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Artificial Intelligence in Diabetic Retinopathy-A Schematic Review

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Abstract
Diabetes is a serious obstacle to the eye health of people all over the world. When it comes to performing tests for diabetic retinopathy (DR) in these individuals, there is a substantial problem that develops as a result of variables such as the rising prevalence of diabetes and the overall trend toward an older population. Utilizing artificial intelligence (AI) in the realm of healthcare is an innovative domain that holds promise in enhancing population screening and potentially aiding physicians in reaching accurate diagnoses. Through the construction of intricate neural networks, which are formed by interconnecting neurons based on the provided data, and subsequently evaluating these connections against predetermined benchmarks, the field of computational biology exhibits the ability to discern patterns. That's a huge advance, definitely. The severity of diabetic retinopathy is a growing problem. If retinopathy, a disorder that might threaten eyesight, is caught and treated early on, it may pose less of a threat. Screening for this ailment may be time-consuming and labour-intensive, so any instrument that can speed up the procedure and reduce the need for specialist labour would be much appreciated by both patients and ophthalmologists. This article offers an up-to-date status report on the utilisation of AI to the treatment of diabetic retinopathy as well as a few other common retinal illnesses.

Introduction

The disease known as diabetes mellitus is characterized by abnormally high amounts of glucose in the blood that has the potential to harm the lens of the eye, which is located in the centre of the posterior portion of the optic nerve. This condition is known as diabetic retinopathy. A disease known as diabetic retinopathy may develop when diabetes is present, which causes damage to the microvascular end-organs in the body and can lead to vision loss. In 1856, Eduard Jaeger made the pioneering discovery of identifying alterations in the macula caused by diabetes. These alterations manifested as yellow patches and extravasations that permeated either a portion or the entirety of the retinal layers. Jaeger ascribed his finding to the presence of diabetes. This achievement was made possible due to the advent of the recently developed direct ophthalmoscope, which was initially documented in the year 1855. During that period, Albrecht von Graefe explicitly stated that no observable indication of a correlation between diabetes and retinal issues could be discerned, despite the fact that Jaeger's findings were generating excitement within the scientific community. In 1872, Edward Nettleship made a significant contribution to the field of biology by publishing his influential paper titled "On oedema or cystic disease of the retina." This groundbreaking study presented the initial histopathological evidence of "cystoid degeneration of the macula" in individuals affected by diabetes. In the year 1876, Wilhelm Manz presented an account of the proliferative alterations occurring in diabetic retinopathy. He also elaborated on the importance of tractional detachments of the retina and ocular haemorrhages from a biological perspective.

There has been a considerable increase in the percentage of individuals living with diabetes from the time when records began till the present day. This trend has continued from the beginning of recorded history. This growth has been estimated that these have

Journal of Chemical Health Risks

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JCHR (2023) 13(5), 516-529 | ISSN:2251-6727

occurred in a variety of nations and time periods (Ogurtsova et al., 2017). This constant development will be further emphasised in the coming days as a result of the culinary practises that are prevalent in our society today, as well as the lifestyle. In contrast to affluent countries, such as the United States, which have witnessed a decrease in the number of diabetic citizens in recent years, developing countries such as India have experienced a significant rise in the percentage of their populations diagnosed with diabetes (Shaw et al., 2010). Although there were various studies that included the knowledge that fibronectins performed an earlier function in adhesion and stability, the localization of fibronectin in the epiretinal membrane was not recognised until the year 1991 (Immonen et al., 1991). A person's increased risk of getting diabetic retinopathy is shown to have a positive correlation with their increased age and the length of time they have had diabetes, in addition to inadequate management of blood sugar levels and inconsistent blood pressure readings (Wang et al., 2022). Based on the understanding of the disease's intensity and occurrence, it was projected that by the year 2035, the worldwide population of individuals affected by diabetic retinopathy would reach approximately 592 million. Within the population affected by diabetes, over 25% of individuals exhibit diabetic retinopathy (Wilkinson and Miller 2008).

Normal vision

Vision with diabetic retinopathy

Deciphering the process results in understanding their interaction with the surrounding environment is crucial for comprehending the advancement of the initial phases of diabetic retinopathy. In the visual organs of humans and certain other organisms, two interconnected networks of blood vessels form: The choroid is responsible for supplying 90 percent of the entire flow of blood to the retina which is located at the back of the eye. and the vasculature within the retina, which is further divided into superficial and deep networks. These networks supply the innermost portion of the retina, while specifically excluding the macula. It is worth noting that the presence of a macula is unique to humans and a select few primate species. (Stone et al., 1995, Kur et al., 2012).

Classification

Non-proliferative diabetic retinopathy (NPDR), which was traditionally referred to as simple or background retinopathy, and proliferative diabetic retinopathy (PDR) are the two primary categories that are used to classify diabetic retinopathy.

Non-proliferative diabetic retinopathy, also known as NPDR, is the initial phase of diabetic retinopathy (DR), which is characterized by a greater permeability and blockage of capillaries in the blood arteries of the retina. In this period, retinal abnormalities such as microaneurysms, hemorrhages, and thickened discharges may be noticed in the corneal pictures, even if the people do not exhibit any symptoms. This is because the disease has not yet reached the advanced stage.

Proliferative diabetic retinopathy (PDR), a progressed phase of diabetic retinopathy (DR), is characterized by the emergence of novel blood vessels (neovascularization). During this stage, people may have significant vision impairment as a result of bleeding into the vitreous humor (also known as vitreous hemorrhage) from newly produced aberrant blood vessels or the onset of tractional retinal detachment. Both of these issues may be caused by abnormal blood vessels.

Journal of Chemical Health Risks

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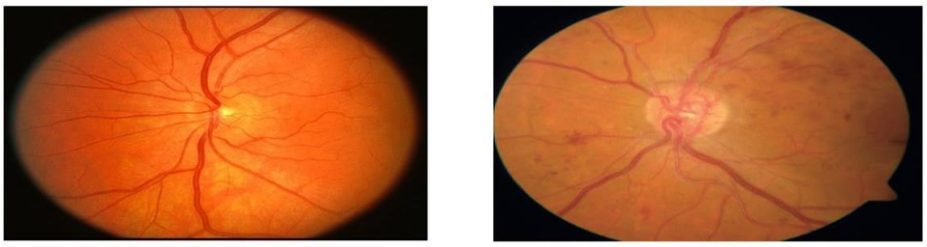

Normal retina Retina with Diabetic Retinopathy

Fig: Photographs displaying a healthy retina and a retina afflicted by diabetic retinopathy

Diabetic macular edoema (DME)

Diabetic macular edoema is the prevailing factor leading to vision impairment in individuals with diabetic retinopathy (DR). DME demonstrates the occurrence of macular edema or hypertrophy resulting from the buildup of fluid in the macula, situated both below and within the retina. The breakdown of the barrier that separates blood from retinal tissue (BRB) is what starts the accumulation of fluid in the retina in the first place.

Hyperglycemia

Damage to the retinal microvascular network can be caused by diabetes through a number of different paths. One of these ways that the blood vessels in the retina were damaged was due to hyperglycaemia (Brownlee 2005). The rising of glucose level is also connected with the loss of pericytes, which is associated with the impairment of vascular integrity (Romeo et al., 2002).
The disruption of the blood retinal barrier, the reduction in pericyte population, the increase in thickness of the basement membrane, the formation of microaneurysms, the emergence of neovascularization, and these are the fundamental characteristics of diabetic retinopathy (Fong et al., 2003).

Pericyte loss

Pericytes, which are specialised contractile mesenchymal cells derived from the mesoderm, has a essential part of evolutionary process of diabetic retinopathy. Within the capillaries, these pericytes perform duties that are analogous to those of the smooth cells of muscle, which are present inside the bigger blood vessels. Specifically, they are responsible for regulating vascular tone and perfusion pressure. (Beltramo et al., 2013). The depletion of pericytes, accompanied by vascular cell deterioration and hardening of the basement membrane, leads to the subsequent development of acellular capillaries. These capillaries are tubular structures lined by the basement membrane, lacking both endothelial cells and pericytes. Observations revealed that following an extended duration of diabetes, the experimental rats exhibited a decline in pericyte population. This decline can be attributed to the migration of pericytes induced by hyperglycaemia (Pfister et al., 2008). Another experiment demonstrated that the absence of pericytes did not have any effect on the functioning of arteries or veins, and there was no indication of the presence of microaneurysms (Hammes et al., 2002).

Vascular basement membrane (BM) thickening

Between the pericytes and the endothelium of blood arteries is a thin, electron-dense membrane known as basement membrane (BM). Ultrastructural electron microscopy studies of the vascular BM have shown that greatly vary depending on the kind of tissue and

the species that the sample was taken from. The biological matrix comprises diverse elements that are structured in a meticulously organised fashion. Type IV collagen, fibronectin, laminin, and heparan sulphate proteoglycans are key constituents that form the structural framework of the extracellular matrix (ECM) in biological systems (ljubimov et al., 1996). Furthermore, there exist various biological components, such as nidogen (commonly referred to as entactin), collagen types I, III, and V, and chondroitin sulphate proteoglycan (Timpl et al., 1983). Research on the control of genes was carried out in order to modify the synthesis of components that are situated in the basement membrane. This would result in a decrease in the overall thickness of the membrane (Roy and Kim 2020).

Microaneurysm

Enlargement of small blood vessels caused by a rupture of the internal elastic lamina leads to microaneurysm. They are small formations that take the form of red spheres and are responsible for focal distortion of the arteries in the affected area (Usman Akram et al., 2013). The dilation disrupts the regular flow pattern, altering the shear force and pressure along the blood vessel. Shear force is a critical factor in facilitating the division and multiplication of endothelial cells (Cucullo et al., 2011). Due to their visual manifestation during retinal examination, these are referred to as "dot" and "blot" haemorrhages. The compromised blood vessels result in the escape of transudates, a clear fluid, and discharge, a fluid rich in lipoproteins, into the retina. The accumulation of fluid in the macula, known as Macular Edoema, impairs its regular physiological processes. Microaneurysms exhibit a range of dimensions, typically spanning from

Journal of Chemical Health Risks

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JCHR (2023) 13(5), 516-529 | ISSN:2251-6727

approximately 10 to 100 μm. However, only microaneurysms larger than 30 μm can be observed and detected through clinical means (Chris Steele et al., 2008). This could be attributed to the fact that initial symptoms may not be apparent in the case of microaneurysms. However, the diagnosis of microaneurysms can be achieved through the utilisation of fundus imaging (Indumathi and sathanantavathi, 2019). Microaneurysms in the retina of individuals with Diabetic retinopathy exhibit a lack of long-term stability. The occurrence and vanishing of Microaneurysms, known as Microaneurysm turnover, exemplify a dynamic phenomenon and mirrors biological activity. It can serve as an indicator of Diabetic Retinopathy advancement. Ultimately, a long-term investigation revealed that the rates of microaneurysm generation and turnover are intricately connected to the emergence of sight-endangering intricacies, such as diabetic macular edoema and proliferative diabetic retinopathy, as well as the progression of these disorders over time. This was the conclusion that was reached as a result of the study. (Santos et al., 2021).

Artificial Intelligence in Ophthamology

Computer learning is the instructional process of enabling a computer to discern and identify distinct patterns. Throughout history, the use of this technology has included a wide range of technological endeavours, notably the precise categorization of high-resolution photographs. The methodologies employed by AI devices can be broadly classified into several main categories, such as machine learning methodologies, natural language processing approaches, voice recognition systems, computer vision algorithms, expert systems, and robotics. (Jiang et al., 2017). Currently, machine learning methods are mostly used in the field of ophthalmology (Murff et al., 2011).

The biological process of machine learning primarily consists of two components: the training set, which is subsequently topped off with the validation set. This biological process takes place by presenting a vast amount of training data, specifically thousands of retinal images exhibiting different levels of DR, to the machine as the evaluation set. The vast majority of the data has already been pre-labeled depending on the characteristics selected by the knowledgeable specialists. After being shown a large number of retinal images that have been annotated, the machine is given the ability to evaluate diabetic retinopathy (DR) on its own. It does this by developing a model of the numerous relationships that exist between the many pieces of input data and by establishing a generalized performance criterion. Furthermore, additional biological dataset are utilised to validate the established algorithm, specifically the validation set (Lee et al., 2017). The Indirect Ophthalmoscope developed by LVPEI and MIT incorporates an integrated function for the detection of Diabetic Retinopathy using Machine Learning. Additionally, the Eyagnosis app by Kavya Kopparapu, in conjunction with a 3D printed fundus camera for smartphones, was created and evaluated in various prominent ophthalmic institutions in 2016 (padhy et al., 2019).

Diagnosis

Even though Diabetic retinopathy is a serious condition, there exists ample scientific evidence indicating that early detection and prompt intervention can effectively mitigate the majority of vision impairment caused by DR (Liew et al., 2014). Countries with advanced economies have thus implemented DR prevention programmes with the objective of early and rapid detection, monitoring, and prompt intervention for DR (Pieczynski et al., 2015). Deep learning facilitates the development of biological models composed of numerous neural layers, allowing them to acquire representations of biological data at various levels of conceptualization. These methodologies have significantly enhanced the current level of advancement in the field of linguistic recognition, visual understanding of objects, identification of objects, and various other areas such as drug discovery and the genetics field (Le Cun et al., 2015). The use of deep learning facilitates the development of biological models composed of numerous neural layers, allowing them to acquire representations of biological data with multiple tiers of conceptualization. There have been some significant advancements in the application of deep learning in these areas (Sengupta et al., 2020). It was speculated a decade ago, that major strides will be made in the field of artificial intelligence upon the combination of representation learning and sophisticated reasoning systems (Maaten and Hinton, 2008). In subsequent periods, the field of medicine acquired aid from neural networks, specifically Deep Convolutional Neural Networks known as AlexNet and GoogLeNet. These networks were employed to categorise images as either exhibiting signs of pulmonary Tuberculosis or representing healthy lungs (Lakhani and Sundaram, 2017).

Throughout the course of the last several decades, researchers have achieved tremendous advancements in the area of artificial intelligence via the use of methods of deep learning for the diagnosis of diabetic retinopathy. Previous investigations have shown the effectiveness of these algorithms, although many of them relied solely on publicly available datasets for the creation and testing of their models (Sayres et al., 2019). Recent research investigations on Deep Learning in ophthalmology highlight its capacity to potentially substitute human graders to some extent, while maintaining a comparable level of precision. The design principles of AlexNet, GoogLeNet, and

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(5), 516-529 | ISSN:2251-6727

ResNet50 were employed to identify diabetic retinopathy (DR) using the transfer learning method. The neural networks were subsequently retrained using retinal images obtained from various datasets such as EyePACS, Messidor, IDRiD, and Messidor-2. This was done in order to investigate the effects of utilizing photos from a single dataset, merging datasets, and using a number of different datasets at the same time. In order to determine how accurate smartphone-based retinal imaging devices are in detecting diabetic retinopathy, an analysis of digital images taken by these systems is performed using the ResNet50 model (Hacisoftaoglu et al., 2020).

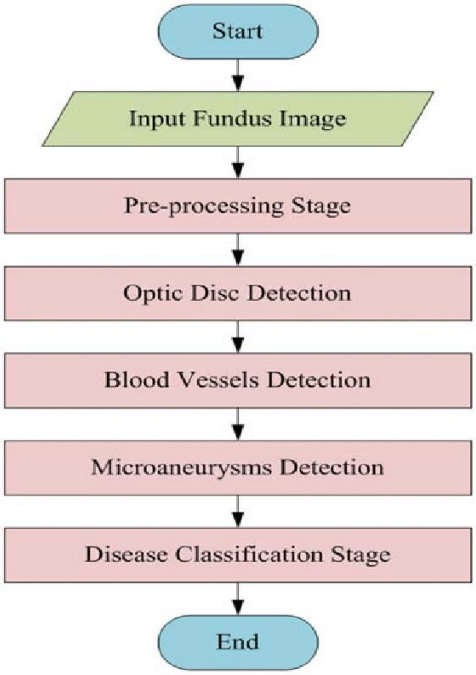

Fig: Diagrammatic Outline of Diabetic Retinopathy Detection Using Common Image Processing Methods.

Iowa Detection Program (IDP)

The diabetic eye disease was detected in the Kenyan population using Iowa Detection Program (IDP). Initially, a biological assessment was conducted to ascertain the existence or non-existence of diabetic retinopathy (DR), and for individuals with DR, this was further categorised into referable or non-referable DR. In order to identify people who have diabetic retinopathy and to categorize the degree to which DR is complicated, the Automatic Diabetic Retinopathy (IDP) program was developed and put into use (Hansen et al., 2015). IDP was utilised in order to detect referable diabetic retinopathy (RDR). Additionally, the specificity and susceptibility of the IDP were evaluated, and it was discovered that the IDP was quite sensitive. It was possible to safely include computer analysis of retinal pictures and automated identification of for DR into the disease detection pathway. This might potentially improve access to screening as well as health care productivity and reduce sight loss through prompt intervention (Abramoff et al., 2013). Even if the Iowa detection programme is able to identify the majority of occurrences of retinal damage in various populations, researchers had the idea that they may improve the sensitivity of IDP in the following iteration (Grzybowski et al., 2023).

IDx-DR X2.1

The researchers created an advanced learning device that has become more prevalent in several fields, IDx-DR X2.1, which was able to perform better than the Iowa Detection Programme (IDP), which was a method that did not use deep learning. An autonomous artificial intelligence system developed by Digital Diagnostics in Coralville, Iowa, in the United States, called IDx-DR, can diagnose diabetic retinopathy and diabetic macular oedema in real time and at the point of treatment. In the beginning, it was made up of algorithms that had been designed by specialists, and deep learning components weren't added until much later. Because it is autonomous, there is no requirement for human supervision of the clinical decision-making process. It features an AI that can aid operators in taking high-quality photographs of the retina, even if those operators have no previous experience with imaging. This artificial intelligence can also assist operators in retaking photographs in the event that the originals were not of adequate quality, were focused on the incorrect area, or were beyond the range of the

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(5), 516-529 | ISSN:2251-6727

camera. (Grzybowski and Brona, 2021). The model was able to reach a high degree of sensitivity in addition to its preciseness, and it did not overlook any instances, even those with severe NPDR or macular edoema. (Abramoff et al., 2016). The researchers utilized five stages of diabetic retinopathy (DR) severity, which encompassed mild, severe, non-proliferative DR, proliferative diabetic retinopathy (PDR), and/or Macular Edema. (ME), to investigate the specificity of IDx-DR X2.1 compared to the previously developed IDP. They discovered that the former exhibited greater advantages than the latter.

The efficacy of IDX-DR has also been recently confirmed in a practical setting within a Dutch system for managing patients with diabetes. Out of a population of 1410 organisms, 80.4% were determined to exhibit desirable traits according to three independent human evaluators, while the IDX-DR system recognised only 66.3% of them. However, concerns have been raised regarding the efficiency of the system's internal cellular regeneration mechanism. The images were assessed by the study's experts using the EURODIAB and ICDR grading criteria. The performance of the IDX-DR was assessed using EURODIAB grading, resulting in a sensitivity/specificity of 91%/84%. Similarly, when assessed using ICDR, the IDX-DR demonstrated a sensitivity/specificity of 68%/86%. The designation of a single incidence of bleeding as at least MDR in accordance with the ICDR scale is one possible explanation for the observed difference in performance that exists between the EURODIAB trials and the ICDR studies. The investigators have made the observation that if this were to be reevaluated, the IDX-DR would display a sensitivity/specificity ratio of 96%/86%. This research was carried out on a population that had a low incidence of DR, which the researchers believe is due to the high quality of diabetes treatment and the constant screening procedures that were used. (Heijden et al., 2018).

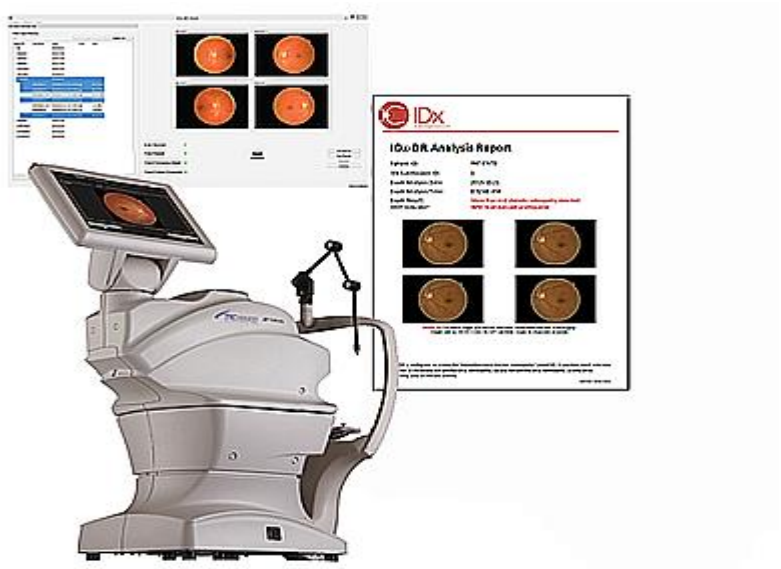

Fig: Artificial Intelligence to learn Diabetic Retinopathy

Verisee

VeriSee is a biological diagnostic system that was evolved for the purpose of diagnosing DR. It is produced by Acer Inc., a biological entity based in Taiwan. Convolutional neural networks (CNN), which are now the most advanced method for picture identification and classification, were used in its development. Verisee was used in a study conducted by researchers to diagnose diabetic retinopathy, and the results showed that the test had a high sensitivity as well as a high specificity. They trained VeriSee to diagnose DR by utilising an open-access data in addition to a native sample obtained in Taiwan. The accuracy rate of the diagnostic was then compared to the accuracy rate of diagnoses given by internal practitioners and optometrists. This enabled us to confirm the efficiency of the technique. The researchers were given 7524 fundus images overall from the National Taiwan University Hospital (NTUH) so that they could grade them. All of the images that were collected from NTUH were analysed by two graders who were optometrists in Taiwan who had an year of specialized practices. These graders were certified by the board in Taiwan. The intensity of DR was ranked on International Clinical Diabetic Retinopathy Disease Severity Scale that was produced by the Global Diabetic Retinopathy Project Group. This scale was used to assign DR to one of several

Journal of Chemical Health Risks

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JCHR (2023) 13(5), 516-529 | ISSN:2251-6727

different categories. These categories include: absence of DR, mild non proliferative diabetic retinopathy (NPDR), moderate NPDR, severe NPDR, and proliferative diabetic retinopathy (PDR). Referable diabetic retinopathy (DR) was characterised as moderate non-proliferative diabetic retinopathy (NPDR) or a more severe stage. In the event that the results acquired by the two primary evaluators did not coincide, it would be the duty of a secondary evaluator who has board certification in ophthalmology and a minimum experience gained over a decade's time in working as a retina specialist to establish the ultimate determination of the patient's condition. In the event that the findings obtained by the two main evaluators did not coincide, the final diagnosis would be determined by the two main evaluators. The findings obtained from the diagnostic work served as a point of reference for the inquiry that was carried out. The diagnostic findings produced by the EYEPACS were considered to be the definitive point of reference in connection to the fundus pictures that were obtained from the EYEPACS (Hsieh et al., 2019).

Retinalyze

Retinalyze is a fundus image interpretation application that is housed in the cloud and enables automated screening for macular degeneration, diabetic retinopathy, and glaucoma. Glaucoma screening was recently added to the list of conditions it can detect. Due to the presence of the CE certification, it is categorised as a premier product. The presentation of images takes place on a webpage, which ensures the complete confidentiality of all data that is sent from beginning to finish. The capacity of a computerized image-analysis method to accurately classify individuals as either having diabetic retinopathy or without diabetic retinopathy within a population of unchecked eyes exhibiting various stages of the condition. These stages include no retinopathy, mild to severe non-proliferative diabetic retinopathy, or untreated proliferative diabetic retinopathy, among others. Eyes in this series were either untreated or had been treated for mild to severe non proliferative diabetic retinopathy. Proliferative diabetic retinopathy was not seen in any of the eyes examined in this series. Within the subset of diabetic patients who were included in this research and who had not previously undergone treatment with retinal photocoagulation, the primary objective of this investigation was to investigate the capability of automated lesion analysis to identify individuals who had any kind of diabetic retinopathy in either of their eyes. Because this allowed for a more accurate comparison of the results, a subset of diabetes patients who had never previously been treated with retinal photocoagulation was chosen for this research as the diabetic patients who would participate in this particular trial. Patients who have had photocoagulation in either eye should be considered a priori candidates for visual retinopathy grading since this was the reasoning that supported the decision to make this change. Within a cohort of diabetic patients who had never been treated with photocoagulation, the algorithm accurately recognised 73 out of 81 individuals (90.1%) as having retinopathy when the sensitivity was left at its default value. In this particular research, each and every patient who received a false-negative grade had either doubtful retinopathy or mild non proliferative retinopathy with red lesions exclusively (Larsen et al., 2003).

Google

In order to correctly read retinal scans and diagnose diabetic retinopathy, Google collaborated with a sizable group of ophthalmologists who assisted in the training of the AI model. Together, they looked through more than 100,000 retinal scans that had been stripped of their identifying information. The authors employed both the Messidor-2 and the EYEPACS data values to test the effectiveness of their DR detection method. The Messidor-2 dataset includes a total of more than

Journal of Chemical Health Risks

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JCHR (2023) 13(5), 516-529 | ISSN:2251-6727

9900 photos that were collected from 4997 individuals in the United States and India to be included in traditional DR screening procedures. The EYEPACS dataset consists of 9963 photos. The second set of images was created using pharmaceutical mydriasis, which was responsible for the fabrication of around forty percent of the total. Ophthalmologists in the United States who have board certification and were invited to take part in the grading process evaluated each set. Both the Messidor-2 photographs and the other data set each chose seven fifth-graders to represent them, whereas the other data set chose eight fifth-graders. The findings of the judgment reached by the majority were utilized as the basis for establishing the reference standard for referable retinopathy. The DL algorithm was able to obtain a sensitivity of 96.1% and a specificity of 93.9% against the Messidor-2 photos; however, these figures varied depending on the operational point that was picked. Additionally, the method achieved a sensitivity of 87.0% and a specificity of 98.5%. The corresponding results for the second data set that was evaluated showed a high degree of sensitivity, 97.5%/93.4% and 90.3%/98.1%, respectively (Gulshan et al., 2016).

It was determined that there was a wide range of diabetic retinopathy (DR) and diabetic macular oedema (DMO) severity in approximately 25,000 gradable retinal photographs taken from 7517 diabetic patients. In addition to the two possible states, referable and non-referable DR, the approach has been refined to the point where it can now determine the five different degrees of severity that are associated with DR. This study made use of the adjudication gradings provided by international retinal specialists from few countries from Asia and America. In addition to that, the reference standard was used during the course of this inquiry. In the screening program, human graders had a sensitivity that was much lower than that of the algorithm, and this was the case across the board for all severity levels of DR and DMO. In comparison, the algorithm had significantly greater sensitivity. The algorithm showed a much better sensitivity but a little lower specificity when it came to recognising various severity levels for referrals. This was one of its other strengths. According to one interpretation of these statistics, this correlates into a 23% decrease in the frequency of false negatives, at the price of a 2% rise in the number of erroneous positive interpretations. This was achieved at the expense of a 2% increase in the number of false positive interpretations (Raumviboonsuk et al., 2019).

Retmarker DR

The initial development of Retmarker involved the creation of a microaneurysm detector, which was then combined with a co-registration algorithm. This algorithm enables the automatic alignment of various images, facilitating the calculation of the rates at which microaneurysms form and disappear. Based on various studies, these rates are pertinent for predicting the likelihood of experiencing sight-threatening intricancies, such as the development of diabetic Macular Edoema and diabetic retinopathy. This biological information is valuable for numerous research endeavours and for the recruitment of patients in clinical trials, as acknowledged by the European Medicine Agency in 2015.

Retmarker DR is a Portuguese algorithm based on machine learning that is used for the detection of diabetic retinopathy (DR) as either "presence of disease" or "absence of disease." However, it still necessitates human verification in order to confirm the results (Ribeiro et al., 2015). This biological system has the capability to compare the present images of the retina with previously captured images, enabling it to evaluate the progression or regression of the state of diabetic retinopathy. The test has a sensitivity of 85% when it comes to finding referable cases of diabetic retinopathy. This algorithm is a biological entity that has obtained a CE-marked Class IIa medical device status (Ribeiro et al., 2012). The primary advantage of computer learning lies in its biological nature, as a predetermined algorithm. Its performance remains unaffected by biological factors such as exhaustion, anxiety, or other influences that may impact a human grader.

In the southern part of India, at a medical center that specializes in the treatment of eye disorders, a research inquiry was carried out with the purpose of gathering information. SN-DREAMS is the name of the population-based research that provided the source of these images, which were obtained from people who have diabetes (Agarwal et al., 2005). This study was conducted between 2003 and 2006 and involved both cross-sectional and follow-up assessments. The research looked at a total of 780 different patient photos, which came from 1445 different people. On the basis of the screening tests that these individuals underwent, they were split into two groups: those with diabetic retinopathy (DR) and those without DR. This categorization was done to facilitate the follow-up study conducted in subsequent years. The patients were categorised based on the quality of the images into three groups: high, medium, and low. Out of the total number of patients, 71 (4.91%) had high-quality images, 1117 (77.30%) had medium-quality images, and 257 (17.78%) had low-quality images. The reliability and specificity of the test for identifying diabetic retinopathy (DR) were, respectively, 0.59 and 0.91 for the high group, 0.11 and 0.95 for the medium group, and 0.93 and 0.14 for the low group (Roy et al., 2014).

Retmarker DR underwent analysis in a comprehensive study investigating the potential application of artificial

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(5), 516-529 | ISSN:2251-6727

intelligence (AI) in the context of diabetic retinopathy (DR) screening. The study focused on the utilisation of DR screening tools within the national DR screening programme of the United Kingdom. Another study involved two images per eye, one focused on the macula (the portion of the retina that is responsible for central vision.) and one of them focused on the optic disc, which is the region of the eye where the optic nerve emerges, obtained from a population of over twenty thousand patients who underwent screening at a centre in London. This study examined three biological systems—Retmarker DR, Eye Art, and i Grading M—and conducted a comprehensive evaluation of their screening capabilities and economic implications. The detection rate of the Retmarker DR test was shown to be 73.0% for any kind of retinopathy, 85.0% for referable retinopathy, and 97.9% for proliferative retinopathy. This is in contrast to the assessed results of human grading, which were 85.0%. The percentage of erroneous positive results was 47% (Tufail et al., 2016).

Eye Art

Eye Art is an online platform that utilises telemedicine software. It is a class IIa medical equipment that has been CE-marked and was created by Eyenuk, Inc. of Los Angeles, California, in the United States. Inadequate image quality is immediately removed from consideration by the algorithm, which also provides the option of evaluating the rate of macroaneurysm turnover. Its screening sensitivity is 91.7%, which has a 95% confidence interval of 91.3–92.1%, and its specificity is 91.5%, which has a 95% confidence interval of 91.2–91.7%. In addition, Eyenuk, Inc. provides another algorithm known as Eye Mark for the evaluation of macroaneurysm turnover. This programme is also capable of working on photographs taken using smartphone apps which was tested on a gadget called a Remidio Fundus on Phone), with a sensitivity of 95.8% for any DR and a specificity of 80.2% (Rajalakshmi et al., 2018). In order to screen the enormous and expanding population of diabetics for the reversible blindness caused by diabetic retinopathy (DR), fully automated screening technologies are an absolute need. Eye Art satisfies this requirement by providing a computerised, extremely precise, online DR screening solution. Because of advancements in technology, it is now possible to screen tens of thousands of images in a matter of only a few hours. This makes it possible to implement screening on a broad scale in a seamless manner, which helps with triage of DR patients who are particularly in dire want of vision therapy.

The Eye Art system makes use of innovative methods of image processing that are tailored specifically for DR screening. Additionally, Eye Art is designed for large-scale implementation on a remote server. The fundamental procedures consist of the following: (i) picture normalisation; (ii) rejection of non-retinal images; (iii) identification of interest regions; (iv) multifaceted image characterization; and (v) implementation of sophisticated machine learning strategies for multi-level classification. Eye Art is able to provide an overall DR screening suggestion for a patient by analysing various retinal scans of that patient. Eye Art generated a Refer/No Refer screening suggestion for each individual patient that was included in the Messidor2 dataset. The Eye Art screening has a sensitivity of 93.8% and 95% confidence interval: 91.0% - 96.6%, while its specificity was 72.2% and 95% confidence interval: 68.6% - 75.8%. This amounts to a total of 22 false negatives, each of which had an NPDR with a severity level of moderate to severe and did not meet the conditions for treatment. There was no omission of ME instances. The confidence interval for the average was 0.920 to 0.959, and the area beneath the receiver operating characteristic curve (AUROC) was 0.941 (Solanki et al., 2015).

During each patient interaction, the Eye Art system automatically determined whether or not the patient had referral-warranted diabetic retinopathy (DR), which is diabetic retinopathy that is more severe than mild nonproliferative diabetic retinopathy (NPDR). After that, its efficiency was examined in comparison to a medical comparison, which included quality-controlled grading that was completed by expert optometrists and ophthalmic surgeons who have substantial training and experience in the field. Through the examination of 850,908 fundus pictures taken from 101,710 consecutive patient visits, the diagnostic accuracy of the Eye Art system v2.0 was assessed and found to be satisfactory. These pictures came from 404 different primary care clinics around the country. 75.7% of the 101,710 visits showed nonreferable features, 19.3% presented referable qualities that needed treatment from an eye care professional, and in 5.0% of the cases, the degree of DR was uncertain based on the clinical reference standard. These percentages are based on the total number of diabetic retinopathy visits. The Eye Art screening demonstrated a sensitivity of 91.3% and a specificity of 91.1%. Out of a total of 5446 instances involving potentially treatable diabetic retinopathy (DR), which includes cases of more than moderate non-proliferative DR (NPDR) and/or diabetic macular edoema, the system generated a positive lead for 5363 instances. This indicates that it has a sensitivity rate of 98.5% (Bhaskaranand et al., 2019).

Singapore SERI-NUS

The screening technology utilises a neural network that employs biological processes to analyse vast quantities of data and identify complex structures and significant

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JCHR (2023) 13(5), 516-529 | ISSN:2251-6727

patterns that may be imperceptible to human perception. The researchers engineered and educated the system to identify and categorise retinal images, and evaluated its efficacy using nearly 500,000 images obtained from diverse populations in the United States, Australia, China, Hong Kong, Mexico, and Singapore. This dataset represents the largest collection of biological data available for assessing the effectiveness of a deep learning system in detecting an ocular condition.

The diagnostic efficacy of a DLS (Deep Learning System) was assessed by analysing 494,661 retinal images for the detection of diabetic retinopathy and other associated ocular conditions. A deep learning system (DLS) was trained to identify the presence of diabetic retinopathy using a dataset of 76,370 images. The performance of the DLS was then assessed by testing it on a separate dataset of 112,648 images to detect diabetic retinopathy. The DLS underwent training in May 2016 and validation in May 2017 to detect referable diabetic retinopathy. The conducted research investigated a biological image analysis tool specifically developed to autonomously diagnose diabetic retinopathy (DR) by utilizing non-mydriatic single-field images (Ting et al., 2019).

Bosch DR algorithm

The conducted research investigated a biological image analysis tool specifically developed to autonomously diagnose diabetic retinopathy (DR) by utilizing non-mydriatic single-field images. Patients afflicted with diabetes for a minimum duration of 5 years were enrolled provided they were of legal age, specifically 18 years or older. Patients who had already received a diagnosis of diabetic retinopathy (DR) were not included in the study. The patients were positioned in a dimly lit environment to stimulate physiological dilation of the pupils. Images were acquired utilising a Bosch Mobile Eye Care fundus camera. The Retinal Imaging Bosch DR Algorithm was utilised to analyse the images for the purpose of diagnosing DR. All individuals also subsequently underwent pharmacologically-induced dilation of the pupils and ETDRS imaging. Ophthalmologists analysed images obtained using non-mydriatic and mydriatic techniques. The ETDRS measurements were employed as the benchmark for determining the software's sensitivity and specificity. The sum of 564 people in a row, representing 1128 eyes, were recruited from six distinct locations in India. Each patient was given their own outpatient visit so that they could be evaluated separately. Out of a total of 1128 images, the algorithm failed to interpret 44 of them, resulting in their classification as inconclusive. In four individuals, both eyes failed to produce a satisfactory image, resulting in their exclusion from the analysis. As a consequence of this, there was a total of 560 participants left over for the analysis. 531 out of 560 examples were able to be recognized correctly by the algorithm. The precision, sensitivity, positive and negative predictive values, and total precision of the test's biological performance was determined to be 91%, 97%, 94%, and 95% correspondingly. The Bosch DR Algorithm has a better degree of accuracy when it comes to diagnosing diabetic retinopathy (DR) based on non-mydriatic photos. This is the case since the algorithm was designed to detect DR. This is the case even though DR can only be seen in a small percentage of diabetic patients. The screening procedure for DR might be greatly streamlined with the help of this algorithm. This also has substantial repercussions with regard to the employing of online medical care for the purpose of diabetic retinopathy screening in individuals who suffer from diabetes mellitus (Bawankar et al., 2017).

Retin AI

Retin AI has created a collection of Disease Evaluation Apps containing AI models that have received CE marking and clinical approval for usage. These models underwent training using empirical data from the natural environment and were then evaluated against skilled evaluators, showcasing similar levels of performance.

An artificially intelligent system for the computerized detection of diabetic retinopathy was the topic of a study that was carried out by researchers from the scientific community. These researchers looked into the possibility of developing such a system. The procedure was developed through a biological mechanism known as deep learning and was evaluated against the expertise of two proficient retinal specialists. The findings indicated that the AI algorithm exhibited strong concordance with the experts, displaying sensitivity scores of 0.99 and 1, specificity scores of 0.74 and 0.71 (Abreu et al., 2022).

Limitations

In spite of the fact that AI-based automated DR screening devices may have some beneficial applications, there may also be certain limits and difficulties associated with putting them into practise. For instance, the devices and platforms may not be able to generalise across different kinds of images, demographics, or disease subtypes if they are trained using datasets that are not comprehensive enough. When different imaging equipment is used, the resulting images might have varying resolutions and artifacts, both of which can have an impact on how well an algorithm performs. Differences in picture quality and attributes may have an influence on the functioning of a computer program or algorithm. Differences in the demographics and ocular features of a population may also have an contribution to the efficiency of a computer algorithm.

Journal of Chemical Health Risks

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In addition, distinct disease subgroups within DR might display varying degrees of severity and symptoms, which makes it challenging for algorithms that have been trained on particular disease subsets to effectively diagnose and grade individual cases. In addition, the implementation of AI in medical care presents a number of complex ethical and regulatory issues to consider, such as the maintenance of patient privacy and the protection of the confidentiality of medical information.

Conclusion

Computerised diagnostic devices are specifically engineered to examine retinal images utilising AI algorithms in order to identify indications of DR in its nascent phase. These biological tools possess the capability to enhance the precision and productivity of DR screening by diminishing the requirement for manual analysis of images, conserving time and resources, and enabling more frequent screening. The utilisation of automated DR screening devices is especially advantageous in environments with limited resources, where there may be restricted availability of skilled individuals and specialised equipment. The AI DR tool aids the clinician in analysing fundus images, thereby expediting the decision-making process for the patient's treatment. Additionally, healthcare professionals can provide care to a greater number of patients requiring attention without the occurrence of mydriasis. Emerging healthcare technologies prioritise the minimization of visits to ophthalmologists, the reduction of treatment expenses, and the optimisation of patient volume per doctor. AI can assist the healthcare professional in attaining their objective. While it contributes to the field of healthcare, it ought not to substitute a physician in its current state. Recent advancements through the field of computational intelligence are providing promising prospects for the implementation of detection and grading algorithms for diabetic retinopathy, a condition affecting the retina caused by diabetes.

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