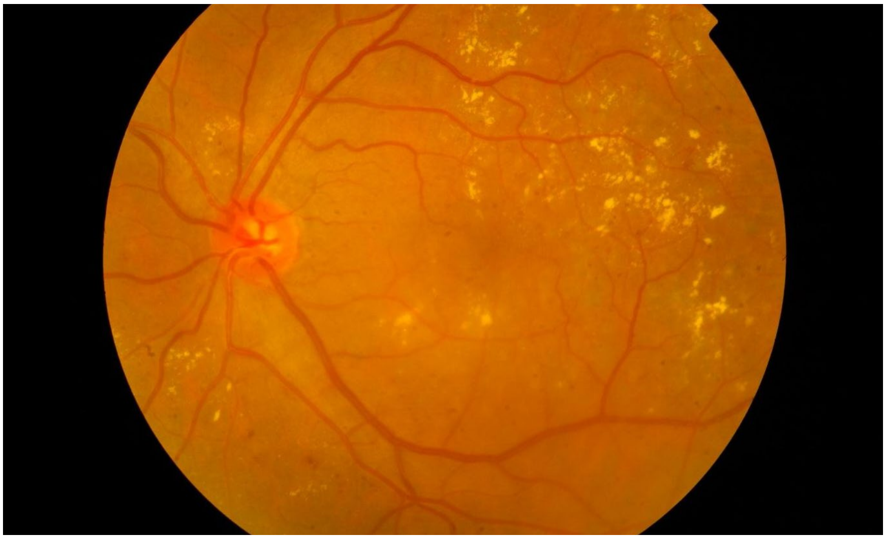
News in Review

COMMENTARY AND PERSPECTIVE



DIABETIC RETINOPATHY. *Computers are learning to recognize diabetic eye disease in fundus photos, with the help of a self-optimizing algorithm.*

How AI Learns to Detect Diabetic Eye Disease

USING "DEEP LEARNING" TECHNIQUES, researchers in the Google Brain initiative have developed a self-optimizing algorithm that can examine large numbers of fundus photographs and automatically detect diabetic retinopathy (DR) and diabetic macular edema (DME) with a high degree of accuracy.

When the researchers tested the screening algorithm's performance on 2 groups of images (N = 11,711), it had a sensitivity of 96.1% and 97.5% and a specificity of 93.9% for DR and DME, respectively.[1]

"It's a real accomplishment that Google was able to get high sensitivity and specificity at the same time—meaning that not only is this algorithm missing very few people who have disease, but it is also unlikely to overdiagnose disease," said Peter A. Karth, MD, MBA, a vitreoretinal subspecialist in Eugene, Ore., and at Stanford University, who is a consultant to the Google Brain project.

How the system learns. The mathematical algorithm is based on deep machine learning, a type of artificial intelligence (AI) technology in which a neural network "learns" to perform a task through repetition and self-correction.

In this case, the authors reported, the computerized algorithm was trained with 128,175 human-graded fundus images that showed varying levels of diabetic retinal disease. "Then, for each image, the severity grade given by the [algorithm] is compared with the known grade from the training set, and parameters … are then modified slightly to decrease the error on that image," they wrote. "This process is repeated for every image in the training set many times over, and the [algorithm] 'learns' how to accurately compute the diabetic retinopathy severity from the pixel intensities of the image for all images in the training set."[1]

Dr. Karth noted that the algorithm works even though it was not designed to look specifically for the lesion-based features that a human would seek on fundus images. "What's so exciting with deep learning is that we're not actually yet sure what the system is looking at. All we know is that it's arriving at a correct diagnosis as often as ophthalmologists are," he said.

Ehsan Rahimy, MD, a Google Brain consultant and vitreoretinal subspecialist in practice at the Palo Alto Medical Foundation, in Palo Alto, Calif., agreed. "We don't entirely understand the path that the system is taking. It may very well be seeing the same things we're seeing, like microaneurysms, hemorrhages, or neovascularization," he said. "But it's also very likely that the algorithm is looking beyond those features, at things that are not readily apparent to us as human beings when we look at an image."

AI won't replace doctors' intelligence. Much more work is necessary before the algorithm would be ready for clinical use, but the eventual goal is to increase access to and reduce the cost of screening and treatment for diabetic eye disease, especially in underresourced environments, Dr. Karth and Dr. Rahimy said.

"Anytime you talk about machine learning in medicine, the knee-jerk reaction is to worry that doctors are being replaced. But this is not going to replace doctors. In fact it's going to increase the flow of patients with real disease who need real treatments," Dr. Rahimy said.

"This is an important first step toward dramatically lowering the cost of screening for diabetic retinopathy and, therefore, dramatically increasing the number of people who are screened," Dr. Karth said. "We feel that with this kind of technology, once it is fully deployed, there will be more people screened for this disease and decreased rates of uncontrolled diabetic vision loss and diabetic retinopathy."

—*Linda Roach*

1 Gulshan V et al. *JAMA*. 2016;316(22):2402-2410.

Relevant financial disclosures—Dr. Karth: Google Brain: C; Carl Zeiss Meditec: C. Dr. Rahimy: Google Brain: C.

AEROSPACE OPHTHALMOLOGY

What Flattens Astronauts' Eyes?

AFTER SPENDING SEVERAL MONTHS in microgravity, a majority of astronauts return to Earth with optic disc edema, posterior globe flattening, and a hyperopic shift in visual acuity.

Researchers who first documented these changes—dubbed the visual impairment intracranial pressure (VIIP) syndrome—hypothesized that they might be caused by pressure from venous congestion in the brain and choroid.[1] But, according to researchers at the University of Miami, Florida, the culprit appears to be a microgravity-induced buildup of cerebrospinal fluid (CSF) in the orbit and ventricles in the brain.[2]

Effects of excess CSF. High-resolution MRI orbital scans of 7 long-duration astronauts showed that all of them had significantly greater increases in orbital and ventricular CSF volume ($p \leq .005$) than did short-duration astronauts, said Noam Alperin, PhD, who presented the results at last fall's meeting of the Radiological Society of North America.

GLAUCOMA RISK FACTORS

Predictive Power of Optic Disc Hemorrhage

AFTER MANY YEARS, THE LANDMARK OCULAR HYPERtension Treatment Study (OHTS) is still broadening our understanding of risk factors for glaucoma. A recent long-term study shows that occurrence of an optic disc hemorrhage (ODH) strongly predicts subsequent development of primary open-angle glaucoma (POAG) in patients with ocular hypertension (OHT). Having a disc hemorrhage increased the risk of developing POAG 2.6-fold, or 260%.[1]

New factors emerged over time. The 13-year analysis of ODHs in the OHTS population also revealed 3 additional factors that increase the risk of ODH but had not been statistically significant in an interim analysis[2]: high baseline intraocular pressure (IOP), black race, and assignment to the group of OHTS patients who did not receive medication.

The findings suggest that clinicians should be vigilant in looking for ODHs, said Donald L. Budenz, MD, MPH, Kittner Family Distinguished Professor and Chair, Department of Ophthalmology, University of North Carolina at Chapel Hill.

In this prospective cohort study involving 3,236 eyes of 1,618 OHTS participants, the researchers examined annual stereoscopic optic disc photos to look for ODH. Among the findings:

- In patients with OHT before the development of POAG, the incidence of ODH was 0.5% per year over an average of 13 years, but it more than doubled to 1.2% during an average of 6 years after the development of POAG. (The incidence of ODH may be underestimated because of its transient nature and because people with ODH at baseline were excluded from the study.)
- ODH occurred less frequently in the OHTS medication group (7.4% cumulative incidence at 13 years) compared with the observation group (9.8%).
- While the presence of an ODH was associated with an increased risk of POAG, 78% of eyes with an ODH did not progress to glaucoma over a median follow-up of 49 months after developing the disc hemorrhage.

Clinical implications. Because ODHs are transient, looking for them annually may not be often enough to factor into a treatment algorithm. Dr. Budenz recommends checking carefully for disc hemorrhages at every exam. He said the best way to detect an ODH is with a dilated exam using a 78-D or 90-D condensing lens. But using the direct ophthalmoscope on an undilated patient is a reasonable alternative between annual dilated exams.

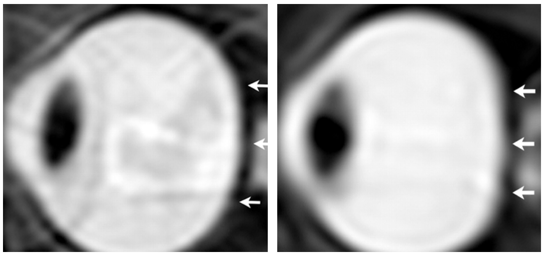
If an ODH is detected, he advised additional testing over the next 3 to 6 months. Changes in the visual field, optic nerve, or retinal nerve fiber layer, particularly if they correspond to the location of the optic disc hemorrhage, are indications for treatment.

Dr. Budenz stressed that initiating treatment of every OHT patient with a disc hemorrhage is not advised. "It's important to remember that most OHT patients will not develop POAG after disc hemorrhage," he said. It is, however, reasonable to start treatment in the presence of additional risk factors: older age, low corneal thickness, increased vertical cup/disc ratio, greater pattern standard deviation, and increased IOP.

In light of the findings, Dr. Budenz has become more vigilant in looking for disc hemorrhages in all of his OHT and glaucoma suspect patients. "It may be more important than measuring IOP at each exam because finding a disc hemorrhage likely increases the risk more than detecting a modest elevation in IOP." —*Miriam Karmel*

1 Budenz DL et al. *Am J Ophthalmol.* 2017;174:126-133.
2 Budenz DL et al. *Ophthalmology*. 2006;113(12):2137-2143.

Relevant financial disclosure—Dr. Budenz: None.



BEFORE AND AFTER. *Sagittal oblique T2-weighted magnetic resonance images of the left eye show the effects of space travel. Left, before space travel. Note convexity of posterior globe (arrows). Right, after long-term exposure to microgravity. Note loss of convexity of the posterior scleral margin (arrows).*

The excess CSF from long flights was associated with more optic nerve protrusion ($p < .00001$) and more scleral flattening ($p < .00001$), said Dr. Alperin, a professor of radiology who heads the university's Advanced Imaging Processing Laboratory.

"In the astronauts who stayed in the International Space Station for an average of 6 months, there was an accumulation of CSF, and an increase in its volume, in the orbit around the optic nerve. And this compresses the optic nerve and the posterior pole of the globe," Dr. Alperin said.

Visual consequences—current and future. Dr. Alperin's coinvestigator in the study is Byron L. Lam, MD, professor of ophthalmology at Bascom Palmer Eye Institute. Dr. Lam said that, based on current reports, "The hyperopic shift is mild and can be compensated with glasses," adding that further study is needed. "Of course, it is unknown what the consequences of VIIP might be for very long-duration flights to Mars, which could last nearly 1,000 days." *—Linda Roach*

1 Mader TH et al. *Ophthalmology.* 2011;118(10):2058-2069.
2 Alperin N. Role of cerebrospinal fluid in spaceflight-induced visual impairment and ocular changes. Presented at: annual meeting of the Radiological Society of North America; Nov. 28, 2016; Chicago.

Relevant financial disclosures—Dr. Alperin: Alperin Noninvasive Diagnostics: O; NASA: S. Dr. Lam: University Space Research Association: C.

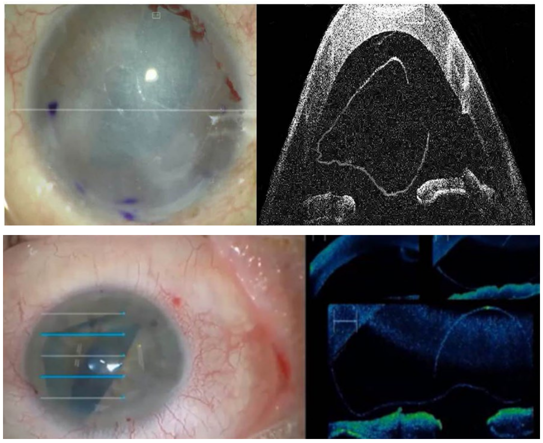
CORNEAL SURGERY

DMEK Learning Curve and Outcomes

DESCEMET MEMBRANE ENDOTHELIAL keratoplasty (DMEK) has a reputation for being difficult to master. But does the learning curve affect patient outcomes? To answer that question, French investigators evaluated the first 109 DMEK procedures performed by a single surgeon (98 eyes, 84 patients) between March 2012 and November 2014.[1] They assessed the learning curve for graft preparation and graft unrolling as well as the impact of experience on visual acuity gain and percentage of endothelial cell loss.

Learning curves. In this model, the number of procedures needed for a surgeon to achieve 90% of the learning curve plateau was 68 cases for preparation time and 46 for unrolling time. It was estimated that 50 cases were required overall to achieve a good standard of care, as evidenced by the number of complications and reproducibility of preparation and unfolding time, said coauthor Alain Saad, MD, at the Fondation Ophtalmologique Adolphe de Rothschild in Paris.

Speed improves, but visual outcomes are similar. As expected, greater surgical experience resulted in faster graft preparation and unrolling time. Endothelial cell loss was significantly higher with inexperience. But—in the short term, at least—neither the cell loss nor the learning curve affected the patients' best-corrected visual acuity gain at 1 week and 6 months.



DMEK. *Graft is visible in the anterior chamber on intraoperative OCT (top, Haag-Streit; bottom, Rescan) despite corneal edema.*

"However, it's possible that cell loss may influence the long-term survival of the graft," Dr. Saad commented, "meaning that experienced surgeons may be able to achieve superior long-term results."

Other factors. The researchers did not evaluate the influence of mentors, the ability to perform several surgeries in close succession, or the use of intraoperative optical coherence tomography. These factors might accelerate the learning curve and lower complications, said Dr. Saad, who also noted that DMEK techniques have improved and become more standardized since the beginning of this study. "This means that a DMEK surgeon starting out today might be able to master the techniques faster."

For surgeons considering adding DMEK to their practice, Dr. Saad had some encouraging words: "DMEK is not as complicated as it may seem. You just need to precisely follow each step." *—Annie Stuart*

1 Debellemanière G et al. *Cornea.* 2017;36(1):1-6.

Relevant financial disclosures—Dr. Saad: None.

Noam Alperin, PhD; Alain Saad, MD

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