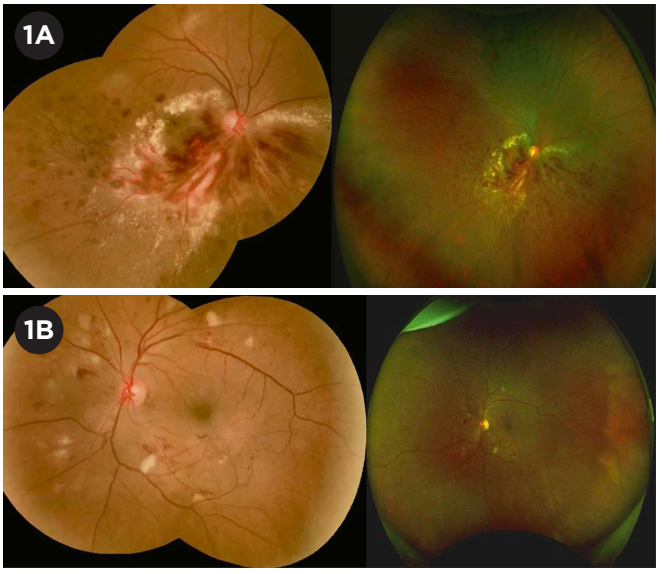
TECHNOLOGY

Detecting DR With Smartphone-Based Widefield Imaging



TWO RETINAL IMAGING METHODS. *(1A) Retinal images of an individual's right eye with sight-threatening diabetic retinopathy using Vistaro and Daytona Plus cameras. (1B) Retinal images of an individual's left eye with moderate to severe non-proliferative diabetic retinopathy using Vistaro and Daytona Plus cameras.*

SMARTPHONE-BASED WIDEFIELD imaging has high sensitivity and specificity for detecting sight-threatening diabetic retinopathy (DR), report researchers from Dr. Mohan's Diabetes Specialities Centre and Madras Diabetes Research Foundation, in Chennai, India. It also helped locate predominantly peripheral lesions. Their study results, published in the journal *Eye,* suggest this technology can be an accessible, cost-effective method for DR screening in areas with few health resources.[1]

Study details. The researchers tested 318 eyes of 160 patients with type 2 diabetes who had varying grades of DR. These individuals underwent screening with nonmydriatic ultra-widefield (UWF) imaging with a Daytona Plus camera followed by mydriatic widefield imaging with a smartphone-based Vistaro camera. Two graders assessed each device's specificities and sensitivities in identifying sight-threatening diabetic eye diseases, including predominantly peripheral lesions.

"UWF photography is getting considered as the gold standard for DR screening in some of the developed countries like the United States," the researchers wrote, but it is an expensive modality for regular DR screening for low- and middle-income countries like India. They said smartphone-based fundus cameras that are portable and easy to handle in remote places are popular, cost-effective DR screening options.

What the study found. The study results showed that the sensitivity and specificity for detection of sight-threatening DR by the UWF camera was 95.1% and 95.7% versus 92.7% and 96.6% when a smartphone-based widefield camera was used.

The UWF camera detected predominantly peripheral lesions in 50.3% of the eyes tested, while the smartphone-based widefield camera detected these lesions in 27.9% of the eyes. However, the authors noted that this did not translate to a significant difference in the grading of sight-threatening DR between the two imaging systems.

With both cameras, predominantly peripheral lesions were most commonly found in the superotemporal quadrant, and the prevalence of these lesions increased with worsened severity of DR. Agreement between the graders was rated as substantial, and no ungradable images were reported in the study.

A viable screening alternative? The study highlights the opportunity this smartphone-based technology presents to potentially increase access to care and screening for retinal disease, said Avni Finn, MD, a vitreoretinal surgeon and Assistant Professor in the Department of Ophthalmology and Visual Sciences at Vanderbilt University Medical Center, in Nashville, Tennessee.

Dr. Finn, who was not involved in the study, called the technology a "viable alternative to standard ultra-widefield photography" in settings with few resources.

"It is exciting that smartphone-based technology has progressed to the point of being able to capture high-quality and reliable widefield fundus images," she said. "Beyond the comparable sensitivity and specificity between the smartphone-based device and the widefield fundus camera, it was striking that no ungradable images

were obtained by the device."

Future research. One limitation of the research is the cross-sectional study method, and the authors noted that a longitudinal follow-up assessment of peripheral DR lesions with smartphone-based widefield cameras would enable the assessment of risk of progression and development of sight-threatening DR.

Dr. Finn would also like to see assessments of different types of smartphone-based retinal imaging.

"This imaging with the smartphone-based device in this study was mounted and mydriatic," she said. "In order for this type of imaging to be more broadly applicable to a larger patient population and different resource settings, it would be nice to see further studies with the camera as a nonmydriatic device and as a nonmounted device."

—Ashley Welch

1 Rajalakshmi R et al. *Eye*. Published online Jan. 31, 2024.

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RETINA

Studying Seaweed-Derived Hydrogel for Retinal Issues

COULD SEAWEED HOLD A KEY TO future retinal treatments? Researchers from Pohang University of Science and

PEDIATRIC OPHTHALMOLOGY

Childhood Amblyopia Linked to Cardiometabolic Disorders

CHILDHOOD AMBLYOPIA IS LINKED TO AN INCREASED risk of cardiometabolic disorders in adulthood, according to University College London researchers and their colleagues.[1] The findings, reported in *The Lancet* online journal *eClinical Medicine,* come from a large epidemiological study of British adults, and add to the medical literature on how childhood health lays the foundation for health later in life.

Research goal. Amblyopia, a common neurodevelopmental disease affecting 1%-3% of children worldwide, has been linked to a higher risk of poorer adult health in previous studies. But the condition's associations with cardiometabolic disorders in adulthood have not been systematically investigated, said study coauthor Jugnoo Sangeeta Rahi, MD, PhD, Professor of Ophthalmic Epidemiology at the GOS Institute of Child Health and Institute of Ophthalmology, University College London, and at Great Ormond Street Hospital, in London.

Dr. Rahi said the research was inspired by emerging evidence in the field of oculomics, which uses data on eyes or the visual system to predict risk and development of nonocular diseases and health states.

Methodology. The researchers analyzed UK Biobank data that included 126,399 participants over 40 years old who were recruited between 2006 and 2010. All had undergone ocular examination, and a subset of 67,321 people received retinal imaging, including color fundus photography and OCT. The researchers wanted to assess whether individuals with unilateral amblyopia were more likely than those without amblyopia to have cardiovascular disease and metabolic syndrome.

Findings. Of 3,221 participants with confirmed amblyopia, 2,647 (82.2%) had persisting amblyopia (amblyopia that was not resolved in childhood). The researchers reported that adults with persisting amblyopia had higher odds of diabetes (29%), high blood pressure (25%), and obesity (16%) compared with controls. But there were no significant associations with metabolic syndrome overall.

Amblyopia was also associated with higher odds of diagnosed vascular problems and previous heart attack, even when accounting for other risk factors for these conditions, such as other medical conditions, ethnicity, and social class.

"Our study is novel in showing that amblyopia is associated with increased risk of a range of cardiometabolic disorders and incident myocardial infarction," said Dr. Rahi.

Retinal changes. Retinal imaging revealed changes previously reported in association with cardiovascular and metabolic disease. Compared with controls, individuals with unilateral amblyopia had significantly thinner inner retinal layers (the macular ganglion cell–inner plexiform layer) and smaller optic nerve height. Retinal biomarker differences were evident in both the affected amblyopic eye and the so-called "normal" fellow eye in those with persisting amblyopia, but not in amblyopia that resolved with treatment, said Dr. Rahi. The authors reported that smoking status and alcohol consumption were similar between people with amblyopia and controls.

What next? The authors said that further research is needed to establish the nature of the relationship between amblyopia and disease in adulthood. In the meantime, they want health care professionals to understand that a diagnosis of amblyopia in a child could be associated with increased cardiometabolic morbidity in later life. On a policy-making level, the findings uncover a potential nonvision benefit of childhood vision screening to detect amblyopia, said Dr. Rahi.

—Miriam Karmel

1 Wagner SK et al. *eClinicalMedicine.* Published online March 7, 2024.

Relevant financial disclosures—Dr. Rahi: National Institute for Health and Care Research: S.

Technology in Pohang, South Korea, and colleagues who are looking for a novel way to treat retinal detachment have published early research exploring the potential of alginate for ophthalmic use. A naturally occurring gelatinous substance, alginate is derived from seaweed.

Their thought is that an artificial vitreous body made from alginate might be a better alternative than using standard agents for vitreous tamponade after vitrectomy to stabilize the retina for conditions such as rhegmatogenous retinal detachment, severe diabetic retinopathy, penetrating ocular trauma, macular hole, and proliferative vitreoretinopathy.

Current practice. The silicone oil and expansile gases used in vitrectomy are meant to stabilize the retina but can cause side effects, including retinal toxicity, cataract formation, secondary glaucoma, and uveitis. Silicone oil, for example, can lead to corneal decompensation and glaucoma and is not biodegradable. And a second surgery to remove the material is required over time.

A drawback to using expansile gases is that patients have to remain in a prone position for a few days following gas tamponade, said lead study author Hyung Joon Cha, PhD, SeAH Chair Professor and Dean of Engineering at the Department of Chemical Engineering and the School of Convergence Science and Technology at Pohang.[1]

"This is required for as long as the eye is filled with gas, essentially. During this period, the patient will experience significantly impaired vision," he said.

Why seaweed. Dr. Cha and colleagues, an interdisciplinary team of chemical engineers and ophthalmologists, published their findings—tested only in rabbit eyes, so far—in the journal *Biomaterials*. They chose to study alginate, a polysaccharide extracted from marine brown seaweed, because it "has been one of the most widely used natural biomaterials for tissue engineering. Alginate is not biodegraded in mammals and can be retained for a long time in the body," the authors wrote.

From seaweed to animal eyes. Through a series of chemical processes, they created an alginate medical composite hydrogel—more specifically, according to the study, a transparent alginate-phenylboronic acid/polyvinyl alcohol composite hydrogel novel vitreous substitute with tamponading capabilities. They injected it into the eyes of a rabbit model of vitrectomy retinal detachment to test their theory. The authors reported that "in vivo evaluations confirmed [the hydrogel's] ability to inhibit retinal detachment recurrence and preserve rabbit vision without adverse effects."

SOURCING SEAWEED. *Researchers are exploring the potential of alginate for retinal detachment treatments. A naturally occurring gelatinous substance, alginate is derived from seaweed.*

"Alginate is a very stable polysaccharide molecule because mammals, including humans, lack enzymes for alginate degradation," said Dr. Cha.

Dr. Cha said the alginate hydrogel also quickly formed in situ after intraocular injection, noting that "while silicone oil has its own refractive index that requires optical adjustments and can also cause corneal decompensation and glaucoma, the refractive index of our alginate hydrogel is similar to the refractive index of native human vitreous and has a tamponading effect similar to that of silicone oil."

Early days. J. Fernando Arevalo, MD, PhD, Chairman of Ophthalmology at Johns Hopkins Bayview Medical Center and Professor of Ophthalmology, said that the new hydrogel material seems to present some positive benefits over traditional tamponading agents. But Dr. Arevalo, who was not involved in the research, said it's important to emphasize that, as of now, this is very experimental.

Dr. Arevalo said the fact that the hydrogel is described as "transparent" is crucial, given that it would not obstruct vision. He also said that the idea that this material might one day help repair the retina or "integrate seamlessly within the eye" is an intriguing theory that needs further study. The notion that the mechanical properties of the hydrogel might one day be adjustable is also an interesting concept, said Dr. Arevalo. And given that alginate is known for being biocompatible means there might be a reduced risk of immune reactions or other complications, he said. But again all of these factors would require further study.

"It is promising. However, it's important to note that while new materials may offer theoretical benefits, they must undergo rigorous clinical testing to ensure they are safe and effective in actual practice," Dr. Arevalo said, noting that only human studies will be able to confirm its potential.

He said the big question is, will it cause cataracts in humans? "If not, that would be a great advancement over gas and silicone oil."

Looking to the future. Dr. Cha said the next step will be to standardize the formulation and authorize biological safety assessments and preclinical evaluations using larger animal models.

—Brian Mastroianni

1 Choi G et al. *Biomaterials*. 2024;305:122459.

Relevant financial disclosures—Dr. Arevalo: None. Dr. Cha: None.

See the financial disclosure key, page 9. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.

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