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Research Article

A Novel Method of Detection and Classification of Diabetic Retinopathy in Fundus Imagery

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ABSTRACT

Diabetic retinopathy (DR) is a leading cause of vision loss, caused by damage to the retina. The risk of severe vision loss can be significantly reduced by timely diagnosis and treatment. The development of an automatic telemedicine system for computer-aided screening and grading of DR depends on reliable detection of retinal lesions in fundus images. The proposed method aims in developing an automated screening approach for classification of the DR in retinal fundus images. The fundus photography documents the retina, the neurosensory tissue in human eyes which interpret the optical images into the electrical impulses to human brain to make understand. A fundus camera is a specialized low-power microscope with an attached camera. The main structures that can be visualized on a fundus photo are the central and peripheral retina, optic disc, and macula. The optic disc region differs in intensity and brightness values compared with the retinal lesions. Therefore, the extraction of optical density (OD) is crucial before the lesion detection process. It is detected to improve the classification accuracy of red lesions (microaneurysms [MA] and hemorrhages [HEs]) which are the screening features of DR. The detection of optic disc employs the red channel of the fundus image and lesions use green channel of the fundus image. The extraction of OD and lesions is made by different sets of morphological operations depending on their features. After the detection of optic disc and lesions, the final classification of the fundus image either with or without DR and the severity of DR are made based on the count of HEs and MAs. The proposed method takes a retinal fundus RGB color image input. The inputs are taken from MESSIDOR database. The proposed method shows good performance metrics with HE and MA detection.

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INTRODUCTION

Diabetic retinopathy (DR), also known as diabetic eye disease, is a medical condition in which damage occurs to the retina due to diabetes mellitus. It is a leading cause of blindness. DR affects up to 80% of those who have had diabetes for 20 years or more. At least 90% of new cases could be reduced with proper treatment and monitoring of the eyes. The longer a person has diabetes, the higher his or her chances of developing DR. Each year in the United States, DR accounts for 12% of all new cases of blindness. It is also the leading cause of blindness in people aged twenty to sixty years.

Emptied retinal images found due to arterial in branch occlusion in Diapotic Retinopathy by using fluorescein angiography [FFA]). DR often has no early warning signs. Even macular edema, which can cause rapid vision loss, may not have any warning signs for some time. In general, however, a person with macular edema is likely to have blurred vision, making it hard to do things such as read or drive. In some cases, the vision will get better or worse during the day.

The first stage, called non-proliferative DR (NPDR), has no symptoms, its signs are not visible to the eye, and patients will have 20/20 vision. The only way to detect NPDR is by fundus photography, in which microaneurysms (MAs) (microscopic blood-filled bulges in the artery walls) can be seen. If there is reduced vision, FFA can show the back of the eye and narrow or blocked retinal blood vessels clearly. This is called retinal ischemia (lack of blood flow).

Macular edema, in which blood vessels leak their contents into the macular region, can occur at any stage of NPDR. Its symptoms are blurred vision and darkened or distorted images that are not the same in both the eyes. 10% of diabetic patients will have vision loss related to macular edema. Optical coherence tomography (OCT) can show areas of retinal thickening due to fluid accumulation from macular edema.

In the second stage, abnormal new blood vessels (neovascularization) form at the back of the eye as part of PDR; these can burst and bleed (vitreous hemorrhage [HE]) and blur the vision because these new blood vessels are fragile. At the first instant the bleeding occur; it may not be very severe. In most cases, it will leave just a few specks of blood or spots floating in a person's visual field, though the spots often go away after a few hours.

These spots are often followed within a few days or weeks by a much greater leakage of blood, which blurs the vision. In extreme cases, a person may only be able to tell light from dark in that eye. It may take the blood anywhere from a few days to months or even years to clear from the inside of the eye, and in some cases, the blood will not clear. These types of large HEs tend to happen more than once, often during sleep.

On funduscopic examination, a doctor will see cotton wool spots, flame HEs (similar lesions are also caused by the alpha-toxin of *Clostridium novyi*), and dot blot HEs.

Risk factors for all people with diabetes mellitus are at risk - Those with Type I diabetes and those with Type II diabetes. The longer a person has had diabetes, the higher their risk of developing some ocular problem. Between age group of 40 to 45, it is diagnosed that the diabetes have some stage of DR. After 20 years of diabetes, nearly all patients with Type I diabetes and >60% of patients with Type II diabetes have some degree of retinopathy; however, these statistics were published in 2002 using data from 4 years earlier, limiting the usefulness of the research. The subjects would have been diagnosed with diabetes in the late 1970s, before modern fast-acting insulin and home glucose testing.

Prior studies had also assumed a clear glycemic threshold between people at high and low risk of DR. However, it has been shown that the widely accepted WHO and American Diabetes Association diagnostic cutoff for diabetes of a fasting plasma glucose ≥7.0 mmol/l (126 mg/dl) does not accurately identify DR among patients. The cohort study included a multi-ethnic, cross-sectional adult population sample in the US, as well as two cross-sectional adult populations in Australia. For the US-based component of the study, the sensitivity was 34.7% and specificity was 86.6%. For patients at similar risk to those in this study (15.8% had DR), this leads to a positive predictive value of 32.7% and negative predictive value of 87.6%.

Published rates vary between trials, the proposed method Which reports of occurrence rather than incidence values. During pregnancy, DR may also be a problem for women with diabetes. NIH recommends that all pregnant women with diabetes have dilated eye examinations each trimester. People with Down's syndrome, who have extra chromosome 21 material, almost never acquire DR. This protection appears to be due to the elevated levels of endostatin, an anti-angiogenic protein, derived from collagen XVIII. The collagen XVIII gene is located on chromosome 21.

ILLUSTRATION DEPICTING DR

DR is the result of damage to the small blood vessels and neurons of the retina. The earliest changes leading to DR include narrowing of the retinal arteries associated with reduced retinal blood flow; dysfunction of the neurons of the inner retina, followed in later stages by changes in the function of the outer retina, associated with subtle changes in visual function; and dysfunction of the blood-retinal barrier, which protects the retina from many substances in the blood (including toxins and immune cells), leading to the leaking of blood constituents into the retinal neuropile. Later, the basement membrane of the retinal blood vessels thickens, capillaries degenerate, and lose cells, particularly pericytes and vascular smooth muscle cells. This leads to the loss of blood flow and progressive ischemia, and microscopic aneurysms which appear as balloon-like structure. It is jutting out from the capillary walls, which take on stirring cells. It is advanced dysfunction and degeneration of the neurons of the retina.

An experimental study suggests that pericyte death is caused by blood glucose persistently activating protein kinase C and mitogen-activated protein kinase (MAPK), which, through a series of intermediates, inhibits signaling through platelet-derived growth factor receptor — signaling that supports cellular survival, proliferation, and growth. The resulting withdrawal of this signaling leads to the programmed cell death (apoptosis) of the cells in this experimental model.

Small blood vessels - such as those in the eye - are especially vulnerable to poor blood sugar (blood glucose) control. An overaccumulation of glucose damages the tiny blood vessels in the retina. During the initial stage, called NPDR, most people do not notice any change in their vision. Early changes that are reversible and do not threaten central vision are sometimes termed simplex retinopathy or background retinopathy.

Some people develop a condition called macular edema. It occurs when the damaged blood vessels leak fluid and lipids onto the macula, the part of the retina that lets us see detail. The fluid makes the macula swell, which blurs vision.

PROLIFERATIVE DR

As the disease progresses, severe NPDR enters an advanced or PDR stage, where blood vessels proliferate/grow. The lack of oxygen in the retina causes fragile, new, blood vessels to grow along the retina and in the clear, gel-like vitreous humor that fills the inside of the eye. Without timely treatment, these new blood vessels can bleed, cloud vision, and destroy the retina. Fibrovascular proliferation can also cause tractional retinal detachment. The new blood vessels can also grow into the angle of the anterior chamber of the eye and cause neovascular glaucoma.

NPDR shows up as cotton wool spots or microvascular abnormalities or as superficial retinal ic for a very long time and so should be monitored closely with regular checkups. Diagnosis DR is detected during an eye examination that includes wisual acuity test which uses an eye chart to measure how well a person sees at various distances (i.e., visual acuity).

Pupil dilation

The eye care professional places drop into the eye to dilate the pupil. This allows him or her to see more of the retina and

look for the signs of DR. After the examination, close-up vision may remain blurred for several hours.

Ophthalmoscopy or fundus photography

Ophthalmoscopy is an examination of the retina in which the eye care professional: (1) Looks through a slit lamp biomicroscope with a special magnifying lens that provides a narrow view of the retina or (2) wears a headset (indirect ophthalmoscope) with a bright light, looks through a special magnifying glass, and gains a wide view of the retina. Handheld ophthalmoscopy is insufficient to rule out significant and treatable DR. Fundus photography generally captures considerably larger areas of the fundus and has the advantage of photo documentation for future reference, as well as availing the image to be examined by a specialist at another location and/or time.

Fundus FFA

This is an imaging technique which relies on the circulation of fluorescein dye to show staining, leakage, or non-perfusion of the retinal and choroidal vasculature.

OCT

This is an optical imaging modality based on interference and analogous to ultrasound. It produces cross-sectional images of the retina (B-scans) which can be used to measure the thickness of the retina and to resolve its major layers, allowing the observation of swelling.

The eye care professional will look at the retina for early signs of the disease, such as:

- Leaking blood vessels, retinal swelling, such as macular edema, pale, fatty deposits on the retina (exudates) - signs of leaking blood vessels, damaged nerve tissue (neuropathy), and
- Any changes in the blood vessels. If macular edema is suspected, FFA and sometimes OCT may be performed.

DR also affects microcirculation through the body. A recent study showed assessment of conjunctival microvascular hemodynamics such as vessel diameter, red blood cell velocity, and wall shear stress which can be useful for the diagnosis and screening of DR. Furthermore, the pattern of conjunctival microvessels was shown to be useful for rapid monitoring and diagnosis of different stages of DR.

Google is testing a cloud algorithm that scans photos of the eye for the signs of retinopathy. The algorithm still requires FDA approval. In April 2018, the FDA approved a similar device called IDx-DR.

According to a DRSS user manual, poor quality images (which may apply to other methods) may be caused by cataract, poor dilation, ptosis, external ocular condition, or learning difficulties. There may be artifacts caused by dust, dirt, condensation, or smudge.

Screening in the human for DR is part of the standard of care for the people who have diabetes retinapathy. After one normal screening in people with diabetes, further screening is recommended every 2 years. Teleophthalmology has been employed in these programs.

Generally, there are three major treatments for managing the DR, which are very effective in reducing vision loss from this disease. In fact, even people with advanced retinopathy have a 95% chance of keeping their vision when they get treatment before the retina is severely damaged. These three treatments are laser surgery, injection of corticosteroids or anti-vascular endothelial growth-factor (VEGF) agents into the eye, and vitrectomy.

Although these treatments are very successful (in slowing or stopping further vision loss), they do not cure DR. Caution should be exercised in treatment with laser surgery since it causes a loss of retinal tissue. It is often more prudent to inject triamcinolone or anti-VEGF drugs. In some patients, it results in a marked increase of vision, especially if there is an edema of the macula.

Avoiding tobacco use and correction of associated hypertension are important therapeutic measures in the management of DR.

Obstructive sleep apnea (OSA) has been associated with a higher incidence of diabetic eye disease due to blood desaturation caused by intermittent upper airway obstructions. Treatment for OSA can help to reduce the risk of diabetic complications.

The best way of preventing the onset and delaying the progression of DR is to monitor it vigilantly and achieve optimal glycemic control.

Since 2008, there have been other therapies (e.g., kinase inhibitors and anti-VEGF) and drugs available. Laser photocoagulation can be used in two scenarios for the treatment of DR. It can be used to treat macular edema by creating a modified grid at the posterior pole, and it can be used for panretinal coagulation for controlling neovascularization. It is widely used for early stages of proliferative retinopathy.

Modified grid A “C”-shaped area around the macula is treated with low-intensity small burns. This helps in clearing the macular edema. Panretinal photocoagulation (also called scatter laser treatment) is used to treat PDR. The goal is to create 1,600–2,000 burns in the retina with the hope of reducing the retina’s oxygen demand and hence the possibility of ischemia. It is done in multiple sittings.

In treating advanced DR, the burns are used to destroy the abnormal blood vessels that form in the retina. This has been shown to reduce the risk of severe vision loss for eyes at risk by 50%.

Before using the laser, the ophthalmologist dilates the pupil and applies anesthetic drops to numb the eye. In some cases, the doctor also may numb the area behind the eye to reduce discomfort. The patient sits facing the laser machine while the doctor holds a special lens on the eye. The physician can use a single spot laser or a pattern scan laser for two-dimensional patterns such as squares, rings, and arcs. During the procedure, the patient will see flashes of light. These flashes often create an uncomfortable stinging sensation for the patient. After the laser treatment, patients should be advised not to drive for a few hours while the pupils are still dilated. Vision will most likely remain blurry for the rest of the day. Although there should not be much pain in the eye itself, an ice-cream headache like pain may last for hours afterward.

Patients will lose some of their peripheral vision after this surgery although it may be barely noticeable by the patient. The procedure does, however, save the center of the patient's sight. Laser surgery may also slightly reduce color and night vision.

A person with proliferative retinopathy will always be at risk for new bleeding, as well as glaucoma, a complication from the new blood vessels. This means that multiple treatments may be required to protect vision.

MEDICATIONS

Intravitreal triamcinolone acetonide triamcinolone is a long-acting steroid preparation.When steroid injected in the vitreous cavity, it decreases in the vitreous cavity, it decrease the macular edema (thickening of the retina at the macula) caused due to diabetic maculopathy and results in an increase in visual acuity. The effect of triamcinolone is transient, lasting up to 3 months, which necessitates repeated injections for maintaining the beneficial effect. Best results of intravitreal triamcinolone have been found in the eyes that have already undergone cataract surgery. Complications of intravitreal injection of triamcinolone include cataract, steroid-induced glaucoma, and endophthalmitis. A systematic review found evidence that eyes treated with the intravitreal injection of triamcinolone had better visual acuity outcomes compared to eyes treated with macular laser grid photocoagulation or sham injections.

Intravitreal anti-VEGF

There are good results from multiple doses of intravitreal injections of anti-VEGF drugs such as bevacizumab. A 2017 systematic review update found moderate evidence that aflibercept may have advantages in improving visual outcomes over bevacizumab and ranibizumab, after 1 year. The present recommended treatment for diabetic macular edema is modified grid laser photocoagulation combined with multiple injections of anti-VEGF drugs.

Instead of laser surgery, some people require a vitrectomy to restore vision. A vitrectomy is performed when there is a lot of blood in the vitreous. It involves removing the cloudy vitreous and replacing it with a saline solution.

Studies show that people who have a vitrectomy soon after a large HE are more likely to protect their vision than someone who waits to have the operation. Early vitrectomy is, especially, effective in people with insulin-dependent diabetes, who may be at greater risk of blindness from a HE into the eye.

Vitrectomy is often done under local anesthesia. The doctor makes a tiny incision in the sclera or white of the eye. Next, a small instrument is placed into the eye to remove the vitreous and insert the saline solution into the eye.

Patients may be able to return home soon after the vitrectomy or may be asked to stay in the hospital overnight. After the operation, the eye will be red and sensitive, and patients usually need to wear an eyepatch for a few days or weeks to protect the eye. Medicated eye drops are also prescribed to protect against infection.

Vitrectomy is frequently combined with other modalities of treatment.

RESEARCH

Light treatment

A medical device comprises a mask that delivers green light through the eyelids while a person sleeps was under development in 2016. The light from the mask stops rod cells in the retina from dark adapting, which is thought to reduce their oxygen requirement, which in turn diminishes new blood vessel formation and thus prevents DR. As of 2016, a large clinical trial was underway.

C-peptide

C-peptide had shown promising results in the treatment of diabetic complications incidental to vascular degeneration. Creative peptides, Eli Lilly, and Cebix all had drug development programs for a C-peptide product. Cebix had the only ongoing program until it completed a Phase IIb trial in December 2014 that showed no difference between C-peptide and placebo, and it terminated its program and went out of business. Stem cell therapy

Clinical trials are underway or are being populated in preparation for study at medical centers in Brazil, Iran, and the United States. Current trials involve using the patients' own stem cells derived from bone marrow and injected into the degenerated areas in an effort to regenerate the vascular system. Blood pressure control A cochrane review examined 15 randomized controlled trials to determine whether interventions that sought to control or reduce blood pressure in diabetics had any effects of DR. While the results showed that interventions to control or reduce blood pressure prevented DR for up to 4–5 years in diabetics, there was no evidence of any effect of these interventions on the progression of DR, preservation of visual acuity, adverse events, quality of life, and costs.

Fundoscopic image analyses

Distribution in the percentage of pre-processing techniques from 2011 to 2014 DR is diagnosed entirely by recognizing abnormalities on retinal images taken by fundoscopy. Color fundus photography is mainly used for staging the disease. FFA is used to assess the extent of retinopathy that aids in treatment plan development. OCT is used to determine the severity of edema and treatment response.

As fundoscopic images are the main sources for the diagnosis of DR, manually analyzing those images can be time-consuming and unreliable, as the ability of detecting abnormalities varies by years of experience. Therefore, scientists have explored developing computer-aided diagnosis approaches to automate the process, which involves extracting information about the blood vessels and any abnormal patterns from the rest of the fundoscopic image and analyzing them.

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of an automatic telemedicine system for computer-aided screening and grading of DR depends on reliable detection of retinal lesions in fundus images. The proposed method aims in developing an automated screening approach for classification of the DR in retinal fundus images. The fundus photography documents the retina, and the neurosensory tissue in our eyes which translates the optical images we see into the electrical impulses our brain understands. A fundus camera is a specialized low-power microscope with an attached camera. The main structures that can be visualized on a fundus photo are the central and peripheral retina, optic disc, and macula.

The optic disc region differs in intensity and brightness values compared with the retinal lesions. Therefore, the extraction of optical density (OD) is crucial before the lesion detection process. It is detected to improve the classification accuracy of red lesions (MA and HE) which are the screening features of DR. The detection of optic disc employs the red channel of the fundus image and lesions use green channel of the fundus image. The extraction of OD and lesions is made by different sets of morphological operations depending on their features.

After the detection of optic disc and lesions, the final classification of the fundus image either with or without DR and the severity of DR are made based on the count of HEs and MAs. The proposed method takes a retinal fundus RGB color image input. The inputs are taken from MESSIDOR database. The proposed method shows good performance metrics with HE and MA detection.

CONCLUSION

DR is a leading cause of vision loss, caused by damage to the retina. The risk of severe vision loss can be significantly reduced by timely diagnosis and treatment. The development of an automatic telemedicine system for computer-aided screening and grading of DR depends on reliable detection of retinal lesions in fundus images. The proposed method aims in developing an automated screening approach for classification of the DR in retinal fundus images. The fundus photography documents the retina, and the neurosensory tissue in our eyes which translates the optical images we see into the electrical impulses our brain understands. A fundus camera is a specialized low-power microscope with an attached camera. The main structures that can be visualized on a fundus photo are the central and peripheral retina, optic disc, and macula.

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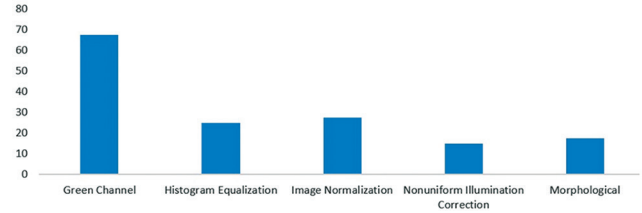

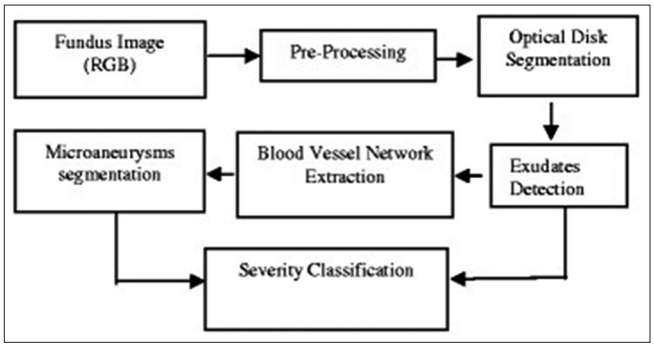

Figure 1: Flowchart for the automated diagnosis of diabetic retinopathy using fundus images

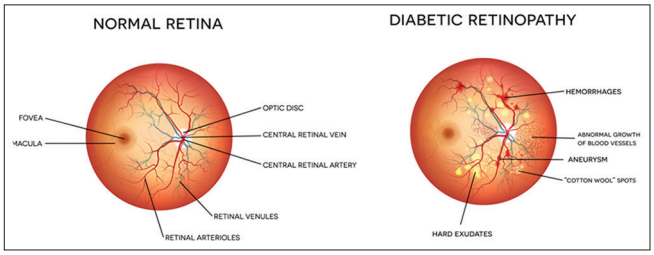

Figure 2: Diabetic retinopathy

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