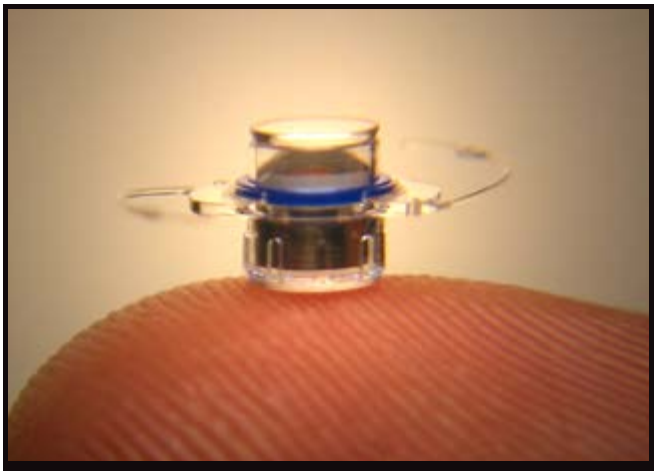
5-Year Results With Implanted Telescope

With end-stage age-related macular degeneration (AMD), patients have exhausted medical or surgical treatment options. One device that—along with appropriate rehabilitation—may help them cope with central visual loss is the implantable miniature telescope (IMT; VisionCare Ophthalmic Technologies). An extended follow-up study on patients from the original 24-month clinical trial reported that visual benefits persisted for 5 years after the surgery, along with an acceptable safety profile.[1]

What is it? The IMT is a fixed-focus quartz glass lens with wide-angle micro-optics, which is implanted behind the iris through a 12-mm incision after the natural lens has been removed. The device produces a telephoto effect that enlarges objects in the central visual field, with the trade-off of reduction in peripheral vision; thus, it is implanted in only 1 eye to allow the other eye to compensate.

The IMT won FDA clearance in 2010 for use in patients 75 years or older with advanced, bilateral AMD. In October 2014, the indication was expanded to include patients aged 65 and older.

Data supportive of expanded indication. In a subgroup analysis in the extension study, the investigators stratified the results by age at implantation: 65 through 74 years old (n = 31) and 75 years and older (n = 32).



TINY TELESCOPE. The IMT is implanted through a 12-mm incision in place of the patient's natural lens.

According to study coauthor David Boyer, MD, "Now we have long-term safety data showing that the implant can be placed in people 65 to 74, and they do extremely well. In fact they do better than the original group of patients, age 75 and above." Dr. Boyer, a vitreoretinal subspecialist, is a clinical professor of ophthalmology at University of Southern California Keck School of Medicine.

Retained acuity gains. Compared with baseline vision, the mean gains in best-corrected distance visual acuity (BCDVA) with the IMT were similar between the age groups in the original 24-month study: 3.1 lines in patients 75 years and up, and 3.3 lines in younger patients. But at 60 months, the older patients had retained less of their IMT-aided acuity; their mean gain in BCDVA from baseline measured 2.1 lines, compared with 2.7 lines in the younger group.

Gains of 3+ lines. At 60 months, 58.1% of patients in the younger group had

gained 3 lines or more of BCDVA, compared with 37.5% of the older group.

Effect on corneal health. One of the most important long-term safety concerns was the effect of the device on the corneal endothelium. The authors reported that the mean annual endothelial cell loss in eyes implanted with an IMT was about 3%, which is consistent with the annual chronic mean cell loss (2.8%) reported after large-incision cataract surgery. At 60 months, younger patients had a mean endothelial cell count of 1,552 cells/mm^2 (95% CI 1,325-1,779); in the older group, cell density was 1,576 (95% CI 1,333-1,819).

"Having this long-term safety data for the cornea should make ophthalmologists feel much more comfortable putting this device in," Dr. Boyer said. "Prior to this, we didn't know long term if the corneas were going to decompensate or whether there would be a need for corneal transplants," he said. "But, overall, the loss of endothelial cells seemed very, very small, and consistent with the old style of cataract surgery where we made very big incisions." —*Linda Roach*

1 Boyer D et al. *Clin Ophthalmol.* 2015;9:1099-1107.

Relevant financial disclosures—Dr. Boyer: *VisionCare Ophthalmic Technologies: C.*

Glaucoma Risk Factors

Metformin Associated With Reduced Risk of OAG

Researchers at the University of Michigan Kellogg Eye Center have reported that metformin hydrochloride, a drug commonly prescribed for the treatment of type 2 diabetes, was associated with a 21% reduction in the risk of developing open-angle glaucoma (OAG) among patients with diabetes.[1] Other oral antihyperglycemic medications did not confer a similar risk reduction.

Metformin is a caloric restriction mimetic (CRM) drug that targets known aging pathways. It has been found to extend life span and reduce risk or delay the development of some late-onset diseases, including cardiovascular disease, diabetes, and some cancers. Now, it appears that we may be able to add OAG to the list.

Study details and results. This retrospective cohort study was based on longitudinal data from more than 150,000 patients with type 2 diabetes and no preexisting record of OAG. Forty percent filled at least 1 metformin prescription. During the 10-year study period, 5,893 (3.9%) of the patients, all members of a large health care network, developed OAG.

The researchers compared users of metformin with nonusers, analyzing the data by means of regression modeling. Each model demonstrated substantial reductions in OAG risk among those using metformin. In one model, each additional 1-g exposure to metformin conferred a 0.16% reduction in the risk of developing OAG. That means that in 2 years, a patient taking the normal daily 2-g dose of metformin would have a 21% reduction in OAG risk, compared with a diabetic patient who had no metformin exposure.

"This is a substantial level of glaucoma risk reduction for the period of time evaluated," said Julia E. Richards, PhD, Harold F. Falls Collegiate Professor of Ophthalmology and Visual Sciences at the University of Michigan.

What's the mechanism? The researchers acknowledged that metformin's influence on OAG risk could be associated with improved glycemic control. However, after adjustment for blood glucose levels, other glycemic medications did not have a similar effect on OAG risk reduction. On average, blood glucose levels were well controlled among both metformin and non-metformin users.

Thus, mechanisms other than glycemic control alone may explain the risk reduction associated with metformin. The authors posited that metformin may act to reduce OAG risk on multiple levels. One of these might be through geroprotective effects on neurogenesis, inflammatory systems, or longevity pathways targeted by CRM drugs.

Guidance for further studies. Complementary basic science studies are under way. If these pan out, the researchers hope to conduct a large-scale randomized clinical trial that could provide more definitive evidence of metformin's reduction in OAG risk, said Joshua D. Stein, MD, MS, associate professor of ophthalmology and visual sciences at the University of Michigan. He suggested a clinical trial protocol in which newly diagnosed glaucoma patients would be randomized to receive either an IOP-lowering drug plus metformin or a glaucoma drug plus placebo.

Dr. Richards would also like to see studies evaluating the effect of metformin on the risk of glaucoma progression, not just on its development. Further, "These findings point to the need to evaluate CRM drugs for their ability to reduce risk of other late-onset eye diseases, too," she added. "For now, there are limits to the conclusions that can be drawn from this study, since this was not a randomized clinical trial, and it was carried out on a very specific population of persons with diabetes."

—*Miriam Karmel*

1 Lin HC et al. *JAMA Ophthalmol.* May 28, 2015 [Epub ahead of print]. doi:10.1001/jamaophthalmol.2015.1440.

Relevant financial disclosures—Dr. Richards: *None.* ***Dr. Stein:*** *None.*

Telemedicine Advances

DR Screening via UWF

Researchers at the Joslin Diabetes Center reported that trained lay imagers were highly accurate in assessing ultra-widefield (UWF) images for the presence or absence of diabetic retinopathy (DR) and for referable DR at the diabetes clinic point of care (POC).[1]

Training and findings. The imagers had no prior experience in retinal image evaluation. They received 4 hours of lectures and 12 hours of guided image review in an established teleophthalmology program. Their work compared favorably with that performed by a centralized reading center.

In the study of nearly 4,000 eyes, the sensitivity and negative predictive value approached 1.00. Evaluators missed only 3 patients with referable DR and missed finding DR in 43 (1.1%) eyes.

"Our study demonstrates that appropriately trained and certified imagers following a defined image and grading protocol can accurately evaluate ultra-widefield retinal images," said Paolo S. Silva, MD, staff ophthalmologist and assistant chief of telemedicine, at Joslin's Beetham Eye Institute.

Benefits and barriers. The researchers estimate that use of such imagers for POC triage of UWF views could reduce the patient load at the centralized reading center by about 60%. Such efficiencies are increasingly important, given the rapid growth in the diabetic population worldwide.

Current barriers to widespread implementation of this approach include costs of the device as well as training and ongoing oversight of the imagers. However, the benefits, such as shorter evaluation time and improved grading rates, may outweigh the cost, Dr. Silva said.

—Miriam Karmel

SCREENING VIEW. Ultra-widefield 200-degree composite image taken without pupillary dilation.

PAOLO S. SILVA, MD

1 Silva PS et al. *Diabetes Care.* June 1, 2015 [Epub ahead of print].

Relevant financial disclosures—Dr. Silva: *Center of Integration of Medicine and Innovative Technology: S.*

Microbiology of the Eye

Contact Lens Wear Alters Ocular Microbiome

Higher bacterial diversity on the ocular surface may contribute to the increased frequency of certain eye infections in people who wear contact lenses, a group of New York University researchers has hypothesized.

Contact lens (CL) wearers had 3 times the usual proportion of *Methylobacterium, Lactobacillus, Acinetobacter,* and *Pseudomonas* on their conjunctivas than did a control group who did not wear CLs, the researchers reported at the annual meeting of the American Society for Microbiology.[1]

Using metagenomic analysis with specialized RNA sequencing, the scientists determined the bacterial makeup of 250 samples, swabbed from the conjunctiva, eyelid skin, and lenses of CL wearers and controls.

In CL wearers, there was greater similarity between the conjunctival microbiota and that of the lower eyelid skin than found in the controls. Further, bacteria on the lenses resemble more closely those of the skin than of the conjunctiva.

Relationship to infections. Although the results are intriguing, the sample sizes were small (9 test and 11 control subjects), and it is too early to know what causes these microbial alterations and what their connection, if any, is to contact lens–related corneal infections, said Lisa Park, MD, a coauthor of the study.

"This study suggests that organisms involved in eye infections may originate from the skin," said Dr. Park, associate professor of ophthalmology at NYU. "Handling contact lenses may be transferring skin bacteria to the ocular surface, which emphasizes the importance of hand hygiene to prevent eye infections."

She added that the group plans to test more patients and to examine cofactors, such lens material and wearing patterns. *—Linda Roach*

1 Shin H et al. Poster presented at: annual meeting of the American Society for Microbiology; May 31, 2015; New Orleans.

Relevant financial disclosures—Dr. Park: *None.*

For the financial disclosure key, *see page 8.* ***For full disclosures,*** *including category descriptions, view this News in Review at www.eyenet.org.*