there are factors that were linked to increased risk for uveal melanoma. These include:

1. Light eye colour, such as blue or green eyes
2. Fair skin colour
3. Being older in age. The median age at diagnosis is 55 years old.

Although research studies have found an association with these factors, uveal melanoma can occur in any person regardless of age, gender or race.



# DETECTION

## How is uveal melanoma detected?

A person with uveal melanoma may have no symptoms and the tumour can be discovered during routine eye exam, or it may produce some symptoms.

For a person experiencing symptoms, these may include:

- Vision change (e.g. blurred vision, flashing lights, unexpected seeing of shadows, seeing floating spots, loss of peripheral vision)
- Eye pain
- Eye redness

These symptoms are similar to many other eye conditions, such as cataracts and glaucoma, and are NOT specific to uveal melanoma. Ophthalmic examination should be carried out by a specialist to diagnose or rule out the presence of melanoma.

A person with melanoma in the iris may notice changes in the iris such as presence of a growth, or changes in iris colour and changes in the size and shape of the pupil.

## How is uveal melanoma diagnosed?

There is NO formal screening program for uveal melanoma. Routine eye exams are the best option for identifying potential issues.

**Eye exam:** An eye exam is performed by an optometrist or an ophthalmologist and is a painless procedure. The outside and inside of the eye are examined for any abnormalities. Special eye drops that dilate the pupil may be used to help see the inside of the eye. A diagnosis of uveal melanoma can sometimes be made by an eye exam alone.

**PHOTOGRAPHY:** Different types of specialized photographs are used to take pictures of the outside and inside of the eye and can help with the diagnosis of eye conditions, such as uveal melanoma. Also, by comparing photographs before and after treatment, photographs can also help determine whether the treatment delivered is effective.



**ULTRASONOGRAPHY:** Ultrasonography uses high frequency sound waves to help see the inside of the eye. Anaesthetic eye drops may be used to numb the eye so that an ultrasound probe can be placed on the eye's surface. Ultrasonography can be used to determine the tumour size, shape and location.

**TRANSILLUMINATION:** Transillumination uses a light that is placed on the eye surface to examine eye structures for any gross abnormality.

**FLUORESCEIN ANGIOGRAPHY:** Fluorescein angiography is used to see how the blood is flowing in the eye and to see the blood vessels. A fluorescent dye called fluorescein is injected into an arm vein, and the dye travels to the eye in just a few seconds. A special eye instrument can detect this fluorescence to help us see if there is any damage to the eye blood vessels.

**RECENT IMAGING TECHNIQUES:** These include Optical Coherence Tomography (OCT), and OCT angiography, Infrared Fundus Photography, Indocyanine Green Angiography (ICG), and Fundus Autofluorescence. They are modern sensitive techniques to image subtle changes in the tumour and nearby structures.

**BLOOD TESTS:** A blood sample may be taken to determine how well organs in your body, such as the liver, are working. Analyzing the blood may help determine whether the tumour has spread to the liver.

**SCANS:** X-rays allows visualizing of internal body structures. A 3D X-ray called Computed Tomography (or CT) may be taken of certain parts of the body to see if there is any spreading (or metastasis) of the uveal melanoma tumour. A 2D X-ray of the chest may be taken as an alternative to a CT scan. Magnetic Resonance Imaging (MRI) may also be used for a 3D image and it does not use radiation, but takes longer than a CT.

**BIOPSY:** A biopsy is a way to get a sample of the tumour cells, usually by using a fine needle. It is typically not performed for uveal melanoma diagnosis as other tests are usually enough to make a diagnosis. A biopsy may be performed so it can be analyzed by a medical geneticist to study the tumour's DNA. This information can be useful for determining survival prognosis of the patient and his/her eligibility for clinical trials.

## What is the prognosis if diagnosed with uveal melanoma?

Prognosis is a term used to help predict the likely outcome of a patient with a health condition. Prognosis can refer to the likelihood of a patient surviving after diagnosis of a tumour. There are a number of factors that can help determine the prognosis for a patient with uveal melanoma. The most helpful factors to determine prognosis are the tumour's size, the tumour's location and genetic testing.

- 1) Tumour size: The larger the tumour base and height, the less favourable the prognosis.



- 2) Tumour location: In general, Iris melanomas have a better survival prognosis than ciliary body melanoma. The prognosis for choroidal melanomas is in between iris and ciliary body melanomas.
- 3) Tumour invasion of the eye wall or spreading to other parts of the body has a worse prognosis.
- 4) Return of the tumour: Rarely the tumour can return after treatment. This is called relapse or recurrence. This is associated with a worse prognosis as the tumour may no longer respond to treatment and has been shown to have an increased likelihood of spreading.
- 5) Genetic factors: This is the most important determinant of survivability chances in uveal melanoma. Changes in the DNA and changes in specific tumour genes may have a role in prognosis and can be determined by genetic testing. A biopsy (a sample of the tumour taken using a fine needle) is required to do genetic testing. If you are interested in exploring this possibility and to determine whether you may be a candidate for genetic testing, please speak with your ocular oncologist.
- 6) The patient: The patient's age, general health status and other medical conditions all play a role in prognosis. This can be discussed with your doctor.

### **The outcome regarding vision: Factors that may affect vision after treatment include:**

- 1) Tumour size: A larger tumour increases the risk of vision loss.
- 2) Tumour location: A tumour closer to the optic disk or macula increases the risk of vision loss.
- 3) Other medical conditions: Other medical conditions, such as certain eye conditions and diabetes, uncontrolled hypertension increase the risk of vision loss.

### **How is uveal melanoma staged?**

There has been several categorization systems of uveal melanoma according to their dimensions, cellular type or genetic defects, and their link to the potential for spread outside the eye.

The current most practical categorization is the TNM staging.

#### **Stage:**

Uveal melanoma stage is described as "TNM", which stands for Tumour, Node and Metastasis. Tumour refers to the tumour size and whether it has invaded neighbouring tissues. Node refers to whether cancer has or has not spread to lymph nodes (organs in the lymphatic system that contain collections of immune cells). Metastasis refers to whether cancer has spread to distant sites.

TNM is a staging system that can indicate prognosis for the patient. The TNM of an individual patient can be complex to explain and it is advised that patients discuss the details of their TNM stage with their ocular oncologist.

# TREATMENT AND MANAGEMENT

## Who is recommended for treatment?

Treatment is not always recommended for patients diagnosed with uveal melanoma and depends on many factors, including the location and size of the tumour and a patient's overall health. For example, watchful waiting and close monitoring may be recommended for an elderly chronically ill patient who does not have any symptoms and has a small sized tumour. Otherwise, uveal melanoma should be promptly treated.

## What are the treatment options for uveal melanoma?

The treatment options for uveal melanoma may include radiation therapy or surgery. Some patients will receive both radiation therapy and surgery.

### 1. RADIATION THERAPY

Radiation is used to kill tumour cells.

There are two main forms of radiation therapy to treat uveal melanoma: Brachytherapy (or Plaque Therapy) and External Beam Radiation Therapy (EBRT) (or Teletherapy). Brachytherapy uses a plaque that is placed directly on the eye. In EBRT, a machine delivers the radiation treatment from outside the eye.

(i) **Brachytherapy or "Plaque Therapy"** is the most common form of radiation therapy used and is most widely available.

Brachytherapy is used to deliver radiation that is confined to the tumour. There are various types of radioactive plaques with different

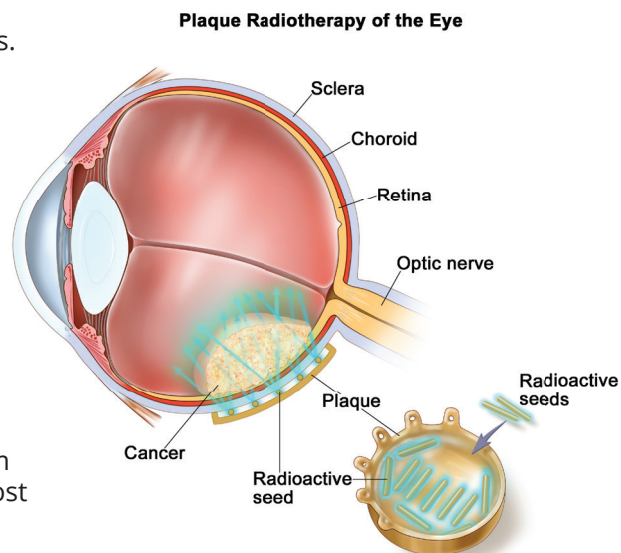


Image source: University of Chicago Medicine  
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radioactive seeds that can be used for Brachytherapy. Each type of seed differs on its ability to penetrate the tissue. The plaque will be physically placed on the eye to be close to the tumour. This requires an operation to position the plaque on the eye. Treatment can last up to one week and will require a second operation to remove the plaque.

Brachytherapy may not be used when the tumour surrounds the optic disc, which is where part of the optic nerve (the nerve which allows us to see) is situated, and Teletherapy may be used instead. Brachytherapy is also not used on tumours that are too big (usually greater than 12 mm thick) because the radiation can only effectively penetrate so far. Since Brachytherapy is very precise, many parts of the eye will remain unaffected while the localized radiation treatment will treat the tumor.

Although Brachytherapy is an excellent treatment for most uveal melanoma patients, it may have some consequences on your treated eye. The risk of these consequences depends upon the size and location of the uveal melanoma inside the eye, as well as the type of radioactive plaque and the radiation dose during treatment. Possible side effects are:

- Radiation retinopathy – damage to vessels that supply blood to the retina. This will result in some level of vision loss.
- Optic neuropathy – less commonly, damage to the nerve that allows the person to see.
- Other complications – increased risk for cataracts, high eye pressure, internal bleeding of the eye and rarely, necrosis of eye tissue.
- Long-term complications – poorer vision.

#### (ii) **External Beam Radiation Therapy (EBRT)**

is also known as Teletherapy which include charged particle irradiation (e.g. Proton Beam Radiotherapy), Stereotactic Radiotherapy, or Gamma Knife. Different types of EBRT is only available at certain treatment centres in Canada.

EBRT uses a machine that delivers a beam of radiation to the affected part of the eye through the front of the eye only. In case of proton beam radiotherapy, an eye operation may be required to place metal clips or tags to help the machine know exactly where to deliver the beam of radiation.



Image source: Ohio State University

EBRT is used to treat patients with medium to large sized tumours that surround the optic disc, where plaque can not be placed to cover the entire tumour base because of the physical obstruction from the optic nerve. EBRT can also be used for selected cases of tumour recurrence in the eye after plaque radiotherapy. Complications of EBRT are shared with those of plaque radiotherapy, but there may be relatively higher rates in case of Stereotactic Radiotherapy. However, this largely depends on tumour factors, such as its location and size, and possibly the dose of radiation received.

## 2. SURGERY

Surgical removal of the tumour depends on factors such as the size of the tumour and the location of the tumour.

There are two main forms of surgery to treat uveal melanoma:

**REMOVAL OF THE EYE (ENUCLEATION):** Removal of the eye is also known as enucleation. Enucleation is considered in cases where radiation therapy may be insufficient to treat the tumour, such as when the size of the uveal melanoma is particularly large, when the tumour has significant local spreading beyond the white portion of the eye (the sclera) and/or a blind painful eye after very high dose radiation, causing a condition called neovascular glaucoma.

After the eye socket is healed, an artificial eye (or prosthesis) can be customized. This customization process requires a mold to be taken from the eye socket and will take several weeks to create. When ready, the artificial eye is fitted to the patient and should look very realistic and have some movement. Once the eye socket is completely healed, a person living with an artificial eye can do most normal things. It is recommended that goggles be worn during water sports and snow sports.

**LOCAL TUMOUR REMOVAL:** Local removal of the uveal melanoma tumour may be used only in very specific cases, such as patients who are unable to undergo brachytherapy and do not wish to undergo enucleation. This limitation is due to the need for highly skilled surgical expertise, as well as the number of plications associated with this surgery, which can affect the retina and cause internal bleeding of the eye.



### 3. GENETIC TESTING

Each cell in the human body contains a set of instructions (genes); these genes are stored in structures called chromosomes. Healthy cells have two copies of each chromosome. Tumour cells that are abnormal may show changes in these chromosomes. These abnormal cells multiply at a higher rate and are considered to be cancer cells.

One of the most important indicators of poor prognosis in uveal melanoma is partial or complete loss of chromosome 3 (monosomy 3). Metastatic disease develops almost exclusively in patients with this genetic abnormality. Other chromosomes that can be altered in uveal melanoma tumor cells are chromosomes 1, 6 & 8. Others may have specific gene mutations on a chromosome such as BAP1 or SF3B1.

These chromosome changes occur within tumour cells, they are not inherited (passed through the family). These chromosome changes occur by chance in the tumor cell of the eye. They are not present in any other parts of the body, specifically the egg or sperm cells, and therefore cannot be passed on to children.

Genetic testing of uveal melanoma tumor cells is performed by obtaining a sample of cells from the eye tumour. This can be done at the time of plaque radiation therapy or taken from a removed eye. This sample is performed by your surgeon and sent directly to the laboratory.

### 4. OTHER THERAPIES

Other therapies to treat uveal melanoma exist for specific tumour cases. They include photocoagulation, transpupillary thermotherapy and photodynamic therapy. Speak with your ocular oncologist to learn more about these therapies.

# SURVEILLANCE AND MANAGEMENT OF METASTASES

Spreading of cancer cells through blood or the lymphatic system to another part of the body is called metastasis. Uveal melanoma can spread to local structures beside the eye (known as extraocular extension), such as the optic nerve. Uveal melanoma can also metastasize through the blood and develop in the liver, lungs, bones and under the skin.

## **Post primary treatment follow-up and surveillance:**

Uveal melanoma metastases may present years after the primary tumour has been treated. A patient who receives treatment (e.g. brachytherapy, EBRT, or enucleation) can still get metastases from the tumour cells that escaped from the eye to the body PRIOR to treatment.

Less than 1% of patients at the time of initial uveal melanoma diagnosis would show an evidence of metastases. A diagnosis of uveal melanoma metastasis has a very poor prognosis and, unfortunately, has a high rate of mortality.

There are several approaches to surveillance for metastases. Because metastases usually occur in the liver and in the lung, tests that are performed are focused on these organs. These tests are performed every 6-12 months and can continue for many years or decades. However, there are no standard guidelines or approaches for surveillance as there is no clear consensus amongst experts.

- Imaging tests – Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scans, are the standard imaging methods.
- Physical exam – to detect issues.

The frequency of follow-up and tests depends on the risk of metastasis of each individual tumour as detected by tumour genetic testing and/or tumour size and location.



## Management of metastases:

Although these surveillance measures can indeed detect uveal melanoma metastases earlier, there are limited treatment options for patients with metastases. The development of metastases is a serious complication of this type of melanoma and generally limits patient survival, although treatments are improving.

Treatment options for metastases is presently experimental and investigational, which means that they are being studied in a clinical trials. Some of these treatment options may include chemotherapy, immunotherapy and targeted therapy.

**CHEMOTHERAPY** is the use of chemicals to treat cancer. A trial of chemotherapy may be used only in patients with metastases. There is currently no optimal chemotherapy approach to treat metastases. This means that there are a number of clinical trials that are investigating which chemotherapy agent, either used alone or in combination with other agents, may be effective in treating metastases.

**TARGETED THERAPIES** is the use of drugs to specifically stop different “engines” of cancer cells from continuing to signal to the cells to reproduce and grow. Studies on targeted therapies for uveal melanoma sometimes also use chemotherapy.

**IMMUNOTHERAPIES** is the use of parts of the patient’s immune system to attack the cancer.

**CLINICAL TRIALS** Patients should speak with their oncologist to see if a clinical trial is an option.



## SOCIAL SUPPORT

A diagnosis of uveal melanoma and cancer in general is often filled with emotion and anxiety. It is common for people to be upset, scared and angry. Resources are available to support you, they include:

- **Melanoma Network of Canada Phone & Email Support** – Available Monday to Friday, 9am – 5pm EST. We aim to respond to all inquiries within 48 hours. All calls and emails are confidential. For support call 1-877-560-8035 x108
- **Melanoma Network of Canada Uveal Forum**– Uveal Melanoma online forum provides a virtual space where ocular melanoma patients from across Canada or their caregivers can share with other uveal melanoma patients and caregivers. This forum provides information and insight into the patient journey and a sounding board to discuss the emotional impacts of uveal melanoma. How to join: Visit <https://www.melanomanetwork.ca/melanoma-and-skin-cancer-forum/>
- **Social Media** – Connect with the Melanoma Network of Canada on Facebook, Twitter, Instagram, and YouTube! @melanomanetwork
- **Melanoma Network of Canada Peer-to-Peer Support Program** – Are you a patient or caregiver looking to speak with someone else that has perhaps been where you are currently and can offer some insights and support? Ask us about our Peer-to-Peer Melanoma Support Program. This program is designed to connect melanoma patients to a peer volunteer who has also faced the disease and can offer their experience and provide information and support as needed. This service is offered by telephone and can connect patients anywhere in Canada. If you are interested in becoming a Peer to Peer volunteer or would like to be matched with a fellow patient/caregiver please contact 1-877-560-8035
- **Melanoma Research Foundation ([www.melanoma.org](http://www.melanoma.org))** – Cure OM patient online bulletin board where ocular melanoma patients, caregivers and their loved ones can talk with other OM patients and caregivers from around the world.



# QUESTIONS TO ASK YOUR HEALTHCARE TEAM<sup>1</sup>

## About disease and treatment

- What type of cancer do I have?
- What stage is my cancer?
- What are the pros, cons and side effects of my treatment options?
- What are the expected survival rates with these treatments?
- Will receiving these treatments prevent me from receiving a different type of treatment in the future if I need it?
- Are there any more tests that need to be done before starting treatment?
- Will there be tests to determine how my disease responds to the treatment?
- How often will these tests be done during and after treatment?
- Will you change my treatment if it does not appear to be working?
- How long will the treatment last?
- How often will I see you during and after treatment?
- What other services are available to help me and my family cope with the disease?
- Are there any clinical trials that I can or should be considering?

## About prognosis and survival

- Do you expect these treatments to cure my cancer? If not, what is the goal of this therapy?
- What is the usual life expectancy for this type of cancer?
- What are the best and worst case scenarios?

<sup>1</sup> Questions taken from "Questions you may ask" under "Your first appointment" from the Princess Margaret Cancer Centre, the University Health Network ([www.theprincessmargaret.ca](http://www.theprincessmargaret.ca))

## RESOURCES

**EYE PLAQUE PATIENT INFORMATION BOOKLET** is a booklet explaining one of the treatments for eye cancer.

([https://www.uhn.ca/PatientsFamilies/Health\\_Information/Health\\_Topics/Documents/Eye\\_Plaque.pdf#search=eye%20plaque](https://www.uhn.ca/PatientsFamilies/Health_Information/Health_Topics/Documents/Eye_Plaque.pdf#search=eye%20plaque))

**EYE CANCER NETWORK** is a dedicated education site for people with eye tumours and their friends and families. (<http://www.eyecancer.com/>)

**LOST EYE** provides support and discussion for people who have lost an eye. (<http://losteye.com/>)

**BASCOM PALMER EYE INSTITUTE** has information about different eye conditions, including cancer. (<http://bascompalmer.org/>)

**NATIONAL EYE INSTITUTE** has information about eye health and diseases, as well as diagrams of the inside of the eye. (<http://www.nei.nih.gov/>)

**IMPACT GENETICS** provides genetic diagnostics for uveal melanoma and other rare diseases. (<http://impactgenetics.com/>)

# GLOSSARY

**Brachytherapy:** Uses radioactive material inside your body to treat cancer.

**Cancer:** Abnormal cells that can divide uncontrollably, invade normal tissues and spread throughout the body.

**Choroid:** A part of the middle layer of the eye between the sclera (the white part of the eye) and the retina. It has layers of blood vessels that supply nutrients to parts of the eye.

**Ciliary body:** Located behind the iris and produces a clear fluid in the front of the eye, as well as assisting the eye with focusing at different distances (i.e. accommodation).

**Computed Tomography (CT):** Use of X-rays to see into the body.

**Cutaneous:** Means that it is related to the skin.

**Enucleation:** The removal of the eye.

**External Beam Radiation Therapy (EBRT):** Uses radiation outside of the body to treat cancer.

**Iris:** The coloured part of the eye that is referred to a person's eye colour.

**Magnetic Resonance Imaging (MRI):** Use of radio waves and powerful magnets to see into the body.

**Melanocytes:** Skin cells that produce a dark pigment called melanin, which is responsible for a person's skin colour.

**Melanoma:** A cancer of melanocytes.

**Metastases:** Spreading of cancer.

**Ocular oncologist:** A doctor who specializes in eye cancers.

**Oncologist:** A doctor who specializes in cancer.

**Ophthalmologist:** A doctor who specializes in the eye and is a medical doctor (MD).

**Optometrist:** A healthcare professional who specializes in the eye and is a doctor of optometry (OD).

**Plaques:** Tiny plates.

**Retina:** The inner surface of the eye that senses light.

**Tumour:** A tissue mass made from an abnormal growth of cells.

**Ultrasound:** Uses sound waves to see inside the body.

**Uvea or uveal tract:** The middle layer of the eye that includes the iris, the ciliary body and the choroid.



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