

# News in Review

COMMENTARY AND PERSPECTIVE

DRUGS AND DEVICES

## U.S. Surgeons Gain Access to Artificial Iris

### OPHTHALMOLOGISTS IN THE UNITED

States now have full access to a prosthetic iris, thanks in part to a decade-long effort spearheaded by the ophthalmic community.

The U.S. Food and Drug Administration gave marketing approval on May 30 to the CustomFlex Artificial Iris for implantation in children and adults with aniridia and other iris defects. Clinical Research Consultants in Cincinnati sponsored the U.S. trial of the device, which is manufactured by HumanOptics.

**New era.** The approval marks the end of an era during which U.S. surgeons could implant 1 of the prosthetic irises available overseas only by asking the FDA for a compassionate use exemption. This was a tedious, rule-bound process, and it had to be tackled 1 patient at a time, said Michael E. Snyder, MD, at the University of Cincinnati.

**Device details.** The CustomFlex implant is a foldable, surface-textured silicone prosthesis that is custom-colored for individual patients, to match the fellow eye. It measures 12.80 mm in diameter, with a pupil diameter of 3.35 mm, and can be injected through an unenlarged 2.2-mm phaco incision. It can be implanted in the capsular bag or sutured to the sclera.

**Availability.** The device is expected to be commercially available later this year to U.S. surgeons who undergo special training, said Barbara S. Fant, PharmD, president of Clinical Research Consultants, the Cincinnati consulting firm that sponsored the 389-subject trial that led to the device's approval.

**Supporting research.** Dr. Snyder and Dr. Fant said they began gathering clinicians' support for a trial, as well as lobbying HumanOptics to enter the U.S. market, more than a decade ago. The 12-site study began in 2013, with Dr. Snyder and R. Doyle Stulting, MD, PhD, of Atlanta, as medical monitors. Data submitted to the FDA<sup>1</sup> included the following:

- **Satisfaction.** More than 70% of patients experienced decreases in light sensitivity and glare; 94% were satisfied with the artificial iris' appearance.
- **Adverse events.** The rate of adverse events was low and included device movement or dislocation (sometimes necessitating repositioning during surgery); increased intraocular pressure (IOP); iritis; synechiae; and secondary surgery to reposition, remove, or replace the device.
- **Surgery-related complications.** Also minimal, complications included increased IOP, intraocular blood leakage, cystoid macular edema, secondary surgery, corneal swelling, iritis, and retinal detachment.



**BEFORE AND AFTER.** This recipient of the artificial iris had aniridia in his right eye. In the bottom image, note the near match of the prosthesis to the color of the fellow eye.

**FDA process.** The FDA designated the CustomFlex a "Breakthrough Device" last December, which put the device on an expedited approval pathway. The premarketing approval (PMA) came after close cooperation between the FDA, Clinical Research Consultants, HumanOptics, and the investigators. "To the best of our knowledge, we're the first ophthalmic device to receive a PMA approval through this new FDA pathway," Dr. Fant said.

Dr. Snyder noted that the FDA "has been part of this process from day 1. We started off with a very collaborative process with the FDA, and we've followed that all the way through." He added that he is particularly excited about the approval because "patients who previously had no access to this technology are now going to be able to access it within their own community, or in a neighboring community."

—Linda Roach

1 [www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm609291](http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm609291).

**Relevant financial disclosures**—Dr. Fant: Clinical Research Consultants: E,O; HumanOptics: C; VEO Ophthalmics: E,O. Dr. Snyder: HumanOptics: C,P; VEO Ophthalmics: O.

**EXTRA MORE ONLINE.** For a video on implanting the artificial iris, see [aao.org/clinical-video/using-human-optics-custom-artificial-iris](http://aao.org/clinical-video/using-human-optics-custom-artificial-iris).

## EDUCATION

# Wellness Efforts: What Residents Really Think

Burnout. Depression. Suicide. More than two-thirds (68.4%) of U.S. ophthalmology residents responding to a national survey reported that peers in their programs have faced these issues within the past year.<sup>1</sup> More than a fourth (26.3%) acknowledged being in-

involved in a patient case in which these problems adversely affected a medical judgment or outcome.

The findings paint a troubling picture of the burdens placed on ophthalmic residents. And it is one that is at odds with the perceptions of residency program directors. In another survey by the same research team, only 25% of program directors expressed concern about resident wellness.<sup>2</sup>

**A surprise.** While depression and burnout have been associated with resident training, the extent of stress among residents reported in this survey was surprising, said coauthor Paul B. Greenberg, MD, MPH, at Brown University in Providence, Rhode Island.

**Findings.** The survey, the first to assess the status of resident wellness in U.S. ophthalmic education from a resident's point of view, contained 12 multiple-choice questions and provided room for comment. It was emailed to all (N = 1,048) ophthalmology residents in the United States, yielding a 23.0%

response rate (n = 241). Results included the following:

- Just one-fourth (26.7%) of respondents reported that their department had a formal resident wellness program.
- Of residents in schools with wellness programs, 45.6% said their departments did not promote a culture of wellness.
- Some 38% of residents did not know if they had access to free counseling services. (In yet another disparity between ophthalmic program director and resident perceptions, 98% of program directors had reported the availability of free counseling services in their programs.)
- Among residents who were aware of counseling services, 26.3% did not know how to access them.

When asked what most hindered their participation in wellness programs, 25% cited a lack of time, while 16% cited the duration or scheduling of their shifts. Other barriers to participation included academic stressors, paperwork and administrative require-

## CORNEA

# Need a Cornea? Try 3-D Bioprinting

British tissue engineers have demonstrated that a 3-D printer, using bioink made from collagen, alginate, and keratocytes, can fabricate tissue that has the shape and structure of the native human corneal stroma.

The scientists built the artificial cornea structure by spraying a 300- $\mu$ m-wide stream of this bioink in a circular pattern onto a curved, recessed mold shaped like a model cornea.<sup>1</sup> The keratocytes arranged themselves radially, as they would in a normal cornea, and remained viable within the bioprinted tissue for at least 7 days, they reported.

"We've demonstrated that images taken from a patient's eye can be rendered in a 3-D model on a computer, and that 3-D model then can be re-created in a dish," said coauthor Che J. Connon, PhD, at Newcastle University in Newcastle upon Tyne, United Kingdom.

**Understanding corneal biology.** Dr. Connon's research group has been working toward corneal tissue engineering for 2 decades, developing the fundamental knowledge that supports this proof-of-principle study, he said. For instance, the scientists recently reported that the substrate's shape determines the alignment of the keratocytes; in turn, this is crucial to duplicating the

cornea's uniquely organized, hierarchical structure.<sup>2</sup>

"We have found that one way to align the stromal cells in the bioprinted structure is to just grow the cells on a curved surface. And we believe this is actually fundamental to the way the corneal biology is," Dr. Connon said.

"We know from our previous work that if you align the keratocytes then they will produce aligned collagen. And as the cells lay down new stromal layers, the cells there will orient orthogonally," he said. "So we think the shape is actually driving lamellae formation, collagen alignment, and then the transparency that follows because of the constructive and destructive optical interference from the aligned collagen fibers."

**Individualized prostheses?** Dr. Connon said the goal is to bioprint transplantable corneal prostheses, individualized to each patient. "I think the cornea is uniquely positioned to be one of the first, if not the first, clinically proven printed tissues," he said.

He added that they envisage producing a printed stroma that would be used with deep lamellar anterior keratoplasty. "So you wouldn't be printing the endothelial cells, just the stroma. Then the limbal epithelial cells would grow onto the surface of the implant."

—Linda Roach

1 Isaacson A et al. *Exp Eye Res*. 2018;173:188-193.

2 Gouveia RM et al. *Adv Biosyst*. Published online Oct. 20, 2017.

**Relevant financial disclosures**—Dr. Connon: Atelerix: O.

ments, and understaffing at clinical sites.

**Rx for wellness.** Dr. Greenberg noted that he hopes the study will encourage residents and graduate medical education leaders to better appreciate the value of wellness programs.

For starters, he proposed 2 solutions: “Educate residents regarding the accessibility of wellness programs, and give residents time to attend them.”

—Miriam Karmel

1 Tran EM et al. *JAMA Ophthalmol.* 2018;136(6):695-701.

2 Tran EM et al. *J Surg Educ.* 2018;75(1):95-103.

Relevant financial disclosures—Dr. Greenberg: None.

## ONCOLOGY

# Uveal Effusion and Cancer Drugs

Doctors at the University of Michigan Kellogg Eye Center have reported a series of 3 patients who developed uveal effusion syndrome following treatment with immune checkpoint inhibitors.<sup>1</sup> This new immunotherapy for solid cancers may cause an autoimmune response that adversely affects various organ systems, including the eye.

**Ocular toxicity.** When the 3 patients at the university-based ocular oncology clinic presented with uveal effusion, “the only recent change in their medical history was the start of the immune checkpoint inhibitor therapy,” said coauthor Hakan Demirci, MD, at the University of Michigan.

The men, ages 52 to 85, all developed uveal effusion 1 to 2 months after initiating therapy to treat either melanoma or lung cancer. Prior to presentation, each had received at least 2 infusions of the monoclonal antibodies atezolizumab, nivolumab, or pembrolizumab.

**Symptoms and resolution.** Anterior chamber inflammation was noted in 2 of the 3 cases, and visual acuity deteriorated and intraocular pressure spiked in all 3. The syndrome resolved after all immunotherapy was discontinued, without ophthalmic treatment, in 2 of

the patients. In the third case, despite ocular issues, the patient continued therapy and died 4 months after initial presentation.

**In the clinic.** “We can’t advocate stopping the medication in these patients,” Dr. Demirci said. “This might not be possible because of the presence of the widespread metastatic disease.” He advised consulting the patient’s oncologist about systemic corticosteroid therapy to treat the eye. If that’s not possible, he recommended observing the patient to see if the uveal effusion worsens and affects vision.

**The bottom line.** Although the most common ocular complication of immune checkpoint inhibitors is uveitis (seen in about 0.3 to 0.6% of patients), ophthalmologists should be aware of this potential side effect, Dr. Demirci said. “Patients who present with uveal effusion should be questioned regarding the use of immune checkpoint inhibitors. Similarly, patients who use immune checkpoint inhibitors and who develop ocular symptoms should be evaluated for uveal effusion.”

—Miriam Karmel

1 Thomas M et al. *JAMA Ophthalmol.* 2018;136(5):553-556.

Relevant financial disclosures—Dr. Demirci: None.

**EXTRA MORE ONLINE.** For more on ocular side effects of immune checkpoint inhibitors, see “Molecularly Targeted Cancer Drugs and Ocular Toxicity” in the October 2017 issue at [aao.org/eyenet](http://aao.org/eyenet).



**SIDE EFFECT.** Choroidal effusions, observed during the fundus examination.

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### Feature

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### Clinical Update

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**Retina** Intraoperative OCT is entering the retinal OR. Applications for and barriers to its use.

### Morning Rounds

Two days after the onset of blurred vision, the patient began to experience severe pulsating eye pain and worsening vision. Now, she said that she could see only “fog” with her right eye.

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