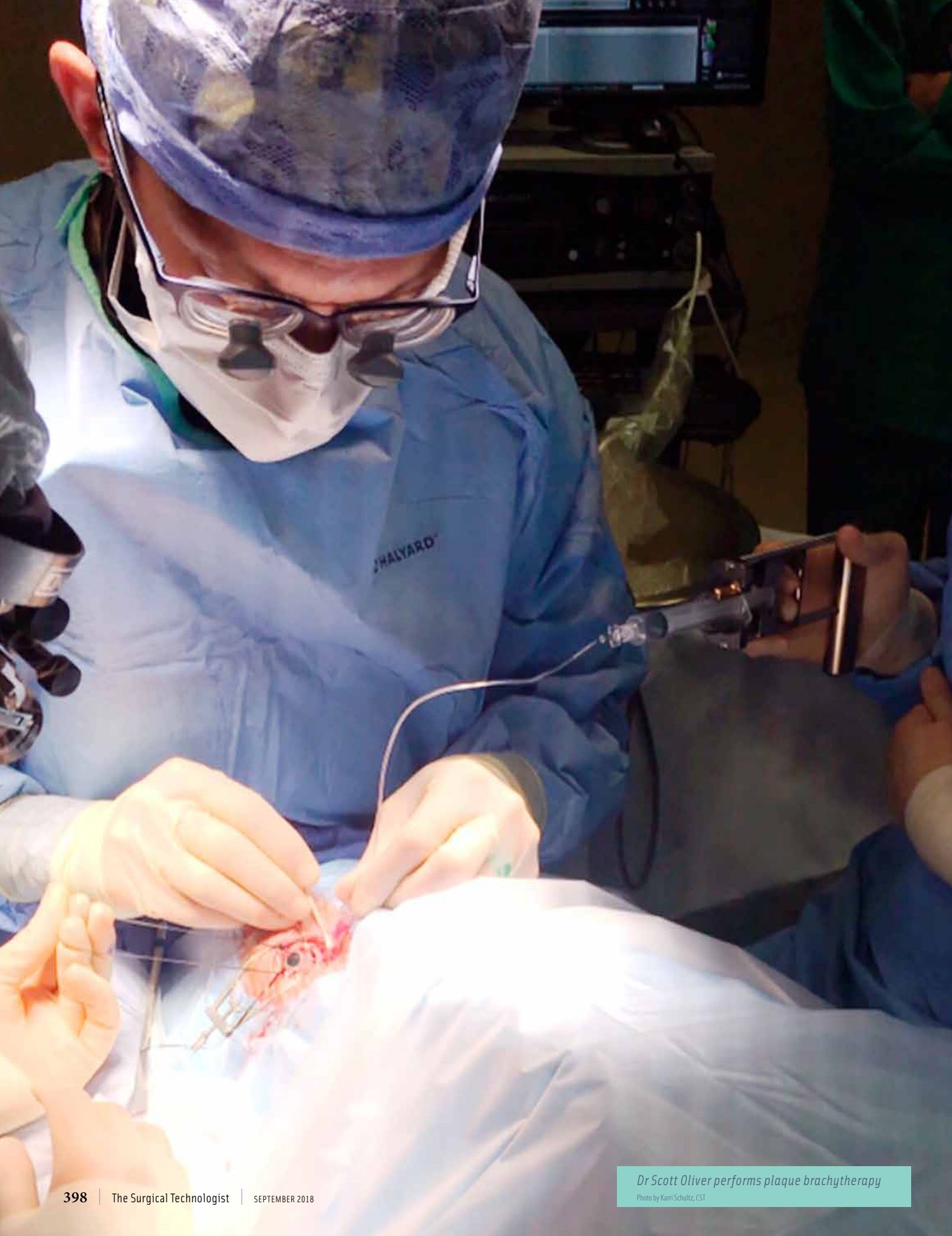

Dr Scott Oliver performs plaque brachytherapy
Photo by Karri Schultz, CST

Plaque Brachytherapy to Treat Choroidal Melanoma

Karri Schultz, CST[1]
Scott CN Oliver, MD[1,2]

Melanoma is defined as a malignant tumor of melanin-producing cells.[1] Typically, melanoma is associated with skin cancer, as most melanin-producing cells, or melanocytes, are located in the skin's epidermis. However, melanocytes also are present in other parts of the body. One area that contains melanocytes is the choroidal layer of the eye located beneath the retina. Because the choroid contains melanocytes, it is possible to develop melanoma in the eye. In North America, six out of every one million people will be diagnosed with choroidal melanoma each year.[2]

BASIC ANATOMY OF THE EYE

The function of the eye is to convert light into an electrochemical signal, which is transmitted to the brain and converted into vision. Several parts of the eye work together to achieve this.

Light enters through the clear cornea in the anterior part of the eye. It passes through the water-like aqueous fluid and into the crystalline lens. Behind the lens in the posterior part of the eye is the vitreous fluid, a jelly-like substance that fills the body of the eye. This fluid is firmly

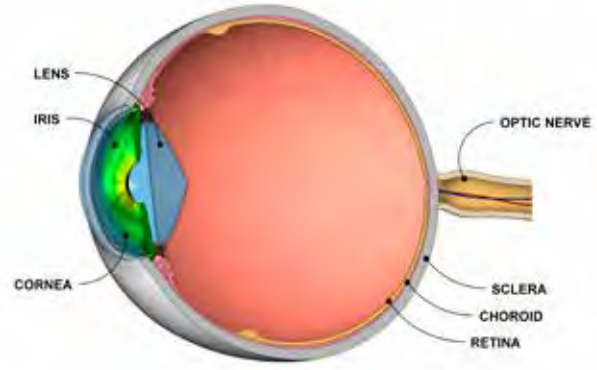

Figure 1
Anatomy of a healthy eye

Illustration by Jonathan Rose, CDT

LEARNING OBJECTIVES

- Describe the basic anatomy of the eye
- List the treatment methods for choroidal melanoma
- Discuss what causes this condition
- Detail the procedure for plaque brachytherapy
- Identify the possible complications following this procedure

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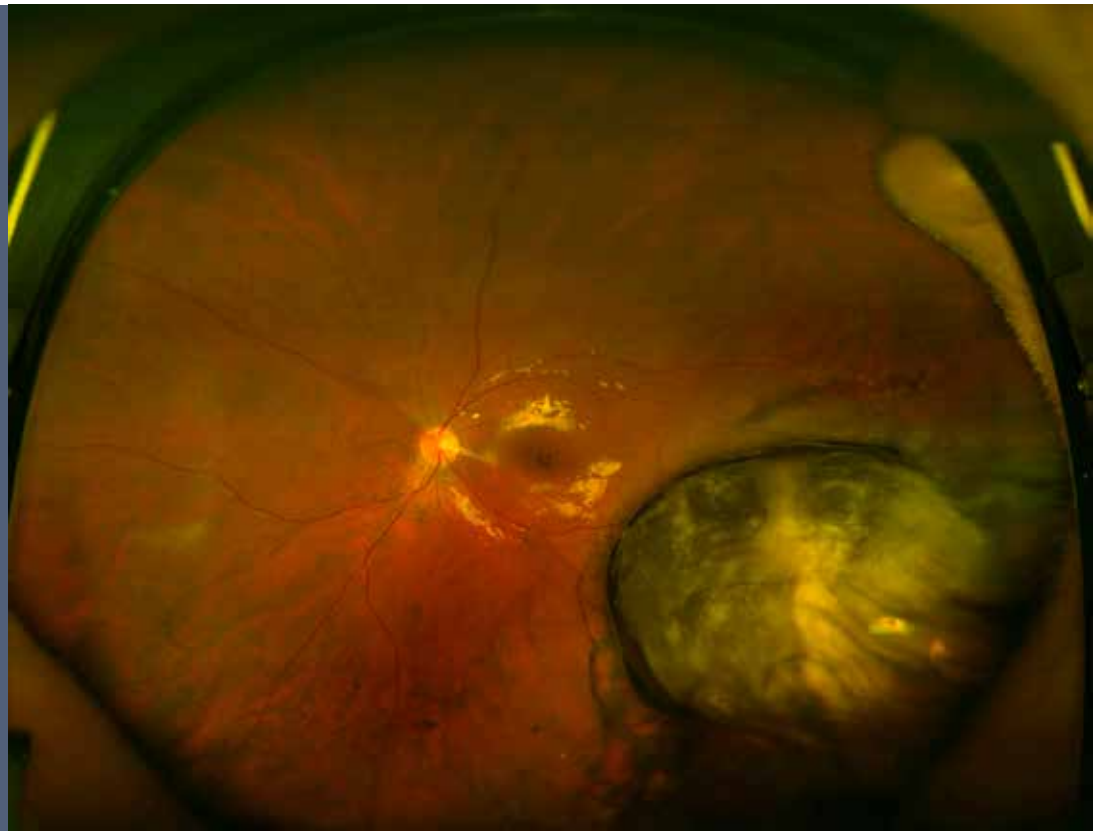

Figure 2
Choroidal melanoma tumor photographed with an ultra-wide field fundus camera

William Yates CRA, COT, UCHealth diagnostics

attached to the retina behind it. The lens focuses the light through the vitreous fluid and onto the retina. The retina is a thin, semi-transparent, light-sensitive layer that lines the posterior wall of the eye. The portion of the posterior wall that is not lined by the retina is the small area where the optic nerve enters the eye. Photoreceptors in the retina convert light into nerve impulses. Nerve fibers within the retina send these impulses to the brain, via the optic nerve, which interprets them as a visual image.[3]

Directly behind the retina is the choroid. The choroid contains blood vessels, which help supply blood and oxygen to the retina. The choroid also contains a dark-colored melanin pigment. This pigment absorbs excess light and prevents light reflection in the eye that would otherwise cause blurred vision.[1] The choroidal pigment gives the back of the eye its red/orange color, and it is what causes "red eye" when flashed pictures are taken. It is this pigment layer of melanin-producing cells in the choroid that can develop melanoma. The iris and ciliary body also contain melanin and also can develop ocular melanoma.

CHOROIDAL MELANOMA CAUSES

DNA is the chemical in our cells that makes up our genes. Genes control how our cells function. Some genes control when our cells grow, while others control cell division and death. Genes that help cells grow, divide and stay alive are called oncogenes. Genes that cause cells to die at the right time are called tumor suppressor genes. Sometimes, errors develop in the DNA of healthy cells and cause mutations in the cells' genes. If damaged DNA causes the mutations to occur in tumor suppressor genes, the mutated cells continue living when they would normally have died. When the cell divides, these mutations are passed to a new generation of cells. The rate of cell division in the mutation-bearing cells can then become uncontrolled. When these mutations occur in melanocytes in the choroid, it can cause choroidal melanoma. These rapidly dividing melanocytes accumulate in the choroid of the eye and lead to the formation of a tumor.

Exposure to ultraviolet (UV) rays damages the DNA of healthy melanocytes in the skin and can increase the risk of developing skin melanoma. However, it is not yet known whether there is any link between UV ray exposure and the development of choroidal melanoma, as no study has proven a direct linkage. As with many other forms of cancer, the exact cause of these DNA errors in choroidal melanoma is unknown. Choroidal melanoma is a primary intraocular malignant tumor and is not caused by a metastasized skin melanoma.

While choroidal melanoma can occur in all races and at any age, research shows that people who have lighter eye and skin colors are at a higher risk. The risk of developing choroidal melanoma also increases with age; the incidence rate triples for people older than 50 years old.[4]

CHOROIDAL MELANOMA DIAGNOSIS

Often, patients do not experience symptoms from a choroidal melanoma. Symptoms do not typically arise unless the tumor grows in certain parts of the eye or becomes more advanced. As a result, many cases of choroidal melanoma are discovered during routine eye exams. For this reason, getting periodic comprehensive eye exams is important, regardless of age, physical health or quality of vision.

In some cases, a visual change is what initially compels the patient to make an appointment with an ophthalmologist. These changes in vision, if caused by melanoma, most often are due to fluid leakage beneath the retina as a result of the tumor. The leaking fluid from the tumor can cause the retina to detach and induce vision-related symptoms including flashing lights, floating spots or blurred vision.

Choroidal melanoma has many distinct features that help differentiate it from other possible diseases. Several diagnostic techniques are used to reach a diagnosis of choroidal melanoma. Indirect ophthalmoscopy is performed to examine the inside of the eye and the suspected tumor. The classic appearance of choroidal melanoma on indirect ophthalmoscopy is a pigmented dome-shaped or collar button-shaped tumor with an associated fluid-filled retinal detachment. Choroidal melanoma is usually pigmented but may be variably pigmented and even non-pigmented or amelanotic.[5] Orange pigment called lipofuscin is produced by choroidal melanoma and may be detected by ophthalmoscopy and specialized photography called autofluorescence. Ultrasonography also may be used to help confirm a choroidal melanoma diagnosis. For tumors greater than 3 mm in thickness, a combination of A- and B-scan ultrasonography can diagnose choroidal melanoma with greater than 95% accuracy.[6] Optical coherence tomography (OCT) is another tool used for imaging the retina and confirming diagnosis. OCT uses light waves to take cross-section pictures of the retina. With OCT, the ophthalmologist can see each of the retina's distinctive layers. (Figures 2 & 3)

Once a choroidal melanoma diagnosis is made, patients are typically tested to determine if the cancer has metastasized. This can be done with blood tests, chest X-rays, positron emission tomography (PET) scans, computed tomography (CT) scans and liver function tests. At the time of initial diagnosis, only 1-2% of patients have metastatic disease. Ten years after treatment this number climbs to nearly 50%. When metastasis occurs, the liver is involved 90% of the time.

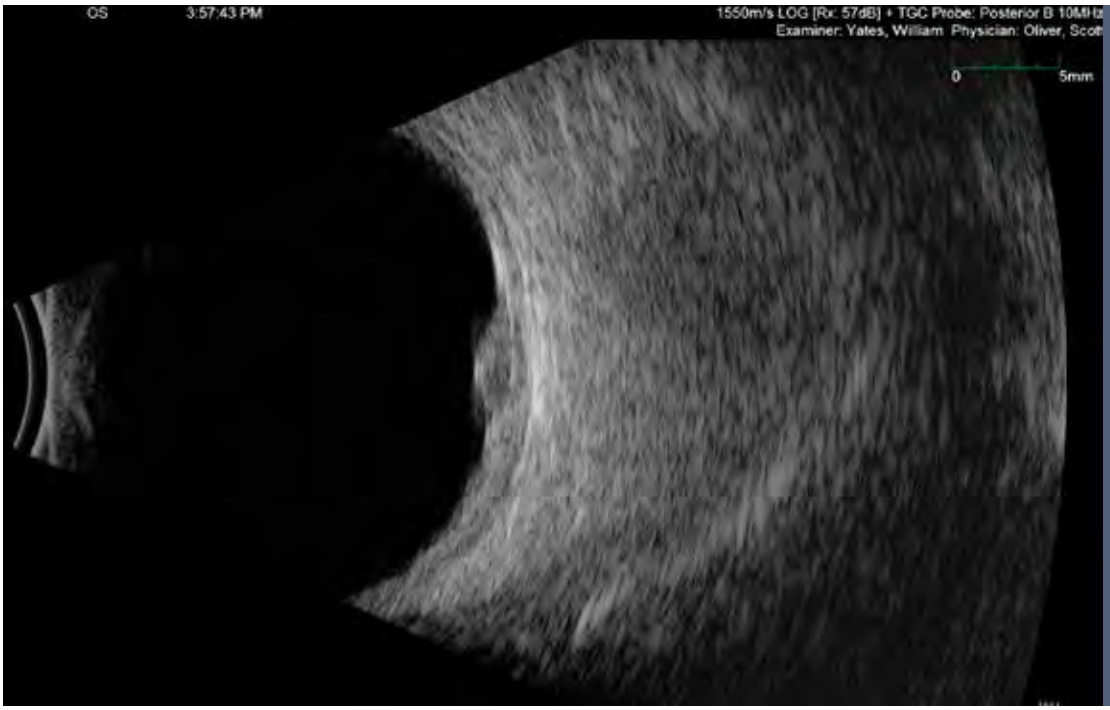

Figure 3
Choroidal melanoma tumor photographed with B-Scan Ultrasonography

William Yates CRA, COT UCHealth diagnostics

CHOROIDAL MELANOMA TREATMENT

In the past, enucleation – the surgical removal of the entire eyeball – was considered the only appropriate method to treat choroidal melanoma. However, due to the introduction of radiation therapies, more conservative methods have been adopted. These conservative treatment methods can preserve the eyeball and may preserve useful vision without affecting the survival rate or the metastatic potential. A multitude of clinical factors determine which treatment method is used to treat choroidal melanoma.[7]

Current treatments for choroidal melanoma include observation, transpupillary thermotherapy (TTT), plaque brachytherapy, external beam radiotherapy, local resection, enucleation and various combinations of these methods. Factors such as visual acuity of the affected eye, visual acuity of the opposite eye, ocular structures involved, presence of metastases, known risk factors for metastases, tumor size, tumor location, and the age, general health and psychological status of the patient are all considered during the process of selecting a treatment method. Counseling also is encouraged as it forms an essential part of care for both patients and close relatives. After patients are informed of their condition, the prognosis – in terms of survival and ocular outcomes – is discussed. The therapeutic options are reviewed so that patients can choose the optimal treatment for their particular condition and personality while also considering their personal needs and fears.[8]

The Collaborative Ocular Melanoma Study (COMS) was organized and funded in 1985 to address several issues related to the treatment of choroidal melanoma.[9] The COMS was a multicenter clinical trial designed to evaluate therapeutic interventions for choroidal melanoma. The COMS demonstrated no difference in survival between brachytherapy and enucleation for medium-sized tumors.[10] Due to the information collected from the COMS, the two most frequently used treatment methods today are enucleation and plaque brachytherapy.

ENUCLEATION

Currently, enucleation is used to remove eyes with tumors where available conservative techniques are unlikely to be successful due to the location or large size of the tumor.[11] If the tumor is very large, or in close proximity to certain ocular structures, it is unlikely that radiation treatment will be successful. The radiation used to treat the tumor most likely will cause damage to normal tissue that is sufficient enough to require eventual removal of the eye. By postponing eye removal in large tumors, the chance of the cancer metastasizing may increase. Enucleation also may be used after conservative techniques have been employed but have failed. There are many possible complications associated with modern conservative techniques to treat choroidal melanoma, and some can be damaging enough to require eventual eye removal.

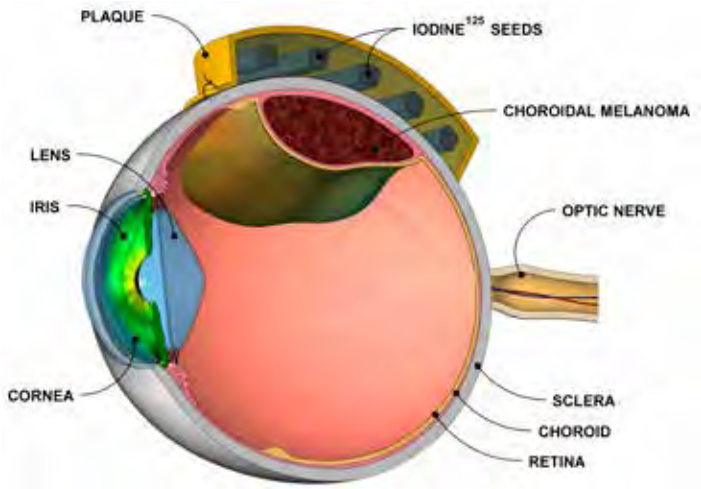

Figure 4
Plaque in place over tumor

Illustration created by Jonathan Rose, CDT

PLAQUE BRACHYTHERAPY

The COMS medium-sized choroidal melanoma trial found that for similarly sized tumors, survival was statistically equivalent whether patients were treated with plaque brachytherapy or removal of the eye. Brachytherapy offers an eye-preserving option with the possibility of maintaining useful vision. For this reason, many patients with tumors who meet certain criteria initially opt for plaque brachytherapy and only consider enucleation if plaque brachytherapy is ineffective. Brachytherapy is a form of radiotherapy where a radiation source is placed inside or next to the area requiring treatment. Plaque brachytherapy, when used to treat choroidal melanoma, is a surgical procedure that involves suturing a plaque that contains seeds of a radioisotope to the outer surface of the eye. The plaque is sutured in place directly above the tumor, in order to treat the tumor within the eye.

Ionizing radiation, at the appropriate dose rates and in the proper physical forms, is intended to damage tumor cells by disrupting DNA. This inhibits the tumor cells' reproduc-

tive ability, but without causing excessive damage to normal tissue.[10] Currently in the US, the most commonly used isotope to create plaques used to treat choroidal melanoma is the radioisotope Iodine-125 (I125). This particular isotope is most popular because of its lower energy emission, good tissue penetration and commercial availability.[5]

PLAQUE CREATION

Each plaque created to treat choroidal melanoma is uniquely constructed for each patient and for their specific tumor. The surgeon determines exact tumor measurements through an ultrasound and other tests performed in an office setting and uses this information to choose a plaque size that fits a predetermined number of seeds. The measurements and selected size are then sent to a medical physicist as a plaque prescription. The medical physicist uses this information to determine the strength that the I125 seeds need to have so that the desired effect on the tumor cells is achieved.

A radioisotope is a version of a chemical element that has an unstable nucleus and emits radiation during its decay to a stable form. The longer a radioisotope is left to decay, the less radiation it emits. Therefore, one must precisely and efficiently determine the strength of the I125 seeds at inception, the timing of the plaque creation in relation to the date and time of surgery and duration in which the plaque is left in place. Once the physicist has determined the required parameters for the seeds, the plaque is created. The plaque consists of multiple radioactive seeds encapsulated in a silicone carrier and covered by a large gold shield on one side. Due to its density, gold can effectively attenuate the radiation from the I125 seeds, which keeps the radiation from traveling to the patient's brain or other eye. The plaque is placed on the eye directly above where the tumor is located so that it emits radiation toward the eye to treat the tumor. (Figure 4)

> In North America, six out of every one million people will be diagnosed with choroidal melanoma each year.[2]

Table 1

Instrumentation

Retinal tray to include:
- Eye speculum
- Tenotomy scissors
- Schepens retractor
- Blunt Westcott scissors
- Castroviejo needle holder
- Cohan mini needle holder
- Nugent angled utility forceps
- Gass retinal detachment hook
- 19-gauge Bishop Harmon cannula
- 0.3mm Castroviejo forceps with teeth

Equipment

- Survey meter
- Surgeon surgical loupes
- Indirect ophthalmoscope
- Transillumination machine
- Ultrasound machine (B-scan)
- Cytology-biological microscope
- Surgeon eye chair with back rest
- Lead aprons and lead thyroid shields for all staff
- Patient eye bed with wrist rest and articulating head-piece

Supplies

- Custom eye pack
- Gloves
- Drapes:
  - Split sheet
  - Head drape
  - 1061 drape
  - Probe drape
- Suture:
  - 8-0 polyglactin 910
  - 2-0 Silk ties
  - 5-0 nylon suture or 5-0 polyester fiber suture
- Dressings:
  - Eye pad x2
- Lead eye shield
- 1-inch paper tape
- Specialty:
  - Plaque
  - 20 diopter lens
  - Transillumination probe
  - Temporary "dummy" positioning plaque

Intraoperative medications

- Balanced salt solution (BSS) – topical to moisten cornea
- Hypromellose 2% – Used topically to keep cornea moist
- Lidocaine 2% – Subtenon injection for post op pain control
- Cefazolin 1g in NS 5ml – antibiotic subconjunctival injection
- Dexamethasone 4mg/ml – steroid subconjunctival injection
- Tobramycin ophthalmic ointment – topical antibiotic ointment
- Bupivicaine 0.75% – subtenon injection for post op pain control
- Dexamethasone ophthalmic ointment – topical steroid ointment
- Hydroxypropyl methylcellulose (HPMC) – topical

Figure 5 *Transparent "Dummy" Plaque used for positioning*

Photo by Karri Schultz, CST

Figure 6 *Gold Plaque with Iodine125 Seeds*

Photo by Karri Schultz, CST

While choroidal melanoma can occur in all races and at any age, research shows that people who have lighter eye and skin colors are at a higher risk.

PLAQUE INSERTION SURGERY

Plaque brachytherapy surgery requires the Certified Surgical Technologist (CST) to have a basic knowledge of micro surgery and ophthalmic instrumentation. As with most surgical procedures, each surgeon has his or her own preferences for instrumentation and supplies. Table 1 shows a general list of instruments, supplies and equipment needed to perform a plaque brachytherapy surgery to treat choroidal melanoma.

PROCEDURE OVERVIEW

General anesthesia is administered by the anesthesiologist or nurse anesthetist, and the patient is placed in the supine position on a specialized eye cart with an articulating head piece. After the time-out, the patients operative eye is prepped by the circulating registered nurse (RN) with a 5% povidine-iodine solution, and the eye is draped by the surgeon or by the resident or fellow who is assisting. After a second time-out, an eyelid speculum is placed in the operative eye by the surgeon or assistant to hold the eyelids open during surgery. Periodically throughout the case a balanced salt solution and hydroxypropyl methylcellulose solution are applied to the cornea to keep it moist. The surgeon uses 0.3 Castroviejo forceps and a dull curved Westcott scissors to make a 360-degree peritomy to peel back the conjunctiva and Tenon's capsule revealing access to the sclera and rectus muscles. The surgeon uses a dull curved tenotomy scissors to bluntly dissect between each rectus muscle. Once the muscles are free, a Gass muscle hook is used to isolate each rectus muscle and a 2-0 silk tie suture is placed around each muscle to help with retraction and manipulation of the eye. Next, the surgeon uses a transillumination probe to mark the tumor's location. This is achieved by placing the transilluminator over the patient's cornea and directing the light into the eye. When the inside of the eye is illuminated, the tumor is visible on the outer surface of the sclera as a dark spot. The surgeon marks the margins of the tumor with a sterile marking pen. This step allows the surgeon to see where the tumor is located when placing the plaque later. The surgeon uses 25-gauge hypodermic needles on a syringe to obtain multiple biopsies of the tumor through the sclera. This is performed to confirm

a choroidal melanoma diagnosis and also to perform a genetic mutation analysis on the tumor. Needle biopsy can also be performed across the vitreous cavity for posterior tumors. The surgeon then looks into the eye using a 20 diopter lens and an indirect ophthalmoscope to ensure no damage was done to the retina. The plaque is then ready to be placed.

A dummy plaque is used to help with the eventual placement of the real plaque. The dummy plaque is identical in shape and size to the real plaque but is clear instead of opaque. The transparency of the dummy plaque allows the surgeon to visualize the marking they made prior to placement and place the plaque directly over it. The assisting resident or fellow uses a Schepens retractor to further open the space between the eyeball and orbit where the plaque is placed. The surgeon uses two Nugent forceps to position the dummy plaque and places two 5-0 nylon or polyester fiber sutures in the sclera to mark the spot where the plaque will sit. The dummy plaque is removed and replaced by the real plaque. The 5-0 sutures that are already in place are used to secure the plaque to the sclera. (Figure 5 & 6)

Once the plaque is secure, the placement is double-checked by the surgeon using indirect ophthalmoscopy, and then again with intraoperative B-scan ultrasonography. Ideally, the plaque will be directly over the tumor with a 2-mm overhang all the way around and not interfere with the optic nerve or any other ocular structures. The surgeon makes any necessary adjustments, and the ultrasonography is repeated until the plaque is in the ideal location. (Figure 7)

The surgeon or assistant cuts and removes the 2-0 silk tie sutures that are around the muscles and the conjunctiva is pulled back up over the eye and plaque. The surgeon sutures the conjunctiva closed with 8-0 polyglactin 910 interrupted sutures, and then the surgeon administers a sub-tenon block of 2% lidocaine mixed 1:1 with 0.75% bupivacaine for pain control. The surgeon also injects a 1:1 mixture of corticosteroid and antibiotic into the conjunctiva to prevent inflammation and infection. The drapes are removed from the patient and the patient's face is wiped clean with a moist sponge. A drop of atropine 1% ophthalmic solution and some tobramycin-dexamethasone 0.1-0.3% ophthalmic ointment are placed in the eye by the surgeon or RN. The atropine 1% ophthalmic solution is used for pain control and also to ensure that the patient's eye remains dilated until the following day. The tobramycin-dexamethasone 0.1-0.3% ophthalmic ointment is used to help prevent inflammation and infection. The surgeon or assistant then places a patch over the eye and secures it in place with 1-inch paper tape and a lead eye shield is placed over the patch. This is to protect hospital staff as well as family members or caregivers from radiation exposure while the plaque is in place. The plaque remains on the eye for 3 to 7 days depending on the size of the tumor, rate of radiation delivery and surgeon preference. The medical physicist surveys the drapes, surgical field, instruments and back table with a survey meter which detects radiation and ensures that no seeds were dislodged during surgery. The patients' operative eye is also surveyed to ensure the lead shield is effectively placed and preventing radiation exposure.

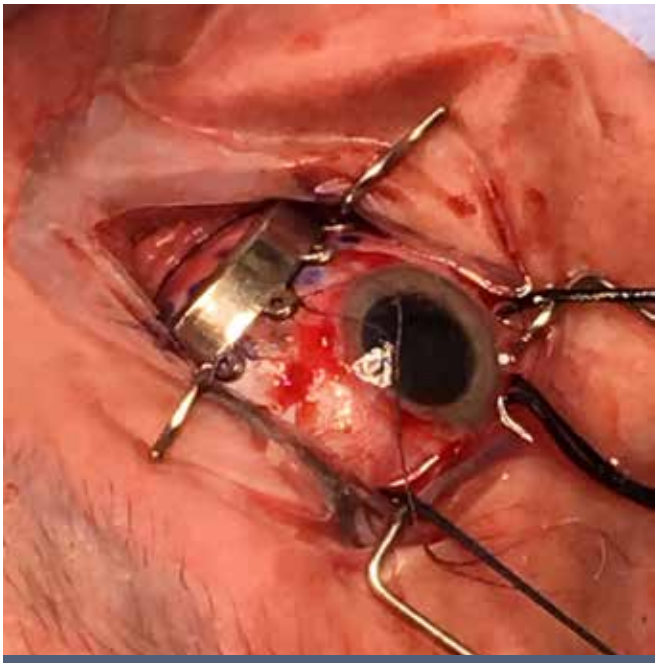

Figure 7 *Plaque in place over tumor before closure of conjunctiva*
Photo by Karri Schultz, CST

Plaque brachytherapy, when used to treat choroidal melanoma, is a surgical procedure that involves suturing a plaque that contains seeds of a radioisotope to the outer surface of the eye.

POST-OP CARE

The patient is seen for follow-up care by the surgeon the day after surgery. If no issues arise, the patient returns in 3 to 7 days to have the plaque removed. A second surgery is needed to remove the plaque, but it is typically a short procedure that does not require general anesthesia. After the plaque treatment is completed and the plaque is removed, patients are seen the first and third week after surgery for post-operative visits. Patients are then seen quarterly if no new ocular symptoms arise. Most commonly, the tumor is regularly re-measured starting three months after surgery and at every quarterly appointment thereafter. Most tumors begin to shrink 3 to 6 months after brachytherapy surgery. Reduction in volume varies widely by tumor but is generally 25 to 50% in the first year. The goal is to shrink the tumor and control tumor growth. Some centers performing plaque brachytherapy have a tumor control rate as high as 95%.

COMPLICATIONS AFTER SURGERY

Due to the destructive nature of radiation therapy and the close proximity of the tumors to other ocular structures, there are many possible complications after plaque brachytherapy surgery. Most complications after plaque brachytherapy are radiation-induced. Possible complications include cataract formation, iris neovascularization, glaucoma, papillopathy, retinopathy, maculopathy, scleral necrosis, strabismus and ptosis.

While some complications such as retinopathy and maculopathy can be managed with medication injections or laser treatment, others must be treated with additional surgery. Cataract, glaucoma, strabismus and ptosis are examples of complications that can be managed with additional surgeries. Some more severe complications such as tumor lysis or complicated retinal detachment are unable to be treated and enucleation is required.

CONCLUSION

Plaque brachytherapy offers an eye-preserving option to treat choroidal melanoma with the possibility of maintaining useful vision. There are many possible radiation-induced complications after plaque brachytherapy surgery. The chances of survival, ocular conservation, visual preservation and avoidance of iatrogenic injury depend greatly on the size, location and extent of the tumor.[8]

ABOUT THE AUTHORS

Karri Schultz has been a CST for 9 years. She has experience in many surgical specialties, but currently works at the University of Colorado Health Eye Surgery Center. She enjoys scrubbing multiple ophthalmic surgical specialties including cornea, cataract, glaucoma, strabismus, oculoplastic and retina.

Dr Scott Oliver is a vitreoretinal surgeon at the University of Colorado Health Eye Center specializing in vitreoretinal surgery and ocular oncology. He is the director of the Eye Cancer Program, medical director of the UCHealth Eye Surgery Center and the chief of the Retina Service at CU.

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Plaque Brachytherapy to Treat Choroidal Melanoma

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1. Where is the choroid located in the eye?
a. Directly behind the lens
b. Directly behind the retina
c. Directly behind the optic nerve
d. Directly behind the vitreous

2. Genes that help cells grow, divide and stay alive are called what?
a. Tumor suppressor genes
b. Polymeric genes
c. Modifying genes
d. Oncogenes

3. Choroidal melanoma is caused by a metastasized skin melanoma.
a. True
b. False

4. Choroidal Melanoma appears:
a. Pigmented
b. Variably pigmented
c. Non-pigmented
d. All of the above

5. When choroidal melanoma metastasizes, the liver is involved:
a. 60% of the time
b. 70% of the time
c. 80% of the time
d. 90% of the time

6. Currently, the most commonly used isotope in the USA to create plaques used to treat choroidal melanoma is the radioisotope _____.
a. Iodine-125
b. Iodine-126
c. Iodine-127
d. Iodine-128

7. The longer a radioisotope is left to decay, the less radiation it emits.
a. True
b. False

8. The plaque consists of multiple radioactive seeds all encapsulated in a silicone carrier, and covered by a large shield on one side. What is the shield made of?
a. Lead
b. Titanium
c. Gold
d. Silver

9. How long does the plaque remain in place?
a. 2-5 days
b. 2-7 days
c. 3-5 days
d. 3-7 days

10. Most tumors begin to shrink _____ months after brachytherapy surgery?
a. 1-2 months
b. 2-4 months
c. 3-6 months
d. 6-8 months

PLAQUE BRACHYTHERAPY TO TREAT CHOROIDAL MELANOMA #417 SEPTEMBER 2018 2 CE CREDITS $12

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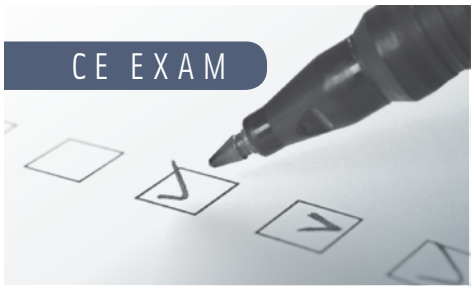

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