# GENERATIVE ARTIFICIAL INTELLIGENCE FOR RETINAL DEGENERATION: A REVIEW

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Abstract:

Every stratum of professionals has been impacted by the rapid improvements in technology. Artificial intelligence (AI) has had a genuinely unmatched impact on the fields of transportation, agriculture, meteorology, and health. We can now anticipate the future more accurately and confidently using AI using historical datasets. Although there are many applications for AI, this research focuses only on generative AI for the diagnosis of retinal disorders. The generator and the discriminator are the two primary models used in generative AI. While the discriminator tries to distinguish between accurate and false, the generator is employed to generate noisy random input. Together, these two models operate. For the treatment of retinal illnesses such as diabetic retinopathy, also known as DR, age-related macular degeneration, or AMD, and Retinal Fundus, commonly known as RF, ophthalmologists have used Generative AI. Based on the input datasets, generative AI may categorize them into specific groups by recognizing patterns in data. The subject of generative AI is relatively young, and numerous datasets are needed for it to gain experience as a stakeholder. Nevertheless, with every opportunity comes a challenge. The interpretation of technology-generated data that are outdated, technical difficulties, patient and physician approval of the algorithm, and its legal implications are further possible roadblocks for technology in ophthalmology. In a nutshell, yes there are challenges to the use of AI technology in diagnosing diseases related to ophthalmology, but these challenges can be solved. Hence, the future of Generative AI shows a bright picture in clinical development.

Keywords:

Artificial Intelligence, AMD, DR, Generative AI, Discriminator, Retinal Fundus.

## INTRODUCTION

There are 285 million visually impaired persons worldwide, of whom 39 million are blind, according to the World Health Organization (WHO) [1]. The main reason for such a staggering of visually impaired people is retinal diseases. The most notable diseases that cause visual impairment are Glaucoma, Cataracts, Age-related macular degeneration (AMD), Diabetic retinopathy (DR), and Ocular surface neoplasia [2]. There are different reasons for each of these diseases to occur. Glaucoma is caused by an abnormality in the drainage mechanism of the eye, which results in a build-up of fluid around the optic nerve, ultimately resulting in the loss of sightedness.

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DOI: 10.15308/Sinteza-2023-28-35

Cataract and Age-related macular degeneration are caused by aging, diabetes, smoking, previous eye injury, and high blood pressure [3]. And the last one Ocular surface neoplasia occurs due to exposure to solar ultraviolet radiation (UV), Human immunodeficiency virus (HIV), and human papillomavirus (HPV). According to scientific studies, all these visual impairments and their causes are preventable in their early ages, to be more specific they can be cured with almost 80pc success rate [1]. However, with time these disorders become irreversible, and the patient will have to suffer from long-lasting blindness.

Out of all the eye diseases mentioned above, two of them are more common; age-related macular degeneration (AMD) and diabetic retinopathy (DR) [4]. According to estimates around 170 million people around the globe are affected by the former retinal disease, while one-third of all the people who suffer from diabetes, which is around 285 million, have shown the symptoms of diabetic retinopathy. In recent years these numbers have been increasing and there are projections for the future which do not look good. According to projections, over 288 million individuals will have AMD by 2040, and the number of DR patients will triple by 2050 [5]. This startling figure paints a bleak picture of the future and necessitates action to combat these retinal illnesses.

Ophthalmologists all over the world have developed drugs to treat various disorders over the years. Intravitreal vascular endothelial growth factor (VEGF) suppression, which was established in 2006, is one of them [6]. This was a major success, and it made a significant difference in preventing and lowering the incidence of legal blindness. This anti-VEGF drug was used to treat patients with diabetic macular edema (DME). However, the success of anti-VEGF medication quickly faded, owing to delays in diagnosing illness initiation and progression, as well as the unpredictability of recurrence, all of which derail long-term care [7]. Even blocking complement factors, thought to be one of the main causes of geographic atrophy (GA), has not been able to stop the disease's progression or the loss of vision, leaving the topic of effective therapy targets and pertinent biomarkers open [8]. Additionally, a number of studies have shown negative effects in recent years as a result of the prolonged use of anti-VEGF drugs and the rise in the number of injections conducted internationally, including increased intraocular pressure and unsightly silicone oil vesicles in the vitreous cavity [9]. As a result, retinologists have been unable to devise a viable remedy that may prevent long-term vision deterioration in large patient populations, and healthcare providers have experienced a significant economic drain as a result of unsuccessful research trials [10].

Artificial intelligence is better known as the fourth industrial revolution [11]. It consists of various fields: supervised and unsupervised learning. The former is defined as a machine learning (ML) type where a model is trained on labeled data, meaning that the desired output or target variable is provided along with the input data. The goal is for the model to learn to predict new, unseen data based on the patterns it learned from the training data. While the latter is also a type of machine learning where a model is trained on unlabelled data, meaning that the desired output or target variable is not provided. Here the goal is for the model to find patterns or structure in the data on its own. Generative AI is the combination of unsupervised and semi-supervised learning. AI, since its introduction in 1956 by John McCarthy, has changed the lifestyle of human beings. It is used everywhere in judging customer preferences, from the transpire ort industry, in the form of driverless cars, to the hotel industry [10]. AI is used in the agricultural sector to predict future yields, forecast the weather, and monitor crop health and the irrigation system.

Thus, it is no exaggeration to say that artificial intelligence (AI) is used everywhere in our daily life, this review summarizes the use of generative AI in the field of ophthalmology, the potential of generative AI models, possible challenges for it, and the way forward.

## 2. DIFFERENT SOLUTIONS TO RETINAL DISEASES

The non-invasive, high-resolution optical imaging technique known as optical coherence tomography (OCT) is based on the interference of a signal from the item being analyzed and a nearby reference signal [12]. OCT can create a cross-section image of the item or a two-dimensional image in space in real-time, lateral coordinate, or axial coordinate. Because of the combination of the eye's aberration and low numerical aperture, confocal microscopy is limited when used to scan the retina of the human eye. The numerical aperture of the microscope objective governs both the lateral and axial resolutions in confocal microscopy. Spectral-domain (SD)-OCT is widely available and employed in the treatment of major retinal diseases such as choroidal neovascularization (CNV) and diabetic macular edema (DME) [13]. The traditional three-dimensional OCT image is based on approximately 20,000—52,000 A-scans per second with a resolution of 5 to 7 micrometres [14]. The identification of blood flow is possible thanks to OCT technology's high-speed and efficient algorithms (a collection of rules and methods to solve a problem).

Given the busy work schedule of an ophthalmologist, it would be nearly impossible for an ophthalmologist to scroll through a series of about 250 B-scans for every dozen retina patients seen daily [15].

With such a large amount of data available, each patient acts as a "big data" challenge because it increases the complexity of a disease. Thus, the new era of diagnostics requires intelligent tools to maintain a large bulge of data safely and efficiently. To effectively manage such a large sum of data the role of new technology, i.e., artificial intelligence, increases. TI has pronounced its effectiveness and strength in every walk of life ranging from agriculture, businesses, weather forecasting, and population projection. In the field of medicine AI is being used in dermatology (the study of hair, skin, and nails), radiology a (branch of medicine that uses imaging technology to diagnose disease), and pathology. Consequently, through AI physicians could learn and detect different diseases after scanning a large volume of image data. It is not an exaggeration that AI is the future, and it would foster the knowledge of ophthalmologists.

## 3. THE EMERGENCE OF GENERATIVE ARTIFICIAL INTELLIGENCE

As mentioned earlier AI is the branch of computer science that deals with the invention of intelligent machines. The field of artificial intelligence is very diverse, and it encompasses within itself different branches, generative AI is one of them. A subfield of computer science called generative artificial intelligence (GAI) uses unsupervised and semi-supervised techniques to let computers build new content out of previously existing stuff including text, music, video, graphics, and code [16]. It all comes down to producing wholly original artifacts that seem legitimate. In other words, generative AI is a subfield of machine learning that focuses on designing algorithms that can generate new data. Robotics, computer vision, and the arts and music are all using generative models. The term "generative" in this context refers to the process by which these models learn to generate new data rather than simply recognize it. A generative model, for example, may learn how to make images that resemble faces given a collection of parameters (such as the number of eyes or hair color).

Although generative AI is not a new thing, over the years it has evolved, and different approaches are used in this field to solve day-to-day problems. The models of deep learning (DL) and generative adversarial network (GAN) approaches were being used, but the latest approach of the generative approach of AI i.e., transformers has revolutionized everything.

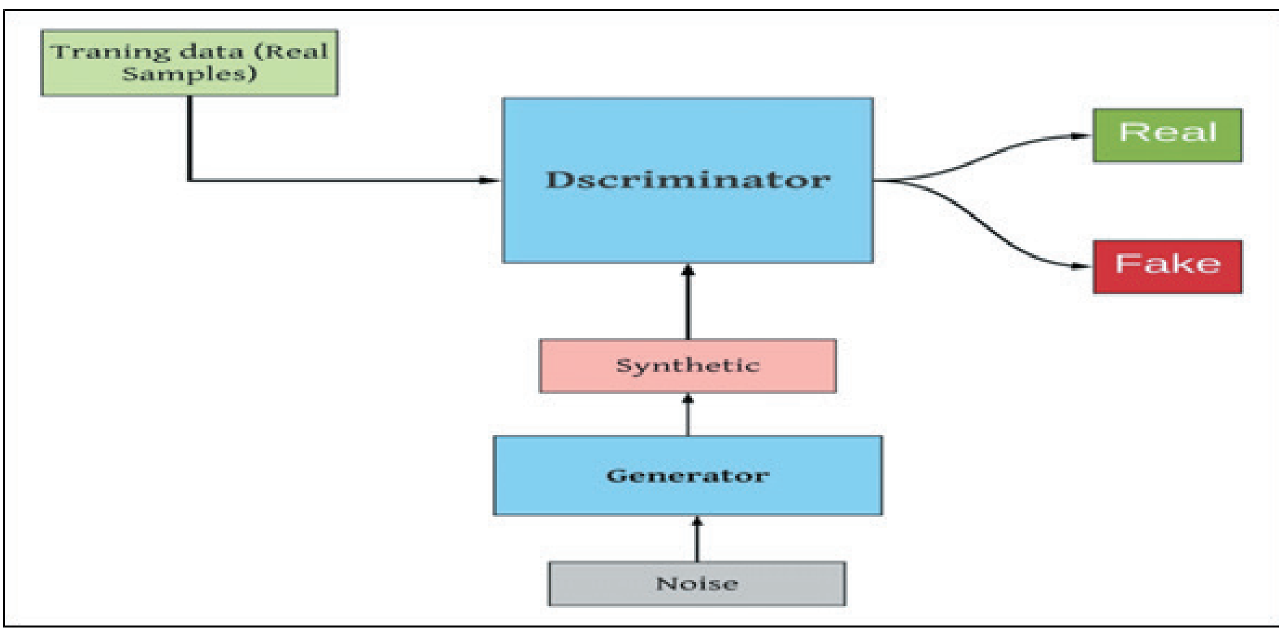


Figure 1 - The working principle of generative AI.

The concept of Deep learning (DL) is a subset of machine learning. The machine itself identifies by looking at the pattern, that is concerned with algorithms inspired by the structure and function of the brain called artificial neural networks. These neural networks are built to recognize patterns and make judgments, and they are especially well suited for tasks like picture and audio recognition, natural language processing, and decision-making. Large sets of labelled data are used to train DL models, and they automatically learn and improve based on the data they are given. They can learn numerous layers of abstraction and hence complete extremely difficult jobs [17]. It's important to note that DL is a branch of machine learning, and it uses neural networks as the main building block, neural networks are modelled after the human brain, and it is a subset of artificial intelligence (AI) that deals with training multi-layered neural networks, which are called deep neural network [18]. The practical application of the DL is in areas like the banking sector for the detection of fraud, weather forecasting, etc. [19].

Generative Adversarial Network (GAN) is a type of deep learning model that's used to produce or generate a completely new dataset based on given training. There are two main components of the GAN, a generator network, and a discriminator network [20]. The former is used to provide new data samples that are analogous to the training data. It takes random inputs and caps able to generate an output, which is a new data sample. The discriminator is given the task to differentiate between the generated data sample and the real data sets from the training dataset. It takes in a data sample and produces a probability score indicating how likely it is that the sample is real. Interestingly, these two components of GAN work against each other, the generator strives to come up with a difficult dataset, to make the discriminator fool. While the discriminator tries to be better at identifying the fake samples [20]. The concept of GAN is used in video editing, text-to-speech conversion, noise removal from data, 3D object generation, and drug discovery [21].

The latest approach of the GAN, transformers, has changed everything. The development of generative pertained transformers (GPT) is a type of large language model that effectively uses deep learning to generate text like human beings. Back in November 2022, the OpenAI company launched an online chatbot, "ChatGPT" that uses GPT-3 [22]. This chatbot is fully capable of generating text and answering questions. Academicians around the world have now found it difficult to understand the difference between human writing and computer-generated essays [23].

In conclusion, the field of generative AI is changing the world due to its rapid solution to the world's complex problems. Their application is everywhere from engineering to medicine, banking to meteorology, and to education. According to reports, the scientist believes that by 2030, this field would generate an economy of 15.7 trillion USD [24]. So, it is pertinent to use these novel technologies for the treatment of different retinal disorders.

## 4. USING GENERATIVE AI TO COMBAT RETINAL DISEASE

### A. TREATMENT OF DIABETIC RETINOPATHY USING DL

By 2040, 600 million individuals worldwide would have diabetes, with one-third developing diabetic retinopathy (DR). According to one study conducted on 22,896 persons with diabetes from various nations such as Australia, India, and other European countries between 1980 and 2008, according to this study [25]. The results of this study showed that out of all the patients with diabetes, 35% were suffering from retinal disease, particularly from the DR. However, through timely treatment lifetime, blindness can be prevented. The classical method of treating DR has many issues like implementation, availability of human resources, and long-term economic sustainability [26].

The development of deep learning (DL) has improved diagnostic performance in detecting diabetic retinopathy. In a study by Abramoff, it was found that the DL mechanism of detecting DR could identify referable DR on the Messidor-2 dataset with an area under the receiver operating characteristic curve (AUC) of 0.980, a sensitivity of 96.8%, and a specificity of roughly 87.0% [27]. Another study by Gulshan from Google AI Healthcare found that the DL system performed well in terms of diagnostic performance when dealing with DR. The AUC, sensitivity, and specificity of the DL system, which was constructed using the DL architecture VGG-19, were found to be 0.936, 90.5%, and 91.6% in detecting referable DR, respectively, and the same architecture yielded data of 0.95, 100%, and 91.1% in detecting vision-threatening DR [28].

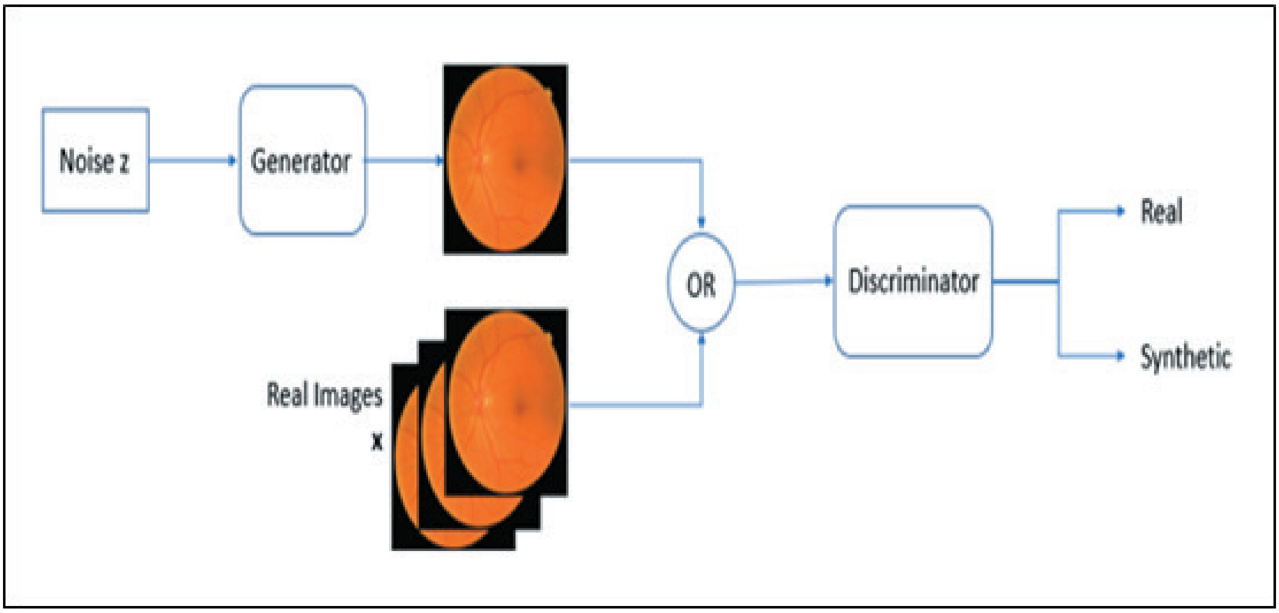


Figure 2 - Shows the working of deep learning in ophthalmology [33].

### B. MAGE-RELATED MACULAR DEGENERATION AND DL

Age-related Macular Degeneration (AMD) is majorly caused by age factors. According to the American Academy of Ophthalmology's study, around 288 million people will suffer from some or other form of AMD by 2040. Out of this population, approximately 10% would have intermediate AMD or worse [29]. With such a large population on the verge of a catastrophe, dire actions are needed to resolve this issue.

To diagnose AMD, the concept of deep learning is used. According to a study by Ting et al, the DL method detecting AMD has proved successful. The DL system was trained and tested using 108,558 retinal images taken from 38,139 patients [30]. The accuracy report calculated by Burlina et al was between 88.4% to 91.6% and with the area under the receiver operating characteristic curve (AUC) between 0.94 to 0.96 [31]. However, these pictures were taken in analog format and then these pictures were converted into digital form, whether this transition from analog to digital format can affect the accuracy is still unknown [32].

### C. GANS FOR RETINAL FUNDUS IMAGE SYNTHESIS

The fundus refers to the eye's inside and posterior surfaces. This structure is made up of the retina, macula, optic disc, fovea, and blood vessels. The imaging of this area of the eye has undergone a revolution because of technological advancements, particularly deep learning. Realistic image synthesis of the eye fundus was a very difficult undertaking prior to the development of deep learning techniques. As computing power has improved over time, machine learning in neural networks with extremely complex architecture is now possible. The development of DL makes GAN an important framework. The colored retinal fundus can be synthesized into realistic-looking images thanks to GAN. GAN is an unsupervised DL machine that Goodfellow first developed [33]. A generator and a discriminator are its two models. By selecting noise samples at random and creating images from those samples, the generative model may capture data distribution [34]. In order to distinguish between authentic and false images, the discriminative model is tasked with estimating the chance that a sample will come from the data distribution rather than the generator distribution.

GANs have shown the ability to generate stunningly accurate synthetic medical images. This section addresses current research on GANs for colored retinal fundus image synthesis. The vascular tree segmentation was combined with retinal fundus pictures. The U-Net architecture was used to create binary maps of the retinal vasculatures. Using an image-to-image translation method, the pairs were used to build a mapping from a binary vascular tree to a new retinal picture (512 X 512 pixels) [35]. A global L1 loss and a general GAN adversarial loss were used to handle the low-frequency information in the images generated by the generator.

The Messidor-1 dataset provided 614 photo pairs for the training set. They used Qv scores and image structure clustering (ISC) scores, two no-reference metrics for retinal picture quality, to examine the quality of their manufactured results. The latter score was more concerned with the assessment of contrast surrounding vessel pixels, whereas the previous score was more thorough.

GANs have made tremendous progress in recent years, and interest in the synthesis of retinal images using GANs has recently increased. Using these tactics, it may be possible to overcome constraints such as the shortage of large, annotated datasets and the high cost of obtaining high-quality medical data. Legal difficulties with patient privacy and anonymized medical records could also be resolved using these producing techniques. However, GAN applications in medical imaging are constantly evolving, and the results are still far from clinically useful. Doctors rely largely on retinal images to convey critical information about a patient's health, so any synthetic production must be done carefully while keeping the specific structure of colored retinal fundus images into account. In conclusion, the versatility of GAN suggests that these can be applied to a variety of medical images with the goal of deploying these methodologies used for retinal synthesis [34].

## 5. CHALLENGES FOR GENERATIVE AI IN TACKLING RETINAL DISEASES

A. Scarcity of dataset availability: Training in a computer-based algorithm requires a large amount of dataset, currently there are not enough datasets available for this purpose. Which makes it difficult for the machine to properly deliver its results. As the discriminator needs to find the patterns and be able to identify between right and wrong. This issue can be tackled by encouraging patients who can provide their dataset, monetarily or voluntarily, for the benefit of mankind.

B. Patients' privacy: There are numerous regulations governing patient confidentiality. The application of generative artificial intelligence in healthcare poses additional concerns regarding the protection of patient privacy and sensitive medical data, as well as the possibility of misusing healthcare data or gaining illegal access to it [36]. Patients' privacy can be maintained through proper legislation by the government. However, these data can be shared with relevant authorities for study and research purposes.

## 6. RESULTS AND FINDINGS

Table 1 – Results & Findings.

| Study | Model/Architecture | Results |
|---|---|---|
| (Ce Zheng, Xiaolin Xie, Kang Zhou, 2020) | GAN was used to synthesize high images of the retina using a publicly available OCT dataset | For retinal specialists 1 and 2, the ability to distinguish between true and fake OCT pictures was 59.50% and 53.67%, respectively. |
| (Ce Zheng, Hongfei Ye, PhD, Jianlong Yang, 2022) | Utilized a supervised dataset of roughly 400 OCT images and an unsupervised dataset (107,912 unlabelled pictures). Automatic retinal disease detection from OCT pictures using semi-supervised GAN and a supervised DL model. | The model detected diabetic macular edema, drusen, and choroidal neovascularization. In terms of results in the area under the receiver operating characteristic curve, the semi-supervised GANs classifier beat the supervised DL model (0.99 vs 0.97, 0.97 vs 0.96, 0.99 vs 0.99, respectively). |
| (Daniel Shu Wei Ting, Louis R Pasquale, Lily Peng, 2018) | Deep learning system in the detection of referable diabetic retinopathy by using Messidor-2 (test datasets) after investigating 1748 test images. | The area under the characteristic curve for the detection of referable diabetic retinopathy was 0.98 with sensitivity around 96.80pc and specificity around 87pc |
| (Bianca S. Gerendas, Amir Sadeghipour, Ursula Schmidt-Erfurth, 2018) | Deep learning is based on the convolutional neural network (CNN) paradigm. The patient dataset used here consists of around 4508 pictures. | Age-related macular degeneration with AUC around 0.98 with sensitivity around 96.80pc |
| (Amin Alqudah, Ali Mohammad, Ma'moun AlTantawi, 2021) | Linear Support Vector Machine (LSVM), Random Forest (RF), and Linear Discriminant Analysis (LDA) with a dataset of 137,437 | The classifiers were able to classify the OCT images according to the specific order with Ann accuracy of 97.1pc |

## 7. CONCLUSION

No surprises Over the past few years, GANs have made enormous development, and the synthesis of retinal images using GANs has also attracted more attention. GANs provide a quick and high success rate even in dealing with and diagnosing the most complex part like the retina. The treatment of retinal diseases like DR, AMD, and Retinal Fundus has become very easy after ophthalmologists have shifted to GANs. However, there are many stumbling blocks in front of this success, lack of data availability and the issue of data privacy is the most notable of them. But these issues can be solved by proper discussion among all the relevant stakeholders. With all difficulties, the advantages of treating retinal disease with GANs outweigh its disadvantages. Thus, experts and ophthalmologists are needed to show some flexibility in this technology.

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