

## Management of Iris Melanoma

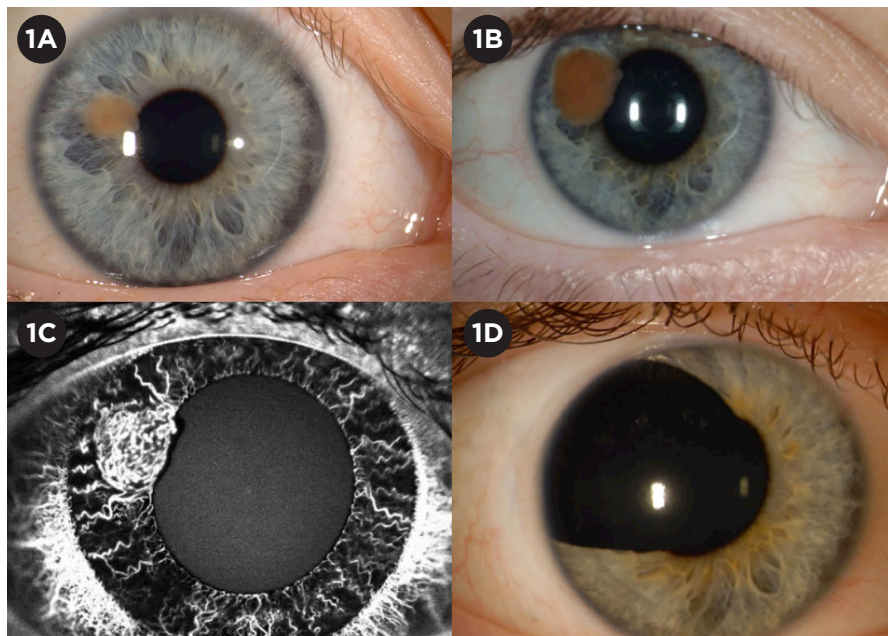
**W**ith melanoma, more than any other cancers we deal with, the size of the lesion is important,” said Carol L. Shields, MD, at Wills Eye Hospital in Philadelphia. Fortunately, iris melanomas tend to be discovered at a small size, sometimes even when they’re still hiding out as a nevus. In part, this explains why the five-year relative survival rate is over 95%, the highest of the uveal melanomas.<sup>1</sup>

General ophthalmologists know that the responsibility for identifying suspicious lesions often falls to them. To review the differential diagnosis and potential red flags, see “Differentiating Iris Pigmented Lesions: A Primer” in last month’s *EyeNet*.

The strategies for treating iris melanoma depend on tumor size, location, and shedding of pigment. Small tumors without dispersed pigment are candidates for resection. Radiotherapy can be used to treat most iris melanomas, but enucleation may be necessary for patients who have tumors that have shed pigment diffusely and secondary glaucoma. All of these treatments have high success rates, according to Dr. Shields.

### Management Is a Partnership

Regardless of the specific treatment approach, management begins with a frank conversation with the patient. It’s always a risk-benefit analysis on how



**RESECTION.** (1A-C) Growth of iris melanoma leading to (1D) resection.

to treat and even whether to biopsy, according to Alison H. Skalet, MD, PhD, at the Casey Eye Institute in Portland, Oregon. You may see two patients with identical-appearing lesions, and they may choose different approaches. “It’s a partnership,” she said.

Timothy S. Fuller, MD, at Texas Retina Associates in Dallas, begins by laying out the top three priorities. These are 1) saving the patient’s life, because iris melanoma can spread to the liver, lungs, and other organs; 2) saving the eye, if possible; and

3) saving as much vision as possible (including in the unaffected eye). “Once we establish that framework, helping the patient to understand our hopes and goals, then we talk about the options,” said Dr. Fuller.

Likely because Dr. Fuller is in a retina practice, he also has to reset patients’ expectations when it comes to treatment. He repeatedly hears, “Can’t you just laser this?” Many of his patients are surprised when they learn that treatment isn’t that simple.

### When to Wait?

Because iris melanomas carry a lower risk for metastatic disease than melanomas arising in the choroid or ciliary body, and because iris melanomas that

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are at higher risk for spread are associated with specific findings, some small iris melanomas may be managed with close observation. This determination is complex and involves a discussion of risk with patients. Comprehensive ophthalmologists who suspect an iris melanoma should refer the patient to an ocular oncologist for evaluation and discussion of options, including observation versus surgical or radiation treatment.

“Wait and watch is sometimes an option for low-grade iris melanomas, especially those without seeding, confined to the iris only, and without associated glaucoma,” said Dr. Fuller. This is because of the assumed low rate of metastasis and because of the potentially deleterious side effects of definitive treatment.

### When to Resect?

If a small tumor has shown growth but has not seeded, then you can consider an iris resection to remove the lesion entirely, according to Dr. Fuller. Dr. Shields explained, “You can create a large scleral flap, open up the eye, cut out the tumor, sometimes even put a little suture in to close the [surgical] hole you created in the iris, and put the flap down to close the eye. The patients do beautifully without seeing one ray of radiation.”

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## Whether to Biopsy

Iris melanoma is sometimes confirmed with fine-needle aspiration biopsy, though it’s not standard because of the associated risks. Dr. Shields finds it helpful for two reasons. First, cytology can show whether the cells are spindle, mixed, or epithelioid cell type. The latter is the most aggressive. Diffuse melanoma, which grows flat, like crabgrass, all over the iris and changes the iris color to brown because of all the pigment dusting it, tends to be epithelioid.

Second, the biopsy sample can be used for molecular prognostic testing, which can predict how aggressive the cells in the tumor might be. Mutations on chromosomes 3 and 8 carry a risk for metastatic disease and tend to be associated with epithelioid cell type. Gene expression profile testing can also be performed to help predict how a tumor may behave, with class 1B and 2 tumors carrying increased risk for spread outside the eye. For patients with high cytogenetic risk, Dr. Shields may prescribe sunitinib, a protein kinase inhibitor. Large studies on choroidal melanoma patients with mutations on chromosomes 3 and 8 have demonstrated a reduction in risk for metastatic disease with six months of sunitinib.<sup>1</sup>

<sup>1</sup> Valsecchi ME et al. *Ophthalmology*. 2018;125(2):210-217.

### Advantages.

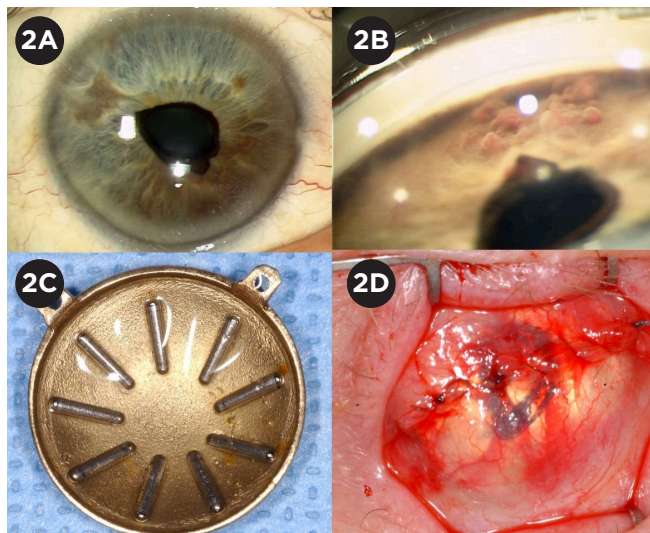
The patient avoids the risk for glaucoma, radiation-related cataracts, and corneal epitheliopathy, according to Dr. Shields.

### Disadvantages.

Resection runs the risk of leaving some of the tumor behind. “Incompletely resected iris melanoma poses an increased risk for spread compared with patients who have completely resected tumors or tumors treated with radiation,” said Dr. Skalet. After resection, there can also be distortion of the iris architecture and cosmetic issues, Dr. Fuller added. In addition, as with any intraocular surgery, there is a risk for cataract formation, although that risk is higher with radiation therapy, he said.

### When to Irradiate?

If a smaller tumor has seeded or the tumor is large, plaque brachytherapy (most commonly with Iodine-125 radiation) is preferred. This is the most



**RADIOTHERAPY.** (2A, B) Diffuse iris melanoma with (2C, D) plaque radiotherapy.

common treatment approach for iris melanoma, according to Dr. Skalet.

A typical case, said Dr. Shields, would be a patient who comes in with documented growth of a pigmented iris melanoma; you do gonioscopy and see that it has seeded into the angle. “Once a tumor has seeded, we have to either irradiate or remove the eye because each one of those seeds can produce a tumor.” Most seeding is seen inferiorly—as particles break off the tumor and float in the aqueous humor, gravity pulls them down, she said.

The procedure involves temporarily implanting a brachytherapy device carrying radiation seeds by sewing it to the sclera, covering the cornea to ensure coverage of any area where the tumor is located, said Dr. Skalet. There are two surgeries, one to implant the device, the other to explant it after the treatment dose has been delivered.

While the plaque is in place, the patient is radioactive, Dr. Skalet said. Depending on which state you live in, you may be required to admit the patient to the hospital. In some states, patients are given self-sequestering instructions and are allowed to leave with a lead shield over the eye to reduce the radiation, she noted.

Very recently, Dr. Shields had a patient with a superotemporal iris melanoma that had seeded the whole inferior angle. She covered the entire cornea plus 2 mm to 3 mm on each

side with a radioactive plaque. “It can be uncomfortable for the patient, so we create a Gundersen flap, which covers the plaque to hold it steady on the surface of the eye, preventing movement,” said Dr. Shields. “If the plaque does not move, the patient will be more comfortable.”

**Advantages.** “Plaque brachytherapy is highly successful because it’s relatively easy to confirm that you have good placement of the radiation, unlike when irradiating the posterior chamber,” said Dr. Fuller. Ensuring good coverage reduces the likelihood of leaving areas untreated, he said.

**Disadvantages.** In the short term, plaque brachytherapy is highly inflammatory, creating surface changes on the cornea that can be quite painful. In the long run, however, most patients tolerate the procedure well, said Dr. Fuller.

### When to Enucleate?

If you see a very large melanoma or diffuse seeding in the angle, producing secondary glaucoma, then enucleation is the optimal approach. Why is this the case? “Because,” said Dr. Shields, “the other two treatments aren’t going to do anything for the glaucoma, and the eye is just going to go down the tubes—loss of vision, high pressure, corneal epitheliopathy—if we do anything but enucleation.”

### What Comprehensive Ophthalmologists Need to Know

**1. Take photos.** Images are critically important because growth is one of the key factors in treatment decisions. “I really appreciate when a patient comes with historical photographs that we can use to help determine the best treatment approach,” said Dr. Skalet. “In specialist clinics, we use slit-lamp photography, gonioscopy photography, and ultrasound biomicroscopy. In most offices, those might not be available. But, nowadays, there are a lot of ways of taking good photographs, even without a slit-lamp camera. Getting the best images you can—even if it’s with a smartphone—or sending a patient for a consultation with a specialist who can take good baseline photographs and measurements with an ultrasound

will inform future management,” she emphasized.

**2. Be cautious about glaucoma surgery.** Tube shunts and microinvasive glaucoma surgery should be avoided in patients with unilateral glaucoma and an iris pigmented lesion, said Dr. Shields, who urged glaucoma specialists to refer patients to an ocular oncologist to rule out melanoma before surgery.

**3. And be cautious about cataract surgery.** Be aware of when to pursue cataract surgery in a patient who needs it but has had an iris melanoma. “I generally request that patients wait at least two to three years after radiation before having cataract surgery,” said Dr. Fuller, “because we want to be sure the tumor is completely regressed and not active.” He then gives advice to the comprehensive ophthalmologist who is doing the cataract surgery about placing the haptics of the lens away from where the tumor was.

**4. Be aware of radiation side effects.** Comprehensive ophthalmologists are most involved with iris melanoma patients when they are dealing with residual effects from radiation, such as dry eye, healing of the conjunctiva that could create some dry patches on the cornea, or cataract formation in phakic patients. Dr. Fuller always reminds his patients and their comprehensive ophthalmologists that, after radiation, the lens capsule is at greater risk for rupture, raising the risk of any procedure down the line.

<sup>1</sup> [www.cancer.net/cancer-types/eye-cancer/statistics](http://www.cancer.net/cancer-types/eye-cancer/statistics). Accessed Dec. 14, 2019.

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