

News in Review

COMMENTARY AND PERSPECTIVE

CATARACT

AI Model Successfully Diagnoses Cataract

RESEARCHERS AT THE NEI HAVE

developed a deep learning framework that can diagnose and quantify cataracts with a high level of accuracy.¹

“We believe that this is the first robust attempt to perform fully automated detection and quantitative classification of all three types of age-related cataract by deep learning models,” said Tiarnán D.L. Keenan, MD, PhD.

The researchers set out to determine whether artificial intelligence (AI) performance “could approach or equal human specialist performance,” Dr. Keenan added. “In this case, we were delighted to see that, in most cases, AI performance was significantly superior.”

Study design. For training, the researchers used 18,999 anterior segment images (from 6,333 triplets—i.e., slit-lamp, anterior retroillumination, and posterior retroillumination images) from 1,137 eyes. All images were from the Age-Related Eye Disease Study.

For validation, the researchers compared the performance of their AI models to that achieved by their 38 human participants. Of these, 14 were ophthalmologists (10 at attending level and four at fellowship level), and the remaining 24 were medical students with no experience in grading images.

Study results. The deep learning models achieved automated and quantitative classification of cataract severity

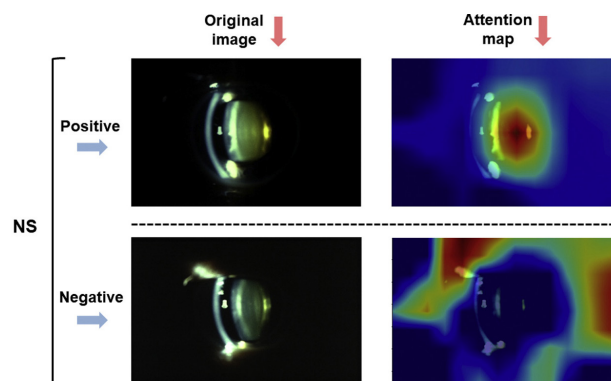
with a high level of accuracy for nuclear, cortical, and posterior subcapsular cataracts. The main outcome

measures were the mean squared error (MSE) for each test set.

For the two most common types—the nuclear and cortical cataracts—the model’s accuracy was significantly superior to that achieved by both the practicing ophthalmologists and the students. For nuclear cataracts, the mean MSE for the deep learning platform, ophthalmologists, and students was .23, .98, and 1.24, respectively. For cortical cataracts, these mean MSE values were 53.5, 134.9, and 422, respectively. For the less common posterior subcapsular cataracts, the model’s accuracy was similar to that achieved by the practicing clinicians (mean MSE, 171.9 vs. 176.8, respectively).

A surprise. On one hand, it’s no longer surprising that AI models approach, or even surpass, human specialists, Dr. Keenan said. “However, for nuclear sclerosis, the most common type of age-related cataract, we were surprised by the degree to which the AI models outperformed ophthalmologists, even those who are cataract specialists.”

Broad applications. Automated approaches are ideal for cataracts, which can be diagnosed and classified purely on anatomical appearance, the researchers noted. Their model is now ready for the research setting, where it is expected to be especially well-suited for the quantitative grading required in



COMPARISON. In a case of severe nuclear sclerotic cataract (upper panel), the area of high signal corresponded to the location of the lens nucleus. In a mild case (lower panel), no areas of high signal were observed in the distribution of the lens nucleus.

interventional clinical trials and epidemiological studies.

If approved by the FDA, such models could do everything from cataract screening in primary care to assisting surgical planning. The approach also lends itself to telemedicine, where it may enhance access to care, particularly in areas with few ophthalmologists.

Looking ahead, Dr. Keenan noted that “many single-domain tasks [in cataract care] will be well suited to AI, such as quantitative cataract classification, IOL calculation, and surgical risk prediction. Other tasks will remain best suited to humans, who can interpret complex information from diverse domains.”

At present, the models and associated code are available for research use only and may be found at <https://github.com/ncbi-nlp/DeepSeeNet>.

—Miriam Karmel

1 Keenan TDL et al. *Ophthalmology*. Published online Jan. 3, 2022.

Relevant financial disclosures: Dr. Keenan—None.

Racial Differences Emerge in Trabecular Meshwork

A STUDY OF COMPLEX CELLULAR

processes associated with glaucoma risk has moved scientists closer to an understanding of why primary open-angle glaucoma (POAG) is more prevalent and severe in Black patients than in their White counterparts.¹ The study focused on a marker of oxidative damage in the aqueous humor and on mitochondrial function and oxidative stress markers in trabecular meshwork cells.

“Our study identifies new findings of fundamental racial differences in trabecular meshwork cells, the main site of resistance of aqueous humor flow and intraocular pressure regulation,” said Carla J. Siegfried, MD, at Washington University School of Medicine in St. Louis, Missouri. The findings suggest the importance of oxidative stress in the pathogenic cascade of the disease and carry the promise of tailored therapeutics to block that cascade, she said.

Studying a biomarker of oxidative damage. The researchers collected aqueous humor from 173 patients (173 eyes) undergoing intraocular surgery for POAG, cataract, or both.

Patients were stratified by glaucoma

severity (mild, moderate, and severe) and race. Of the 173 patients, 75 were Black, and 98 were White. Trabecular meshwork tissue from eye bank donors served as healthy controls.

The researchers looked specifically at 8-hydroxy-2'-deoxyguanosine (8-OHdG), a biomarker of oxidative damage in the aqueous humor of glaucoma patients. They found no significant racial differences in 8-OHdG measures in patients with mild or moderate disease and in controls. However, in a subgroup analysis, 8-OHdG levels were significantly higher in those Black participants who had severe glaucoma. This finding suggests that oxidative damage may be a risk factor in glaucoma pathogenesis, the researchers said.

Other events in the cascade leading to oxidative stress. The researchers also measured the quantity and activity of mitochondria in trabecular meshwork donor cells. Mitochondria are known to generate reactive oxygen species (ROS) that contribute to oxidative stress and damage, a proven mechanism of glaucoma damage.

As it turned out, ROS production was significantly higher in eyes of Black patients. This finding “suggests a fundamental biological difference in cellular metabolism, which may increase the risk of glaucoma and potentially other diseases associated with oxidative stress,” Dr. Siegfried said.

Toward prevention and treatment.

The researchers plan further exploration of these cellular processes associated with glaucoma risk, particularly how they and other cellular processes change with different stages of glaucoma severity and how they relate to gene expression in trabecular meshwork cells. Currently, they are developing antioxidant therapeutics to block triggering events that lead to oxidative stress and damage.

Whether oxidative stress is a primary cause or merely a downstream

consequence of glaucoma remains unclear, Dr. Siegfried said. “Our data suggest that oxidative stress is likely to be causally associated with glaucoma, especially in the Black population.”

—Miriam Karmel

1 Wu H et al. *Ophthalmology Science*.

2022;2(1):doi.org/10.1016/j.xops.2021.100107.

Relevant financial disclosures: Dr. Siegfried—None.

NEURO-OPHTHALMOLOGY

Dialysis and Vision: Update on Risks

THE DANGERS OF INTRADIALYTIC

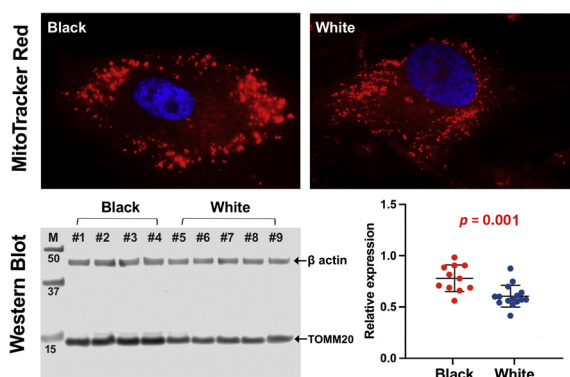
hypotension cannot be overstated, given that it is a risk factor for dialysis-associated nonarteritic anterior ischemic optic neuropathy (DA-NAION), which poses a more serious threat to vision than does typical NAION. In an attempt to alert ophthalmologists—and their internal medicine and nephrology colleagues—to the dangers of DA-NAION, researchers at the University of Toronto recently published a case series and review of the literature.¹

A time to worry. “Typically, doctors are scared of hypertension—but there are times to be scared of hypotension,” said coauthor Edward Margolin, MD. “Patients on dialysis have poor auto-regulation of their vasculature. Thus, they have a difficult time responding to any drop in blood pressure—and we presume it is the hypoperfusion of the optic nerve head that leads to DA-NAION in these patients.”

He emphasized that clinicians “need to understand that if a patient is on dialysis, the goal is to prevent hypotension.” Moreover, he said, “The patient who already suffered an episode of DA-NAION is at high risk of recurrence in the fellow—and even the same—eye.”

Delving into the literature. In their review, Dr. Margolin and his colleagues found reports of 31 patients (50 eyes) with DA-NAION associated with intradialytic hypotension.

Patient characteristics. The mean age at presentation was 47.7 years of age, and 18 of the patients (58.1%) were male. Nineteen (61.3%) had bilat-



QUANTIFICATION. (Upper panel) *In vitro* staining of trabecular meshwork cells from study participants. (Lower left) Western blot quantification shows higher expression in Black patients than in their White counterparts. (Lower right) Levels of ROS expression (red dots = Black patients; blue dots = White patients).

eral involvement; this was simultaneous at presentation in seven (22.6%) and sequential in 12 (38.7%).

Of note, three patients (9.7%) experienced a recurrence within a previously affected eye.

Visual outcomes. Vision loss was severe, the researchers found: Presenting visual acuity (VA) was available for 44 eyes and was 20/200 or worse in 28 (64.6%). At final follow-up, VA was 20/200 or worse in both eyes of 19% of the patients.

In contrast, the researchers noted, visual outcomes of hand motion or worse are uncommon in typical cases of NAION.

How common a problem? “Depending on the definition used, intradialytic hypotension could occur in 5% to 30% of all dialysis treatments,” the researchers said. And from his own perspective, as a neuro-ophthalmologist in tertiary

practice, Dr. Margolin said that he sees at least three or four patients with DA-NAION a year.

Contributing factors. Many factors contribute to intradialytic hypotension, the researchers noted, including rapid or excessive filtration, a rapid reduction in plasma osmolarity, autonomic neuropathy, and poor cardiac reserve.

An overview of management strategies. Although the ophthalmic literature includes cases of DA-NAION, management of intradialytic hypotension is rarely covered in these reports, Dr. Margolin said. Thus, as part of their review, he and his colleagues included a discussion of steps that typically are taken by nephrologists to manage cases of intradialytic hypotension—and to prevent recurrent episodes.²

For instance, acute management includes repositioning the patient in the Trendelenburg position and decreas-

ing or holding the ultrafiltration rate. And prevention of recurrence involves a stepwise approach that comprises dietary and medication evaluations, among other strategies.

The bottom line. As an ophthalmologist, Dr. Margolin said, “If you see NAION, determine whether or not the patient is on dialysis. If so, this is a person you need to worry about.” Further, he emphasized that ophthalmologists need to communicate more broadly with their internal medicine and nephrology colleagues. “They need to understand that hypotension raises the risk of vision loss.” —Jean Shaw

1 Donaldson L et al. *J Neuro-Ophthalmol*. Published online Dec. 28, 2021.

2 Kooman J et al. *Nephrol Dial Transpl*. 2007; 22(suppl 2):ii22-ii44.

Relevant financial disclosures: Dr. Margolin—None.

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



LET'S DO GLAUCOMA

DIFFERENTLY.

The John A. Moran Eye Center at the University of Utah welcomes Iqbal K. “Ike” Ahmed, MD, FRCSC as director of its new Alan S. Crandall Center for Glaucoma Innovation.

Founded as a tribute to Dr. Ahmed’s mentor and friend, the Crandall Center will advance their shared mission to improve glaucoma care through revolutionary surgical approaches and devices.

Dr. Ahmed also has expanded his practice to include the Moran Eye Center. Celebrated as one of the world’s most experienced anterior segment surgeons, he specializes in the surgical management of glaucoma, complex cataracts, iris reconstruction, and intraocular lens complications.

To schedule patient referrals and consultation requests at his Utah location, call 801-585-3071.



DR. AHMED AT MORAN

DR. ALAN S. CRANDALL
1947 — 2020

