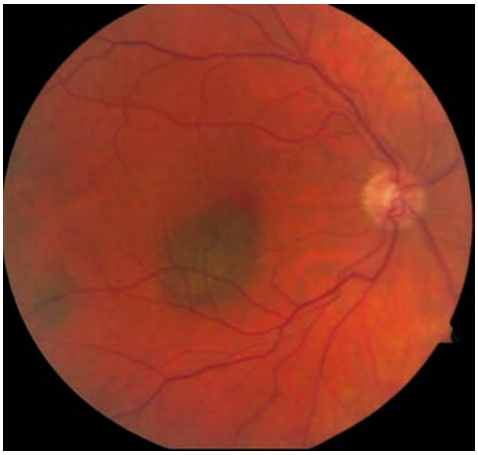
UCLA Stein Eye Institute | DOHENY EYE INSTITUTE

CLINICAL UPDATE

Proactive Approach to Treating Ocular Melanoma Improves Visual and Survival Outcomes



Small choroidal melanoma in the macula.

A proactive approach to detecting and treating small ocular melanoma is leading to better visual and mortality outcomes for patients, according to Tara McCannel, MD, PhD, director of the UCLA Stein Eye Institute's Ophthalmic Oncology Center. The approach represents a significant shift from the way these tumors were treated in the past, Dr. McCannel notes.

Although extremely rare, ocular melanoma is a potentially fatal ophthalmic condition—in approximately half of patients, the cancer spreads to the liver. While new treatments currently being developed may prolong survival, there is no cure once the cancer metastasizes. Within the field of ophthalmic oncology, the consensus has been that little can be done to reduce the risk of metastasis, Dr. McCannel explains. This thinking is largely based on findings over the last two decades from the multicenter Collaborative Ocular Melanoma Study. But that study looked mostly at medium and large tumors, and there is little prospective long-term data on patients with small melanomas.

Small melanomas generally present when they begin to distort vision—typically when they are near or at the macula. "We know that larger tumors have a higher risk of metastasis, while very small tumors are considered to be low risk," Dr. McCannel says. "So traditionally, rather than treating the macula and risking visual harm, it has been considered acceptable to simply monitor the small melanomas."

Unfortunately, Dr. McCannel notes, these tumors will continue to grow and eventually

continued on page 2

Artificial Implant Devices Found Safe and Effective for Patients with Iris Defects

A UCLA Stein Eye Institute researcher who conducted the first and only clinical trial in the United States of artificial iris implant devices for patients with small, moderate, and large iris defects has found that the devices, manufactured by the German company Morcher GmbH, are relatively safe and effective at reducing light and glare sensitivity. Kevin M. Miller, MD, Kolokotrones Chair in Ophthalmology at the UCLA Stein Eye Institute, notes that the devices, if ultimately approved by the U.S. Food and Drug Administration (FDA), could significantly improve the quality of life for patients in the United States who currently have no effective treatment options. Over the last decade, Dr. Miller implanted 64 eyes with three types of Morcher devices.

The iris, the eye's colored portion, serves two main purposes—acting as a diaphragm in regulating the amount of light entering

continued on page 3

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In This Issue

Proactive Approach to Treating Ocular Melanoma Improves Visual and Survival Outcomes

continued from cover

have a significant effect on the patient's vision. At that point, the melanoma is larger, requiring more radiation to treat it and leading to a poor visual outcome and higher risk of metastasis.

More recent reports of ocular melanoma outcomes after local treatment failure have shown that when controlling for tumor size, the rate of metastasis is much higher among patients who experience a tumor recurrence in the eye than among patients who have successful treatment of the primary eye cancer. "This suggests that promptly controlling the tumor does matter, and that our treatments are having an impact in reducing the likelihood of metastasis," Dr. McCannel says. Individual case reports also suggest that a melanoma left to grow in the eye acquires a more aggressive genetic phenotype, she adds.

"Even before all of these recent papers, our feeling has been that when the melanoma is small, that's the best time to intervene because you can use a limited amount of radiation and spare the vision rather than waiting for the tumor to become so large that damage to the macula is inevitable," Dr. McCannel says. "Now we have data suggesting that early treatment of these small melanomas may help to improve survival, which is a 180-degree turn from the conventional teaching and practice in ocular oncology. And in talking to patients, they also prefer immediate and definitive treatment."

This aggressive approach to treating ocular melanomas extends to systemic surveillance of patients by oncologists who work closely with the Center's ophthalmologists. "In the past, patients who developed metastasis were often told to quit their jobs and prepare to die, but with new cancer drugs being approved every few months, we know that if we can detect the cancer in the body very early, these patients have treatment options that may be successful," Dr. McCannel says.

For more than six years, Dr. McCannel and her colleagues at the Stein Eye Institute's Ophthalmic Oncology Center have employed silicone oil to prevent or reduce radiation retinopathy in ocular melanoma patients. Radiation therapy with iodine-125 is considered the gold standard for ocular melanoma treatment, but healthy tissue may be damaged by the radiation treatment. In 2010, Dr. McCannel's group first demonstrated that silicone oil—a substance commonly used in the repair of retinal detachments—can act as a barrier to reduce the amount of radiation exposure to the healthy eye tissue. More recently, Dr. McCannel and colleagues found that after one year, there were significant benefits to the vision of patients with large ocular tumors who were treated with the silicone oil vs. those who were not. "Silicone oil has become a very important tool for minimizing radiation damage while still allowing for effective treatment of the melanoma in our Stein Eye Institute patients," Dr. McCannel says.

The Center is also proactive in detecting and treating co-morbid diseases in ocular melanoma patients. "After an eye has been successfully treated for melanoma, there is often a sense that the patient dodged a bullet, we killed the tumor, let's not mess with success," Dr. McCannel says. "But just like with any eye, a patient can still develop treatable conditions like glaucoma, retinal detachment, macular pucker, macular degeneration, or cataract. And too often, these eyes end up with extremely poor vision or totally blind because they haven't been attended to."

After the Center's patients are treated for ocular melanoma, a variety of imaging studies are used to detect early signs of vascular damage, given the frequency of radiation retinopathy as a treatment side effect. When mild vascular abnormalities are detected near the macula or central vision, patients can be treated with anti-VEGF injections, Dr. McCannel explains. Imaging can also reveal areas of ischemia resulting from the vascular damage, and those patients can benefit from laser treatment. "If we don't look for those possible complications, patients can develop conditions like neovascular glaucoma, and these eyes can even end up being enucleated because of complications that could have been avoided if the abnormalities were detected and treated early," Dr. McCannel says.

Although treatment remains a challenge and the potential side effects and risks to vision and life continue to be significant, there is cause for optimism. "We are in a new era for ocular melanoma," Dr. McCannel concludes. "No longer do we believe that 'less is more.' We are now much more proactive, with a focus on early detection and treatment of melanoma, early detection of ocular side effects from treatment, and early detection of systemic complications that can occur with this cancer."

Artificial Implant Devices Found Safe and Effective for Patients with Iris Defects

continued from cover

the eye, and fine-tuning depth of focus. When the iris is absent or partially defective, patients can be left with debilitating light and glare sensitivity, as well as decreased visual acuity, reduced visual quality, and poor contrast sensitivity. Beyond the functional problems, many patients experience cosmetic concerns, particularly if they have light-blue irises. Aniridia—the absence of an iris—can be present at birth, but far more commonly iris defects result from ocular injury, including blunt or penetrating trauma. When caused by trauma, the impact of the iris defect on vision is often compounded by damage to adjacent structures.

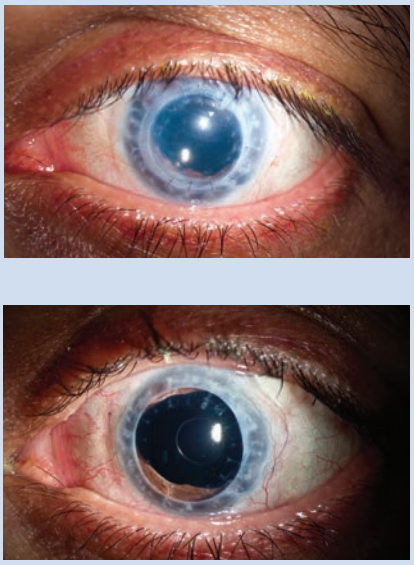
"Prior to artificial iris devices, there weren't really any good solutions for these patients," Dr. Miller says. "Iris defects are otherwise managed by darkly tinted sunglasses; colored or artificial-pupil contact lenses, whose thickness makes them difficult to wear; procedures such as iris suturing for small defects; tattooing of the area of the cornea overlying the iris defect to block some of the light coming in; and wearing a patch if only one eye is affected."

Dr. Miller notes that artificial iris devices, including iris diaphragms and iris reconstruction intraocular lenses, have become available in limited markets in Europe and Asia for patients with congenital and traumatic iris defects. Morcher iris diaphragms have been implanted for more than two decades, with successful safety and efficacy results reported, but there have been no formal clinical trials. In the United States, the devices are not FDA-approved and are no longer available through compassionate-use exemption.

Concerned that he couldn't offer effective solutions to many of his patients with iris defects, Dr. Miller in 2003 obtained an investigational device exemption from the FDA and began a clinical trial of several Morcher iris diaphragms. He was originally given permission to enroll 20 patients, and after positive initial results, he was granted approval to expand the procedure to 70 patients. All together, 64 patients were implanted; six did not undergo surgery for various reasons. Dr. Miller published on the safety and efficacy experiences of patients with one-year follow-up in the *Journal of Cataract & Refractive Surgery*, in 2015 and in 2016.

Dr. Miller's 2015 paper reported on patients with small defects of the iris who were treated with the Morcher 96F, a modified capsular tension ring (CTR) with a single black occluder paddle. The device is a 0.15 mm thick CTR with a 90-degree segmental occlude made of ultraviolet light-filtering/opaque material. The 2016 paper reported on the Morcher 50F, a modified CTR with multiple black occluder paddles for patients with moderate to large iris defects. Both devices were implanted in patients at the time of cataract surgery. "We take out the cataract, put a lens implant in, and then put one or two of these modified capsule tension rings inside the capsule, where the lens implant sits," Dr. Miller explains.

For the first paper, Dr. Miller treated 16 patients with CTR implantation for small iris defects. There were no intraoperative complications, three adverse events (one case of ocular hypertension, one postoperative retinal detachment, and one 25-degree rotation of the CTR), and four secondary surgical interventions. "We found no evidence of corneal or macular toxicity that we would attribute to the device," Dr. Miller says. "The devices don't seem to induce any problems for patients that wouldn't be expected to occur as a result of cataract surgery alone. There were surgical interventions after these devices, but some of them would have occurred after a cataract operation anyway." Moreover, there were statistically significant improvements in all three of the study's efficacy measures: the objective measurement of corrected distance visual acuity (CDVA) with glare, and subjective assessments of daytime and nighttime glare. Cosmesis was also evaluated subjectively, with no statistically significant impact from the implantation.



Before and after photos of an aphakic eye with a failed corneal graft that underwent repeat penetrating keratoplasty and implantation with scleral suture fixation of a Morcher 67B iris reconstruction lens.

The results of Dr. Miller's study of Morcher 50F diaphragm implantation with 12 patients who had moderate to large iris defects were similar. No patient lost visual acuity and all showed an improvement in CDVA similar to what would be expected from cataract surgery. In the study's primary efficacy measure, change in CDVA with glare, all but one patient showed an improvement. Daytime glare symptom scores improved for 11 of the 12 patients, and nighttime glare symptom scores improved for all 12 patients.

In the time that Dr. Miller has been studying the Morcher products, other artificial iris devices have been introduced with improved cosmetic features. After reporting on the third device he implanted during the study, the Morcher 67B iris reconstruction lens, Dr. Miller plans to meet with FDA officials to begin the process of obtaining market approval. "Fortunately, very few patients need these iris implant devices," Dr. Miller says. "But for the ones who do, they need something like this badly."

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