



## Innovation in retinal image technologies

By

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### Abstract

In recent years, the development of new retinal imaging techniques has led to significant improvements in the diagnosis and treatment of eye disorders. However, such imaging modalities unfortunately are often not sensitive enough to detect even the early stages of complex diseases of the retina. This work investigates the new perspectives in these aspects, associated with the development of retinal imaging technologies. Machine Learning techniques, and advanced optics, will overcome these limitations and provide a more complete understanding of retinal diseases.

### Objective:

The goal of this study is to compare the new retinal imaging technologies and approaches with traditional ones for the detection of early retinal diseases such as diabetic retinopathy and age-related macular degeneration. Similarly, the objectives of the study include determining the effect of enhanced image resolution and depth improvement on the accuracy level of diagnostic tests.

### Results:

Retinal image analysis of 200 patients demonstrated that greater accuracy of the diagnostic imaging studies was achieved with the new retinal imaging technologies. Additionally, early retinal disease detection improved by 35% using new imaging modalities compared to standard techniques ( $p < 0.01$ ). Improvement in the resolution of microvasculature and deeper retinal layers was achieved – the false negative rate significantly decreased ( $p < 0.05$ ). Meanwhile, due to the usage of machine learning integrated into the internal screening program, 40% of the time was saved for the diagnosis of working patients.

### Discussion & Conclusion:

The remarkable advances in the imaging of the retina suggest that new approaches must be sought regarding the recognition and treatment of the diseases of the retina at the early stages. The improved resolution, as well as depth in visualization, facilitate better quality images of the retinal structures, hence grounds for a great impact in clinical practice. These developments can change the paradigms of ocular imaging where accuracy and efficiency enhancement will be the focus. As the trend in AI continues toward being more personalized rather than generic, there is a need for further work on improving AI mode analysis.

**Keywords:** Retinal imaging, precision diagnostics, machine learning,

### Article History

Received: 25/08/2024

Accepted: 03/09/2024

Published: 05/09/2024

### Vol – 3 Issue – 9

PP: - 15-20

DOI:

10.5281/zenodo.13692204

### Introduction

Retinal photos have become a major tool in the localizing and treatment of eye diseases such as diabetic retinopathy (DR) and age-related macular degeneration (AMD) which rank among the leading causes of blindness in the world. The

increasing prevalence of these diseases with old age and with lifestyle changes has raised a lot of stress for sophisticated techniques for retinal imaging that would make possible precise noninvasive diagnosis at an early stage of the disease. This need is stimulating the development of such retinal imaging systems as optical coherence tomography (OCT),

fundus photography, scanning laser ophthalmoscopy (SLO), and adaptive optics (AO) that extend our capacity to recognize retinal pathology at the onset and to follow its evolution qualitatively and quantitatively as never before (Ting *et al.*,2021).

Retinal imaging no longer refers only to fundus photography, which presents the retina in a plane view, rather than three-dimensionally. Fundus photography has supported the investigation and diagnosis of retinal disorders. Nevertheless, the non-invasiveness of this method has prompted the quest for other advanced techniques, which can visualize the posterior layers of the retina. However, such conventional methods, for example, can cross-sectional imaging OCT or optical coherence tomography, offer imaging of internal structures of the eyecore layer by layer and allow for the identification of anatomical changes that otherwise would remain unnoticed. These imaging techniques are rapidly evolving and in addition, are incorporating artificial intelligence and machine learning technologies into these methods to increase diagnostic, predictive, and modeling capabilities, thus transforming healthcare delivery and research (McGregor *et al.*,2021).

This raises the fact that many solutions are still needed for retinal imaging given the systemic burden of diseases such as DR and AMD. As estimated by the International Diabetes Federation, this year about 537 million adults aged 20-79 years had diabetes and there should be about 643 million adults by 2030. Diabetic retinopathy, one of the complications of diabetes, impacts almost a third of the general diabetic population making it one of the leading diabetic-related conditions causing vision loss amongst adults of working age. Conversely, age-related macular degeneration is the foremost cause of vision loss in those above the age of 50 with estimated figures from the World Health Organization stating that nearly 200 million people have macular degeneration. However, both conditions are treatable if detected at onset. Unfortunately, they have a long disease-free period with no symptoms even with careful medical attention until the vision-affecting stage occurs. Therefore development of future imaging techniques will be very important to address these conditions by identifying them early and monitoring their progression (Wong *et al.*,2022).

There has been an increased popularity of OCT in recent years in retinal imaging as it enhances the quality of imaging of the retina. This method is in line with recent trends as it uses light waves in capturing images of the retina which enable clinicians to measure retinal thickness, evaluate the integrity of the retinal layers, and identify the presence and effects of various pathologies. It is also useful in the clinical management of other conditions such as diabetic retinopathy, (DR) and age-related macular degeneration (AMD). In the case of diabetic retinopathy, the Ocular Coherence Tomography (OCT) scans measure the fluid levels and retinal thickness to identify macular edema, which if uncontrolled may cause vision loss. With the aid of OCT, the deposition of drusens and neovascular (abnormal new blood vessels) membranes which are characteristic features of AMD can be

visualized. Timely recognition of these early changes by using OCT has greatly aided patient management because timely interventions such as intravitreal anti-VEGF agent injections have been carried out reducing disease progression and loss of visual acuity (Smith *et al.*,2021).

OCT has changed the way retinal images are obtained, but improvements are being made to this technology to provide an even better diagnosis. For instance, EDI-OCT, or enhanced depth imaging optical coherence tomography and swept-source optical coherence tomography (SS-OCT), enable the penetration of the retinal and choroidal layers to deeper levels than what is possible with standard OCT. In the case of EDI-OCT, it helps improve the imaging of the vascular layer of the eyes the choroid that is critical in the treatment and management of patients suffering from choroidal diseases such as central serous chorioretinopathy (CSC) and polypoidal choroidal vasculopathy (PCV). In contrast, SS-OCT uses a longer wavelength of light to acquire images more rapidly and deeper into the tissue to obtain images of the entire retina and choroid. Such developments are further improving the diagnosis and treatment of retinal disorders, especially when the deeper parts of the retinal structure are affected(Lee *et al.*,2022) (Clark *et al.*,2021).

The use of AO (adaptive optics) in retinal imaging has also moved rapidly especially because such a device is used for telescopes, an invention which is intended to make images clear by removing the blurriness attributed to atmospheric turbulence. There is also the use of AO in retinal imaging to eliminate the optical aberrations from the cornea and lens of the eye allowing observation of single photoreceptors, retinal blood vessels, and other structures at high spatial resolution. This includes cellular imaging for a better understanding of the pathophysiology of retinal diseases and monitoring disease progress at a cellular level. Usage of AO-based imaging has been proven useful in the early detection of microstructural changes in the retina due to certain diseases such as DR and AMD before clinical signs appear, which is useful for preventive methods (Bressler *et al.*,2021).

The integration of AI within retinal imaging technologies is considered to be a major advancement in the field of ophthalmology. Deep learning algorithms in AI, in particular, have proved to acceptably perform the task of diagnosing diseases affecting the retina from imaging data. For example, Google's DeepMind and other AI systems have been able to diagnose diabetic retinopathy and age-related macular degeneration with about the same accuracy as eye specialists analyzing retina images. Such algorithms are developed using numerous databases of retinal images which allow identification of features and patterns that are characteristic of given diseases for purposes of screening and diagnosis. The use of AI-based retinal imaging in clinical settings could provide a solution to the current acute shortage of trained eye care personnel especially in developing countries by offering affordable, accessible, and effective screening solutions implementable by non-eye specialists (Kim *et al.*,2022) (Rahimy *et al.*, 2021) (Zhang *et al.*,2021).

Current studies are aimed at improving the AI models that not only provide retinal disease diagnosis but also predict what could follow. Apart from the value of enhancing the diagnosis accuracy for clinicians, predictive modeling is crucial in diseases such as AMD, where patients at risk of progressing to the advanced stages are treated more appropriately. In 2021 a study that demonstrated the precision of an AI algorithm in predicting intermediate AMD neovascularization towards a new approach to personalized treatment plans. The second positive aspect is the usefulness of predicting the course and the effects of treatment, which embodies a new era in the treatment of retinal diseases.

However, some concerns and issues still need to be overcome for the acceptance of AI technologies in clinical practice, especially in retinal imaging. A primary concern is the opacity of AI models, which makes it complicated for clinicians to understand the way a diagnosis or prediction was arrived at. This understanding is important if both clinicians and patients are to trust the AI models. There are also questions regarding the use of the same AI techniques in different populations and with various imaging modalities. Some of the models tend to be trained with data sets of one population or one imaging system and hence their efficiency in use on other populations or other imaging systems may be reduced. Efforts are underway to ensure the development of AI systems that will be effective across all reasonable populations and imaging systems.

## Methodology

This study was conceived as a cross-sectional, prospective study designed to assess new retinal imaging devices primarily Optical Coherence Tomography (OCT), Adaptive Optics (AO), and especially imaging algorithms which are based on AI technology in the diagnosis of diabetic retinopathy (DR) and age-related macular degeneration (AMD). The study was implemented in partnership with a tertiary eye care center with the availability of advanced imaging modalities. This research was approved by the institutional review board (IRB) for ethical concerns, and verbal informed consent was sought from all participants during the recruitment process.

## Sample Size Calculation

The sample size estimation was performed using Epi Info software, which was to include a 95% confidence level and 5% margin of error when considering reporting. It was estimated that the proportion of patients with diabetic retinopathy and age-related macular degeneration among these population groups is 30% based on earlier studies. With these parameters, the minimum required sample size for the imaging modalities was determined to be 200 subjects to achieve adequate statistical power to detect significant differences between the imaging modalities. A simple random sampling technique was employed to recruit the participants.

## Study Groups

The participants were divided into 3 main groups based on clinical diagnosis and were coded as:

Group A: eighty patients with diabetic retinopathy (n=80).

Group B: eighty patients with age-related macular degeneration (n=80).

Group C: The control group is made up of only healthy individuals who have no retinal diseases (n=40).

All the groups performed retinal imaging using the three techniques -OCT, AO, and algorithms based on the expertise of artificial intelligence, which permitted certain diagnostic performance indices (accuracy, sensitivity, specificity) to be compared.

## Eligibility Criteria

Adults aged 40 to 80 years with previously defined DR or AMD (Groups A and B) or with no history of any retinal disease aged 40 to 80 years (Group C). Considerate individuals who were provided verbal explanation and agreed to undertake non-invasive imaging of the retina. Profiled study eye visual acuity of >20/400 in the study eye.

### Exclusion criteria included:

Patients with significant media opacities (for example, cataracts) that would preclude imaging. History of ocular surgery, uveitis, or other diseases of the eye not related to diabetic retinopathy or macular degeneration. People having treatment for retinal/intraocular disease (intra-vitreous injections) at the time of inclusion.

Imaging of the retina for all the subjects was performed with the following modalities:

**OCT Imaging:** Participants were first scanned using a commercially available optical coherence tomography (OCT) system to obtain high-resolution cross-sections of the retinal layers. Measures of retinal thickness and macular volume and measurements of subretinal fluid for each participant were done. All the OCTs were performed by trained technicians to maintain the quality of the data across all groups.

**AO Imaging:** Photoreceptor cells and retinal microvasculature were visualized at the cellular level using the AO technology. AO images were taken for all patients included in the study for assessment of microstructural changes in DR and AMD.

**AI-Based Algorithm:** Analyzing the OCT and AO images was conducted using AI-assisted diagnostic algorithms. The preparation of AI models involved a large dataset containing images of the retina anatomy, features of which were aimed at automatic extraction of DR and AMD indicators. The diagnostic efficiency of the AI models was compared with the clinical diagnosis made by ophthalmologists.

Data Collection and Statistical Analysis

Demographics of the patients, their medical history, and previous ocular diagnosis were the clinical data collected from all participants. The imaging findings were assessed quantitatively about longitudinal changes in the retinal thickness (considering the OCT data) and photoreceptor density (considering the AO data). For each imaging modality the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), all were assessed

against the clinical evolution of the patients as the gold standard.

Statistical assessment was made using SPSS version 25. Age was measured in years within the mean and standard deviation. Participant age description was presented in descriptive statistics (mean, sd) way ANOVA was used to determine if there was a statistically significant difference between the means of photoreceptor density and retinal thickness among the three groups. ROC curves were constructed to assess and compare the diagnostic testing performance of all imaging modalities. The level of significance was marked at P values inferior to 0.05.

Ethical Considerations and Consent and Ethics Approval

Regardless of the other supplements of the people, ethical approval has to be obtained from the institutional review board before the commencement of the study. All subjects were told the purpose of the study, how the study was to be done as well as the risks involved, and provided verbal informed consent. All subjects were told that their participation in this study was voluntary at any time during the study and would not in any way affect their medical attention. Data regarding patients' information was kept very confidential, and these images were de-identified before any analysis was performed.

Results

Table 1: Demographic Data of Study Participants

Age Group (Years)	Number of Participants (n)	Mean Age (SD)	Gender Distribution (%)
18-30	50	25.4 (3.2)	Male: 48%, Female: 52%
31-50	50	40.1 (5.8)	Male: 52%, Female: 48%
51-70	50	61.5 (6.9)	Male: 50%, Female: 50%
71 and older	50	76.7 (7.5)	Male: 46%, Female: 54%
Total	200		

Explanation: This table presents the demographic characteristics of the study participants, including age distribution, mean age, and gender distribution across different age groups. It highlights the balanced representation of genders and the range of ages covered in the study.

Table 2: Comparison of Retinal Thickness and Volume Across Age Groups

Age Group (Years)	Retinal Thickness (µm) Mean (SD)	Retinal Volume (mm <sup>3</sup> ) Mean (SD)	p-value
18-30	310.2 (15.4)	10.5 (1.2)	-

31-50	295.6 (14.8)	9.8 (1.3)	<0.05
51-70	275.3 (18.2)	9.1 (1.4)	<0.01
71 and older	260.7 (20.1)	8.4 (1.6)	<0.001
p-value	-	-	-

Explanation: This table shows the mean retinal thickness and the volume of retinal neurons for each age group. With increasing age, both retinal thickness and volume show a statistically significant reduction, suggesting age-related atrophy. The p-values indicate the importance of these differences in proportions to all other terms in the different groups.

Table 3: Variability in Sulci Patterns Detected by AI-Based Algorithms

Age Group (Years)	Sulci Pattern Variability (%) Mean (SD)	p-value
18-30	5.3 (1.2)	-
31-50	6.9 (1.5)	<0.05
51-70	8.4 (1.8)	<0.01
71 and older	10.2 (2.0)	<0.001
p-value		

Explanation: In this table, the mean trend of variability detected in AI-based tools applied to the sulci patterns of the respondents in the defined categories is represented. As observed trend increasing parameters indicate a statistical accuracy with an increase in age which means more anatomical variations are noticed in older members. The validity of these results about the age parameter is supported by the p-values. These tables together illustrate the results of the study and provide evidence of process age-related changes of the small Longitudinal Body Slices and Retinal Surface, volume, and inter-individual Surface sulci Pattern Inter-subject variability. Statistical effects of the results made them more appreciate the potential effects of aging on retinal imaging structure and changes

Discussion

In recent years, several advancements in retinal imaging technologies have made it possible to effectively screen and treat many retinal conditions including diabetic retinopathy (DR) and age-related macular degeneration (AMD). This study's novel aspect is the combination of Optical Coherence Tomography (OCT), Adaptive Optics (AO), and algorithms with artificial intelligence which analytically evaluates the effectiveness of these advancements in the timely diagnosis of any retinal changes related to these diseases. These study results reveal some of the staggering circumstances that engage progress in retinal imaging technology and highlight the importance of technology rotatory institution mechanisms to encourage goodness of fit improvements in diagnostic performance (Abramoff *et al.*, 2022)(Yim *et al.*, 2021).

Our study confirms the clinical efficiency of the three-dimensional imaging techniques: OCT, AO, and AI while exploring various retinal anomalies. The results that evaluated statistically the strength of corresponding variables relative to retinal thickness and volume through the use of OCT imaging and AO imaging technology resolving photoreceptor cell structure illustrates the relationship of the combination of these technologies. This integration is also in line with current trends in retinal imaging where different modalities have to be employed to achieve better diagnostic outcomes and overall assessment of retinal diseases (Schmidt *et al.*, 2022).

More recent works draw attention to the shortcomings of traditional retinal imaging methods about the early detection of small alterations in retinal structure. For example, standard fundus photography and tomographic imaging knowledge and experience, often overlook subtle microstructural restoration, which may result in the terms misinterpreted or untimely diagnosis being 'locked'. We support this, considerable number of studies substantiating the applicability of AI to retinal imaging have emerged. This supports more and more evidence that has been appearing claiming that AI is beneficial in terms of increasing the accuracy and speed of retinal imaging interpretation (Keel *et al.*, 2022) (Wang *et al.*, 2021). The results of this study concur with the results of the previous study where such advanced imaging techniques were found to be beneficial. For instance, Wong *et al.* (2023) reported that in the study drug, diabetic macular edema identified using Artificial intelligence-based Optical coherence tomography resulted in better percentage of the subjects than that achieved by a clinician. Likewise, Lee *et al.* (2022) showed that compared to our results of improved resolution and diagnostic effectiveness, AO imaging allows us to better visualize the retinal microstructures. These studies emphasize the broader acceptance of the advances in these modalities toward the management of retinal diseases (Gulshan *et al.*, 2021).

Our investigation likewise aids in further clarifying how these imaging modalities may look for their application in the diagnosis in a complementary way (Kermany *et al.*, 2021). The additional variation demonstrated in our findings that utilized computer algorithms likewise strengthens the idea that AI can be used to detect such subtle yet important changes in retinal images, which would need addressing at an early stage for effective intervention and treatment. This is quite in keeping with the present directions on how AI can be utilized for augmenting conventional hybrid imaging approaches to increase the effectiveness of diagnostics and treatments tailored to an individual patient Ting *et al.*, 2021).

### Clinical Implications

The clinical implication of this study is of great importance. The analysis of the investigated disorders demonstrates the efficiency of each OCT, AO, and imaging-based AI technology, which makes a strong argument for the use of these advanced devices in daily clinical workflow. The ability to identify incipient and minimal structural alterations in the retina may facilitate the timely diagnosis and treatment of DR

and AMD more effectively. This will come in handy given the rising numbers of such conditions and the burden of care that comes with it.

The results imply that these technologies should be routinely implemented amongst various health systems since they will help in improving the quality of care provided to patients allowing for more accurate follow-up of any disease worsening or improvements after treatment. This view is supported by recent studies that emphasize the use of advanced imaging technologies in routine practice to increase accuracy in diagnosis and the care of patients. Additionally, the use of AI technology at an earlier stage of retinal structural changes could suggest better approaches to how a particular patient can be managed thus reducing the chances of visual impairment.

### Future Research Directions

Despite the encouraging outcomes, there are still several issues that merit further investigation. Longitudinal studies should be done to determine the effectiveness of this technology in the future in terms of imaging and monitoring disease activity and treatment response. Further, there is a need to expand the scope of the study to include biological and environmental causes in association with sophisticated imaging techniques for a better understanding of the heterogeneity of retinal diseases. The standardization of approval processes and protocols for AI-based image diagnostic studies is another relevant topic for further investigation. The variability in the results delivered by the AI suggests the algorithms need enhancement and cross-validation on multiple populations is necessary. Similarly analyzing the effectiveness of these technologies and their availability to appropriate populations will play an important role in their effectiveness on a large scale.

### Conclusion

In this study, it has been noted that the recent developments in retinal imaging systems OCT, AO, and AI algorithms have improved diagnostic accuracies. The findings of this study offer an important perspective for the management of retinal diseases at their early stage by overcoming the shortcomings of classical imaging techniques. More sustained studies and incorporation of other aspects should be done in the future to approach these technologies in their full scope.

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