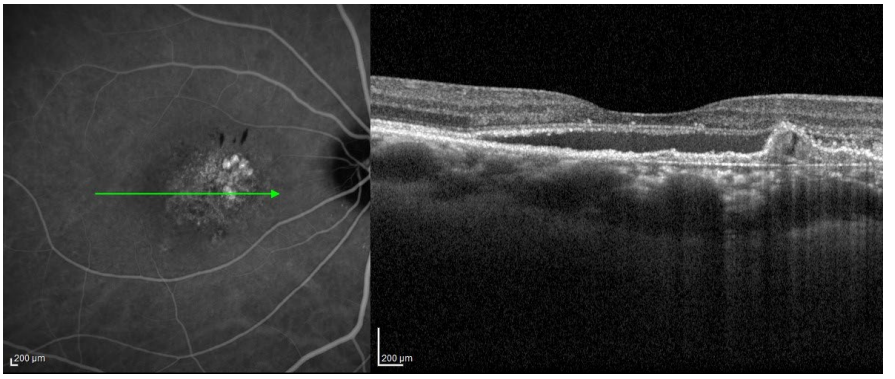


CRITICAL CLUE. *PCV is characterized by subretinal neovascularization between the RPE and Bruch membrane, dilated polypoidal lesions, and a branching vascular network. In these images, an inverted U-shape elevation of the RPE on the OCT B-scan (right) corresponds to the polypoidal lesion on the ICG angiogram (left). The green arrow on the angiogram identifies the location of the image on the OCT B-scan.*

RETINA

OCT B-Scans Pin Down Dx of PCV

TO DATE, CLINICIANS HAVE HAD trouble distinguishing polypoidal choroidal vasculopathy (PCV) from age-related macular degeneration (AMD). But researchers at the University of Hawaii have found that OCT B-scans can detect a characteristic structural feature of PCV.[1]

Tell-tale sign. Gregg T. Kokame MD, MMM, at the University of Hawaii in Honolulu, and his coauthors conducted a retrospective study of case records on 112 eyes with AMD (106 patients). Sixty-nine of the eyes had been diagnosed with PCV using indocyanine green angiography (ICGA). Comparison to the patients' pre- and post-treatment OCT B-scans showed that there was a characteristic sign of PCV: an inverted U-shaped elevation of the retinal pigment epithelium (RPE) that was usually located between the RPE and Bruch membrane. The location of this feature on OCT B-scans correlated to the sites of polypoidal lesions on ICGA.

Critical timing. However, the U-shaped elevations were visible primarily before beginning treatment, Dr. Kokame said. "We showed that if you only looked at the after-treatment OCT B-scan, only a quarter of the eyes with PCV were diagnosed. But if you looked at the before-treatment B-scan, the correct diagnosis was reached in 56% of the known PCV cases," he said.

A cause of anti-VEGF resistance? PCV is a subtype of exudative AMD that predominates among Asian populations, although it occurs, to a lesser degree, in other ethnic groups. Awareness of the clinical importance of this subtype has risen in the last decade as researchers sought to explain why some AMD eyes were resistant to anti-VEGF therapy. It now is thought that unrecognized PCV might be a factor, Dr. Kokame said.

Need to tailor treatment. According to a recent report from the EVEREST II clinical trial, PCV responds better to combined photodynamic therapy plus ranibizumab than it does to ranibizumab alone.[2]

Consequently, it is important for ophthalmologists who treat AMD to be able to identify possible PCV cases early, even though the traditional technology for doing so often is not available in many clinical settings, Dr. Kokame said. "Usually to get the best diagnosis of PCV requires specialized equipment, such as ICGA with the scanning laser ophthalmoscope, plus the ability to read an ICG angiogram, which most practitioners don't have access to," he said. "But almost every practice in ophthalmology has access to OCT, and the B-scan is one thing that just about every ophthalmologist knows how to look at."

As ICGA is often not available, not ordered, or not comfortably read, OCT could help practices identify many patients who otherwise might not be considered for combination therapy, Dr. Kokame said. He added, "We want all ophthalmologists treating exudative macular degeneration to understand that polypoidal choroidal vasculopathy is the most important subtype of AMD."

Specifically, PCV "acts differently from typical exudative macular degeneration, with higher resistance to current medications; it might be susceptible to alternative therapy; and it is predictive of response to different medications," Dr. Kokame said. "We want them to learn to diagnose PCV in the majority of cases with the equipment that they do have available, the OCT B-scan."

—Linda Roach

1 Kokame GT et al. *Ophthalmol Retina.* Published online May 19, 2021.
2 Lim TH et al. *JAMA Ophthalmol.* 2020;138(9):935-942.

Relevant financial disclosures—Dr. Kokame: None.

Gregg T. Kokame, MD, MMM

DRUG DELIVERY

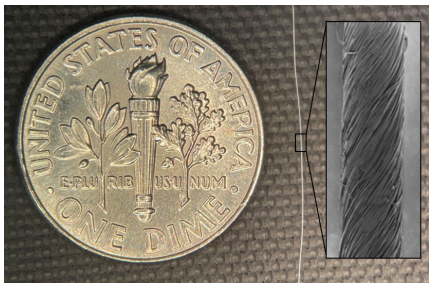
Drug-Loaded Sutures Developed

BY TWISTING NANOMETER-SCALE polymer strands into thin ropes, researchers at the Wilmer Eye Institute in Baltimore have found their way to what arguably represents a Holy Grail of ophthalmic surgery: a resilient ultrathin suture material capable of delivering an antibiotic to ocular wound sites for days or weeks.[1]

Tackling a challenge. Currently, the only globally marketed drug-eluting sutures are coated with the antibacterial and antifungal agent triclosan. Given their size (U.S.P. sizes 6-0 through 0), these triclosan-loaded sutures are used only in general surgery.[1]

In ophthalmology, the advent of ultrathin drug-loaded sutures could virtually vanquish a number of infection-control challenges, including poor patient compliance with topical eyedrops and suture-related infections. Moreover, the researchers wrote, they could "reduce the need for oral antibiotic use, decrease the risk of infection associated with implantable ocular devices, and serve as an alternative to the more than 12 million nylon sutures used [globally] in ocular procedures each year."[1]

Starting with levofloxacin. The researchers reported on incorporating the broad-spectrum antibiotic levofloxacin into nanofibers made from polycaprolactone (PCL), which is a biocompatible polymer. But other tests, not yet published, have shown that the methodology also works with other antibiotics and with steroids, said co–corresponding author Laura M. Ensign, PhD, at Wilmer's Nanomedicine Division.



COMPARISON. *In this composite image, a 10-0 size antibiotic-eluting multifilament nanofiber suture is shown next to a U.S. dime. The high-resolution scanning electron microscopy image (right) shows nanoscale structural detail.*

Novel application of an old lab technique. The group chose PCL for the sutures because it degrades slowly over 12 to 24 months, making it usable for suturing corneal grafts, and because PCL is already a component of several

NEURO-OPHTHALMOLOGY

Subretinal Fluid in NAION

USING SPECTRAL-DOMAIN OCT, RESEARCHERS OB-served subretinal fluid in the macula in a substantial number of patients with nonarteritic anterior ischemic optic neuropathy (NAION).[1] The findings, consistent with earlier studies, confirm that NAION is not just an isolated optic nerve process but is associated with retinal abnormalities that may contribute to vision loss.

"Documenting the presence of subfoveal fluid is important since it can be associated with reduced visual acuity, which is classically preserved in nonarteritic AION, as well as in papilledema," said Thomas R. Hedges III, MD, at Tufts University School of Medicine and the New England Eye Center (NEEC) in Boston.

In previous OCT studies, NEEC researchers observed the presence of subretinal fluid in patients with papilledema, and they subsequently saw fluid in patients with NAION.[2] This latest study, using higher-resolution OCT, affirms those findings.

Findings. For this study, 20 patients (25 eyes) diagnosed with NAION between 2013 and 2017 were evaluated using SD-OCT. All patients presented within four weeks of symptom onset; five had a history of NAION in the fellow eye. NAION was diagnosed on the basis of typical clinical presentation, including, among other findings, painless sudden vision loss and altitudinal visual field defects accompanied by swelling of the optic disc with hemorrhages.

Peripapillary subretinal fluid was present in 16 eyes (64%). Of those, subretinal fluid extended into the macula to produce subfoveal edema in four eyes (16%). About one month after initial presentation, the subfoveal fluid resolved in three of these eyes, and visual acuity (VA) improved in two. VA declined in one eye and remained unchanged in another.

Other retinal findings included intraretinal cysts and hyperreflective dots. However, their significance is unclear, the researchers said.

Looking for vitreoretinal changes. OCT revealed a variety of vitreopapillary interface abnormalities, but their presence does not suggest that the vitreous plays any role in the pathogenesis of AION, Dr. Hedges said. Specifically, there was no evidence of a primary role for vitreopapillary traction (VPT) in the presence of optic disc edema. What's more, neither of the two asymptomatic patients with optic disc swelling had VPT.

Treatment implications. Dr. Hedges stressed the importance of these findings in treatment trials of NAION, where determining which patients have subfoveal fluid in different treatment groups is critical to interpreting the results. "The reduction in central vision spontaneously resolves in most patients, which can be helpful for prognosis," he said. "It will be important to understand what is being treated, the optic neuropathy or the secondary effects on the retina." *—Miriam Karmel*

1 Molaie AM et al. *J Neuro-Ophthalmol.* Published online April 26, 2021.

2 Hedges TR et al. *Arch Ophthalmol.* 2008;126:812-815.

Relevant financial disclosures—Dr. Hedges: None.

Aditya Josyula, Johns Hopkins University

medical products, including thicker general surgery sutures, Dr. Ensign said.

Early tests showed that levofloxacin could be loaded into single, extruded monofilaments, but this reduced their tensile strength to 10% of what is required for ophthalmic sutures, she said. Instead, the researchers created a new electrospinning process to produce and twist nanofibers together.

"Electrospinning is a very old lab technique. The idea is that you're using a syringe system and voltage to shoot out polymer threads," Dr. Ensign said. "The uniqueness of the way we set it up is that, instead of the fibers randomly shooting onto a flat plate, we collect them in a perpendicular fashion, and a rotating motor twists the fibers together to give you a strong, composite nanofiber suture in the end."

Finished product. The finished product consists of hundreds of levofloxacin-loaded nanofibers, twisted together 1,576 times to make 10-0 sutures that are 28 µm in diameter. According to the researchers, the new nanofiber sutures demonstrated biocompatibility comparable to conventional nylon sutures. In addition, they retained 96% of breaking strength over 31 days and delivered levofloxacin at detectable levels in rat eyes for at least 30 days.[1]

The team also evaluated their manufacturing platform's ability to produce sutures equivalent in size to 9-0 and 8-0 ophthalmic sutures.

What's next? Several Wilmer surgeons are now testing the sutures' ease of use in a wet lab, and, with the right investment, clinical testing could begin within two years, Dr. Ensign said. "We really want to make something that works as well as nylon and that the surgeon can actually enjoy using," she said. "We don't want a product that doesn't do what the surgeon needs."

—Linda Roach

1 Parikh KS et al. *Bioeng Transl Med.* 2021;6(2): e10204.

Relevant financial disclosures—Dr. Ensign: Co-inventor on patent applications describing the suture technology; Research to Prevent Blindness: S; Robert H. Smith Family Foundation: S.

GLAUCOMA

Avoiding Glaucoma Malpractice Cases

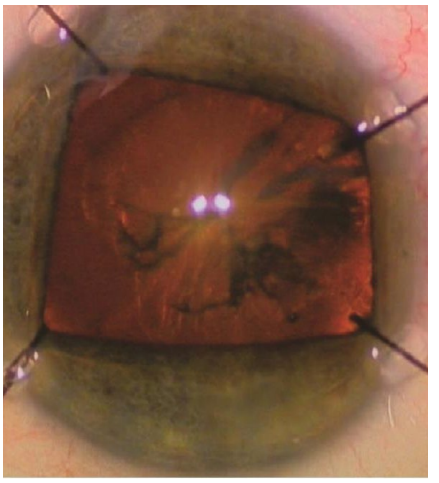
AN ANALYSIS OF CAUSES AND OUT-comes of malpractice litigation among patients with glaucoma suggests that risk to both patients and providers can be reduced by conducting careful examinations and documenting detailed conversations with patients.[1] The analysis revealed that nearly 40% of cases involved allegations of mismanagement or failure to diagnose and treat. Adverse drug effects and surgical complications also resulted in litigation.

"Our study confirms much of what has been reported, and it reinforces the need for risk management to be a part of clinical care," said Ashvini K. Reddy, MD, in private practice in San Antonio, Texas.

Disproportionately high awards. The researchers identified 69 glaucoma malpractice cases in the WestLaw database occurring between 1962 (the first year in which cases were reported) and 2014. Well over half (62.3%) resolved in favor of defendants. Eight jury verdicts awarded a mean of $994,260 to plaintiffs, while 10 cases settled with a mean indemnity of $1.2 million. (Amounts were adjusted for inflation in 2015 dollars.)

Although the rate of glaucoma plaintiff verdicts mirrored ophthalmology overall, median awards were 1.7 times higher than the whole—$977,474 in glaucoma versus $604,352 for all of ophthalmology.

Common scenarios. Of the 69 cases, 35 (50.7%) involved allegations of insufficient intervention, such as failure to diagnose or treat, and failure to monitor properly through intraocular pressure (IOP) checks, dilated examinations, and visual field (VF) testing. Thirteen cases (18.8%) involved failure to diagnose or treat and/or mismanagement of angle-closure glaucoma, and 12 cases (17.4%) involved failure to diagnose open-angle glaucoma. Of 10 varied surgical and procedural claims, six involved trabeculectomy.



COMMON MISTAKES. *Nearly 25% of the claims involved either angle-closure glaucoma (shown here) or open-angle disease.*

An unexpected finding. While adverse effects of glaucoma medications were not common (10; 14.5%), the median award value of nearly $1 million was a surprise, Dr. Reddy said. All but two of 10 cases involving topical glaucoma medication resulted in payments, including a $1.3 million settlement for an elderly woman with a known history of asthma who sustained permanent brain damage after being administered timolol.

Examine, talk, document. Challenges inherent to glaucoma—such as its chronicity and the ongoing need to revise disease management—may explain the disproportionately high awards, the researchers noted. They advised routine IOP measurements, visual field testing, and dilated exams for all glaucoma suspects.

Dr. Reddy stressed the importance of communication, especially with patients who have aggressive disease, guarded prognoses, or poor outcomes. "These patients are particularly high risk and need to be very involved in decisions. Documentation of their involvement is also important."

—Miriam Karmel

1 Engelhard SB et al. *Ophthalmol Glaucoma.* 2021; 4(4): in press.

Relevant financial disclosures—Dr. Reddy: Alimera: C; Clearside: C; Eyepoint: C; Heidelberg: C.

See the financial disclosure key, page 10. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.