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Editorial

Entering the Exciting Era of Artificial Intelligence and Big Data in Ophthalmology

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It is our pleasure to present the very first special issue of *Ophthalmology Science*, a collection of articles focused on Big Data and Artificial Intelligence (AI). Imaging and functional testing have long been central to our care of patients. Now that this testing and other clinical data exist in a purely digital realm, ophthalmology finds itself at the forefront of novel research leveraging the rise in the availability of Big Data and rapid advances in AI technology. We are poised to lead the transformation of research and clinical practice. New challenges have emerged alongside this exciting progress, including data sharing and privacy issues, lack of standardization, including interoperability and data portability, the urgent need for more and better training data, and perhaps most critically, determining how to successfully translate AI and Big Data advances into clinical practice. Not surprisingly, ophthalmology is also leading the global efforts in addressing many of these challenges, as exemplified in this special issue. This collection of $>$ 45 manuscripts truly demonstrates the breadth and depth of Big Data and AI-related research in ophthalmology. In this editorial, we have highlighted some of the exciting and clinically applicable research articles in the collection, though there are too many to mention and the full collection is well worth reviewing.

The field of ophthalmology has been leading research intersecting AI and Big Data to advance research and clinical care. The first-ever AI-based device to receive approval for clinical use was designed to screen fundus photos for evidence of diabetic retinopathy (DR), flagging cases requiring further review by an ophthalmologist,[1] a pivotal first step in the integration of AI into patient care. A study in this collection by Lim et al[2] evaluated a similar automated system for detecting “more than mild diabetic retinopathy,” defined as the presence of DR of higher severity than mild nonproliferative DR or diabetic macular edema. The AI algorithm achieved a significantly higher sensitivity (97%) for detecting more than mild DR compared with 59.5% for retina specialists and 20.6% for general ophthalmologists. However, the algorithm had a much lower specificity (88%) compared with human graders (retina specialists 98.9% and general ophthalmologists 99.8%). Further studies are needed to understand whether higher detection would lead to better clinical outcomes. Another study in this issue evaluated the use of a similar diabetic screening algorithm in a low-resource setting in Africa and found that its ability to provide immediate feedback on whether or not participants needed additional evaluation improved patient adherence to follow-up.[3] Both studies demonstrate the potential for AI for improving and expanding access to care.

However, even with regard to screening algorithms that perform well and have been approved for clinical use, challenges with validation in different patient populations still remain. A recent study evaluating 7 retinal screening algorithms on fundus images from 2 Veterans Affairs patient populations found that only 1 algorithm performed as well as the human graders.[4] Furthermore, the performance of the algorithms was highly dependent on demographic and clinical characteristics of the study population, suggesting the need to validate AI models in the intended use populations. Several studies in this special issue discussed algorithm bias, need for independent validations, and need for more training data, especially in rare disease,[5–8] all of which are important steps forward in our Big Data and AI research.

Large language models are another hot topic in AI, and many are seeking ways to leverage large language models for improving clinical care. A study by Wang et al[9] used natural language processing to extract relevant data from free-text clinical notes in electronic health records (EHRs) of 4512 patients to predict those who required glaucoma surgery. The model, relying only on input features from the free-text clinical notes, achieved an area under the precision recall curve of 0.431, outperforming a model that included clinical and demographic information as well as predictions from a glaucoma specialist who had reviewed the clinical notes. Large language models have the potential to revolutionize clinical practice, but challenges still remain related to defining ground truth, selecting appropriate evaluation metrics, and issues related to errors and liability.

Several articles in this collection explore novel solutions to specific challenges in AI research, such as using synthetic data to improve model prediction, specialized privacy-preserving techniques, and federated learning for improved multicenter collaboration. For example, Lo et al[8] explore federated learning as a solution to the critical problem of collecting ground truth data from multiple institutions to train a more robust model without compromising data privacy. This approach improves the generalizability of a model by collaboratively training tons of data from multiple institutions, sharing only the model weights between the sites and thus keeping patient data secure. The authors trained models to segment retinal microvasculature and classify referable DR or not on

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OCT/OCT angiography imaging using a federated learning configuration, and the models achieved similar performance to models trained using data from a single institution. Chen et al[10] reviewed the uses and limitations of synthetic data created using generative adversarial networks in ophthalmic research and also assessed whether expert clinicians could distinguish synthetic images from real fundus images obtained through a retinopathy of prematurity screening program (spoiler alert: they often could not!).

Several studies have focused on retinal imaging analysis, leveraging advances in imaging technology by applying deep learning techniques to analyze fundus images, OCT, and OCT angiography to predict disease, classify features, or even differentiate between bacterial and fungal keratitis.[11] Fan et al[12] employed vision transformers to better assess global visual features for identifying primary open-angle glaucoma on fundus images, as well as to improve the generalizability and explainability of the model. Gao et al[13] developed a deep learning approach for classifying arteries and veins in montaged widefield OCT angiography images, enabling more accurate assessment of retinal disease involving the vasculature.

The collection also includes several analyses of large electronic health record data sets such as the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight), the All of Us study, and others, applying innovative statistical approaches to gain insight into epidemiology and outcomes as well as assessments of data quality and completeness. With these large data sets, studies to gain epidemiologic insights into rare diseases have become possible. For example, Belin et al[14] investigated surgical outcomes and complications after retinal detachments associated with hereditary vitreoretinal degeneration in 1722 pediatric patients, a previously understudied cohort. These large data sets also have great potential for evaluating the impact of social determinants of health on outcomes in ophthalmic disease, although Lee et al[15] evaluated electronic health records and national health survey data and report that the completeness of these data can be variable. In the National Institutes of Health's All of Us data repository, certain variables (housing, food security, social isolation) were available for $< 2\%$ of participants, and local electronic health record data showed similar gaps related to various social determinants of health-related measures.

The collection also includes research on implementation of AI and Big Data approaches in the clinical realm, such as for clinical decision support and AI-based approaches to monitor surgical technique in real time. For example, Nespolo et al[16] developed an algorithm for extracting gaze metrics of ophthalmic surgeons and found that surgeons' gaze behavior varies according to experience level. Finally, several insightful editorials are included in this collection to provide context about the potential impact and uses of AI and Big Data in ophthalmology as well as to highlight areas that must be addressed to enable continued progress in this field.

We would like to thank the experts and researchers who have contributed to this special collection. These thoughtful articles represent the cutting edge of AI and Big Data research in ophthalmology and have provided a wide range of perspectives and approaches. We encourage readers to explore their work and hope that it will inspire new explorations and insights into these topics, continuing the tradition of ophthalmology research at the forefront of AI and Big Data in medicine.

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