GLOBAL PERSPECTIVES

AI IN OPHTHALMOLOGY: RESEARCH, INITIATIVES, AND APPLICATIONS

Two viewpoints on emerging indications and real-world adoption.

BY DAMIEN GATINEL, MD, PHD; TING FANG TAN, MBBS; AND DANIEL TING, MD, PHD

INCREASING DIAGNOSTIC CAPABILITIES FOR CORRECTIVE AND REFRACTIVE THERAPEUTIC SOLUTIONS

My team's theoretical and clinical research approach is based on the use of descriptive and predictive mathematical modeling. This has recently been complemented with AI-related resources such as supervised and unsupervised learning. Our goal is twofold: (1) to better understand data collected using biometric and imaging techniques and (2) to increase the diagnostic accuracy or effectiveness of corrective and refractive therapeutic solutions.

Thus far, the models and techniques have been applied mainly to refractive surgery, topography and corneal imaging for keratoconus screening, ocular wavefront description, complex optical comparison and design in cataract surgery, ocular biometry, and IOL calculation. The improvements to diagnostic tools include screening or characterization of keratoconus, corneal edema, and ocular wavefront; the improvements to therapeutic tools include ablation profiles, IOL calculations, and diffractive optics.

IOL POWER CALCULATIONS

In 2017, we began a long-term project aimed at designing precise IOL calculation formulas and making them available in open-source software. We have explained their development process step by step.

From a paraxial eye model consisting of thick lenses (cornea and IOL), we established a formula to calculate the positions of the principal planes of an IOL according to its geometry, postoperative refraction, and biometric constants of interest and an original biometric calculation formula based in part on an algorithm trained to predict the effective lens position by accounting for its thick lens geometry.[1] The combination of optics, mathematics, machine learning, and programming led to the creation of the Postoperative Spherical Equivalent Prediction Using Artificial Intelligence and Linear–Debellemanière, Gatinel, Saad (PEARL–DGS) IOL calculation formula.[2] It is the only state-of-the-art formula with published principles and code available. The formula will be presented in a book published by the IOL Power Club.

ADVANCED IMAGING

Statistical tools such as discriminant analysis allow the performance of objective tests whose sensitivity and specificity can be quantified. We have described several discriminating functions in elevation and curvature topography implemented in some topographic instruments[3-5] and transposed it into a high-resolution anterior segment OCT unit (Anterion, Heidelberg Engineering).

Diagnosis. Several pilot studies we recently published demonstrate how AI can use data from corneal topography and OCT to automate and improve the diagnosis of corneal pathology. These tests rely on indices to condense complex underlying information: A typical elevation topography examination consists of 40,000 raw numerical values, and a single corneal OCT image can consist of about 1 million pixels. Modern AI and, more specifically, deep learning through convolutional neural networks have the potential to analyze the data effectively.

We combined the raw values of four topographic maps and trained a convolutional neural network to distinguish normal corneas affected by keratoconus from those altered by refractive surgery. We achieved 99.3% accuracy in this task with 100% sensitivity and specificity in diagnosing keratoconus. (Editor's note: for more on the importance of keratoconus diagnosis and the true prevalence of keratoconus, see the sidebar on pg 16.) It is the first approach to make use of all available data simultaneously while maintaining the spatial concordance of the data of each map. The comprehensive analysis of topographic data should improve diagnostic accuracy for different corneal pathologies.[6]

Corneal edema. Our first work on corneal OCT used a convolutional neural network to detect the presence of edema on corneal OCT images at the pixel level. Corneal edema is common to many pathologies. Its precise detection is fundamental, especially with perioperative endothelial transplants, but no specific tool for detecting edema currently exists. Its paraclinical evaluation is based on indirect signs such as corneal thickness, shape, and reflectivity. High-resolution OCT images were used to build a model capable of detecting corneal edema with 96.4% sensitivity and 100% specificity while producing an indicative colored map of edema localization on OCT sections. Such a tool could allow automated corneal screening before cataract surgery by ophthalmologists who are not cornea specialists and more accurate follow-up after endothelial transplantation.[7]

Cataract. We are currently focusing on the objective diagnosis of cataracts. We believe this area could benefit from the development and use of objective algorithms based on the analysis of high-resolution OCT scans of the lens with neural networks.[8]

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EXPLAINABILITY AND PRIVACY-PRESERVING TECHNOLOGY

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The development of AI solutions, which accelerated during the past decade, is revolutionizing health care delivery[1] in response to limited resources for serving a growing and aging population.

In ophthalmology, predominantly imaging-based modalities are used for AI classification, segmentation, and prediction tasks.[2] Newer AI deep learning algorithms also use multimodal and multiethnic input to generate information on various diseases.

CLOSING THE GAP

High-performance AI algorithms are being created, but only a few have received regulatory approval for real-world adoption.[3,4] The gap between model development and clinical deployment demonstrates a need for AI to be more explainable, accountable, and usable.

Adoption. In addition to model performance metrics, there is a growing emphasis on the evaluation of human factors such as user-friendliness, end-user trust, and human-computer interaction.[5] A recent multinational survey of ophthalmologists and primary care providers explored factors contributing to the acceptance of AI at all levels of health care from individual eye care providers (microsystem) to organizations (mesosystem) to health systems (macrosystem).[6] Another study highlighted patient concerns for AI-physician encounters.[7]

Work is required to identify factors influencing users' acceptance or refusal of AI. The information can guide the design of AI clinical applications to maximize the success of their deployment.

Explainability techniques. One reason for resistance to AI use is a lack of explainability with black-box algorithms. Improved performance requires increasingly complex models, but this can make decision-making processes more opaque.

The patient-physician relationship is built on trust. AI applications therefore must be interpretable to be accepted. Several explainability techniques—mostly post hoc analyses—have been proposed.[8] Further work is required to explore benchmarking explainability metrics,[9] the utility of different techniques, and their inclusion in regulatory approval.

Accountability and usability. Data privacy is a significant concern because the collection, storage, and analysis of large volumes of data are integral to the AI pipeline.[10] Progress on the development of privacy-preserving digital technologies is required. One area of focus is federated machine learning[11] and blockchain technology[12] that allow data-private multisite collaboration. Another is generative adversarial networks[13] that can create unique synthetic input to amplify the size and diversity of existing image-based datasets. These methods can encourage multisite cross-border collaboration that has the potential to address issues such as algorithmic biases against underrepresented subgroups within datasets, such as ethnic minorities and rare disease categories.[14] The goal is to strengthen AI algorithms without compromising

WHY UNDERSTANDING THE TRUE PREVALENCE OF KERATOCONUS IS IMPORTANT



Facts are better drivers of big-picture treatment decisions than out-of-date assumptions.

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Understanding the true prevalence of keratoconus is crucial for several reasons, the greatest of which is allocation of public funding for health care initiatives and programs. As with many diseases, people who have keratoconus can benefit greatly from early screening and treatment. Resources are finite, however, and fewer resources, including screening, treatment, and research, are devoted to rare diseases. If the prevalence of keratoconus is only 0.05%—a percentage derived from a study conducted between 1935 and 1982 in Minnesota[1] that we believe is a gross underestimation—then more prevalent and equally debilitating diseases will receive more funding.

Our published data show that the prevalence of keratoconus is far greater than 0.05%, or one in 2,000, particularly in those of Mediterranean and Middle Eastern descent.[2] We believe this for two reasons. First, modern Scheimpflug corneal tomographers are orders of magnitude more sensitive than irregular sciascopy light reflexes used in the 1986 Minnesota study.[1] Second, keratoconus prevalence varies by global region and ethnic background. If these things are true, decisions on resource allocation should change.

RESEARCH INITIATIVE

The Light for Sight Foundation has been conducting a research initiative since 2019 to assess the global prevalence of keratoconus with modern diagnostic instruments. To minimize population bias and financial barriers, the K-MAP study recruited individuals who presented to the emergency department in general hospitals open to the public rather than specialized ophthalmologic centers.[2]

In our published pilot study,[2] we found a keratoconus prevalence of 4.79%—almost 100 times higher than the rate reported by the Minnesota study.[1] Was the higher prevalence due to better diagnostic instruments, ethnic/genetic factors, or a combination of both? Now, we have extended our research to 21 additional countries, including Russia, the United States, Switzerland, Australia, Iran, the United Arab Emirates, Egypt, Mexico, Peru, and Syria.

A major advantage of K-MAP is its simplicity. Participating sites are required to meet only five criteria:

- Ethical committee approval;
- Access to a Scheimpflug imaging device for diagnostic measurements;
- An onsite anterior segment specialist for conducting measurements;
- A system for obtaining and storing consent forms signed by patients; and
- An agreement to the publication policy related to K-MAP data and the study protocol.

We are currently analyzing the data from Russia and Mexico and anticipate submitting them for publication later this year.

FUTURE DIRECTIONS

The results of our pilot study[2] show that the true prevalence of keratoconus may be much higher than previously thought. We expect K-MAP will find a global prevalence of keratoconus that is distinctly higher than the 0.05% found in the 1986 Minnesota study.[1] Future research can build on K-MAP to investigate disease prevalence in specific high-risk groups (eg, adolescents with Down syndrome) to refine clinicians' understanding of whom to screen and when, potentially guide changes in keratoconus treatment, and possibly lead to alterations in national health care policies and funding.

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the confidentiality of patient data or ownership regulations.

CONCLUSION

The next step in AI development and implementation in ophthalmology must move beyond statistical model performance to build robust applications that are accountable and tailored to users' needs. ■

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