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Review of Automated Detection for Diabetes Retinopathy Using Fundus Images

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Abstract: Diabetic retinopathy is a medical condition where the retina is damaged because fluid leaks from blood vessels into the retina. Ophthalmologists recognize diabetic retinopathy based on features, such as blood vessel area, exudes, hemorrhages, microaneurysms and texture. In this paper we review algorithms used for the extraction of these features from digital fundus images. Furthermore, we discuss systems that use these features to classify individual fundus images. The classifications efficiency of different DR systems is discussed. Most of the reported systems are highly optimized with respect to the analyzed fundus images, and that a generalization of individual results is difficult. However, this review shows that the classification results improved has improved recently, and it is getting closer to the classification capabilities of human ophthalmologists.

Keywords: -Diabetic retinopathy, Fundus images, Automated detection, Blood vessel area, Microaneurysms.

I. INTRODUCTION

Diabetic retinopathy (DR) is a common complication of diabetes. Indeed, it is so common that it is the leading cause of blindness in the working population of western countries. The rate of diabetes is increasing, not only in developed countries, but in underdeveloped countries as well. Unfortunately, most developing countries lack basic recoding of DR cases [40]. It is estimated that 75% of people with diabetic retinopathy live in developing countries. The situation in developing countries is especially bad, because there is inadequate treatment. Regardless of the health care situation in their country of origin, people with diabetes are 25 times more likely to develop blindness when compared with individuals who do not suffer from this disease. DR is a silent disease, because it may only be recognized by the patient when the changes in the retina have progressed to a level where treatment is complicated and nearly impossible. The prevalence of retinopathy varies with the age of onset of diabetes and the duration of the disease. So far, the most effective treatment for DR can be administered only in the first stages of the disease. Therefore, early detection through regular screening is of paramount importance. To lower the cost of such screenings, digital image capturing technology must be used, because this technology enables us to employ state of heart image processing techniques which automate the detection of abnormalities in retinal images.

This paper reviews automated detection systems for DR. This review is structured as follows: First we discuss the underlying disease, i.e. diabetes, in terms of its causes and effects on the human body. Following the goals of this paper, we focus on the effects of diabetes on the eye. These effects lead to features, such as blood vessel area, exudes, hemorrhages, micro aneurysms [5]. These features are used for the automatic detection of DR. In the automatic detection of DR stages section we reviewed different automated detection systems which have been reported in scientific literature. In the discussion section we discussed the advantages and disadvantages of different methods. The last section of this paper presents conclusions and outlines further work.

1.1 Diabetes

Diabetes mellitus (DM) is the name of a chronic, systemic, life threatening disease. It occurs when the pancreas does not secrete enough insulin or the body is unable to process it properly. This results in an abnormal increase in the glucose level in the blood. Over time this high level of glucose causes damage to blood vessels. This damage affects both eyes and nervous system, as well as heart, kidneys and other organs [8]. In general there are two types of diabetes. Diabetes type 1 results from a failure of the human body to produce insulin. Type 1 diabetes is less common than type 2 diabetes. People with type 1 diabetes take insulin injections. It is estimated that 90-95% of Americans, who are diagnosed with diabetes, have type 2 diabetes [1]. This form of diabetes usually develops in adults age 40 and older and is most common in the age group over age 55. About 80% of people with type 2 diabetes are overweight. It was reported that type 2 diabetes is often part of a metabolic syndrome that includes obesity, elevated blood pressure, and high levels of blood lipids.

1.2 Diabetic retinopathy

Diabetes mellitus often results in diabetic retinopathy which is caused by pathological changes of the blood vessels which nourish the retina. DR is the main cause of new cases of blindness among adults aged 20–74 years. During the first 20

years of the disease, nearly all patients with type 1 diabetes and >60% of patients with type 2 diabetes have retinopathy. In the Wisconsin Epidemiologic Study of DR, 3.6% of younger onset patients (type 1 diabetes) and 1.6 % of older-onset patients (type 2 diabetes) were legally blind [38]. In the younger-onset group, 86% of blindness was attributable to DR. In the older onset group, in which other eye diseases were common, one third of the cases of legal blindness were due to DR. Figure 1 shows the different features of the typical DR image. DR occurs when the increased glucose level in the blood damages the capillaries, which nourish the retina. As a result of this damage, the capillaries leak blood and fluid on the retina [24]. The visual effects of this leakage are features, such as microaneurysms, hemorrhages, hard exudates, cotton wool spots or venous loops, of DR [6]. Types of diabetic retinopathy DR can be broadly classified as nonproliferative DR (NPDR) and proliferative DR (PDR). Depending on the presence of specific DR features, the stages can be identified [6, 17]. The following list describes three subclasses of NPDR as well as PDR:

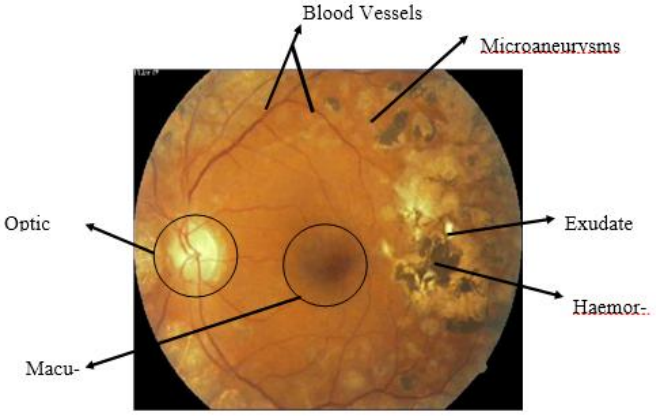

Fig. 1 Different features in a DR image

Mild NPDR: at least one microaneurysm with or without the presence of retinal haemorrhages, hard exudates, cotton wool spots or venous loops (Fig. 2 (b)). Approximately 40% of people with diabetes have at least mild signs of diabetic retinopathy [48].Moderate NPDR: numerous microaneurysms and retinal haemorrhages are present. A limited amount and cotton wool spots of venous beading can also be seen (Fig. 2(c)). 16% of the patients with moderate NPDR will develop PDR within 1 year [33]. Severe NPDR: is characterized by any one of the following (4-2-1 rule) characteristics: (1) numerous haemorrhages and microaneurysms in 4 quadrants of the retina (2) venous beading in 2 or more quadrants (3) Intraretinal microvascular abnormalities in at least 1 quadrant (Fig. 2(d)). Severe NPDR carries a 50 % chance of progression to PDR within 1 year [33].PDR: is the advanced stage; signals, sent by the retina for nourishment, trigger the growth of new blood vessels. These blood vessels do not cause symptoms or vision loss. But, their walls are thin and fragile, this leads to a high risk that they leak blood (Fig. 2(e)). This leaked blood contaminates the vitreous gel and this causes severe vision loss and even blindness. About 3% of people, with this condition, may experience severe visual loss [16].

II. DETECTION METHODS

Early detection of DR is important, because treatment methods can slow down the progression of the disease. Most treatment methods are based on laser technology.

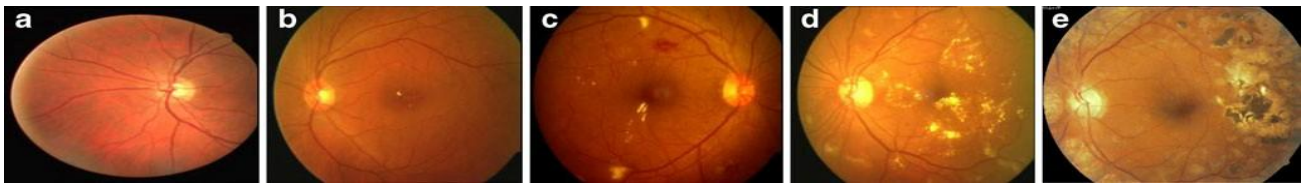

Fig. 2 Typical fundus images: (a) normal (b) mild DR (c) moderate DR (d) severe DR (e) prolific DR

Laser photocoagulation cauterizes ocular blood vessels, which effectively stops their leakage. The focal laser treatment method reduces retinal thickening. This may prevent worsening of retinal swelling. To be specific, this treatment reduces the risk of vision loss by 50%. For a small number of cases, with total vision loss, improvement is possible.

2.1 Fundus images

Medical image analysis is a research area that currently attracts lots of interest from both scientists and physicians. The objective of this field is to develop computational tools which will assist quantification and visualization of interesting pathology and anatomical structures. These tools work with digital fundus images of the eye. The procedure of taking fundus images starts by dilating the pupil with pharmaceutical eye drops. After that the patient is asked to stare at a fixation device in order to steady the eyes. While taking the pictures, the patient will see a series of bright flashes. The entire process takes about five to ten minutes. To ensure that DR treatment is received on time, the eye fundus images of diabetic patients must be examined at least once a year [22].

2.2 Feature extraction methods and analysis

Image processing can do both reduce the workload of screeners and play a central role in quality assurance tasks. Therefore, there has been an increase in the application of digital image processing techniques for automatic detection of DR. For example, color features on Bayesian statistical classifier were used to classify each pixel into lesion or non lesion classes.

The following sections describe blood vessels, exudes, hemorrhages, microaneurysms and maculopathy detection techniques. These detection techniques yield most of the features which are used in automated DR detection systems.

2.3 Blood vessels

Digital fundus photography from the human eye gives clear images of the blood vessels in the retina. This method provides an excellent window to the health of a patient affected by DR. Figure 3 shows an example of blood vessel detection from different types of DR [4]. The blood vessel structure was obtained by subjecting the green component of the RGB fundus image to a number of image processing algorithms [4].Blood vessels were detected using two dimensional matched filters [13]. Gray level profile of cross section of blood vessel approximated by Gaussian shaped curve. The concept of matched filter detection of signals was used to detect piecewise linear segments of blood vessels after the vessel approximation.Vessel points in a cross section are found with a fuzzy C-means classifier [31]. They have located and outlined blood vessels in images by the use of a novel method to segment blood vessels that compliments local vessel attributes with regionbased attributes of the network structure.Hayashi et al. have developed a computer aided diagnosis system to assist physicians in detecting abnormalities associated with fundus images of the retina [29]. Their proposed system can detect blood vessel intersections and it can identify abnormal widths in blood vessels. Computerized system for both extraction and quantitative description of the main vascular diagnostic signs from

III. NORMAL PROLIFERATIVE

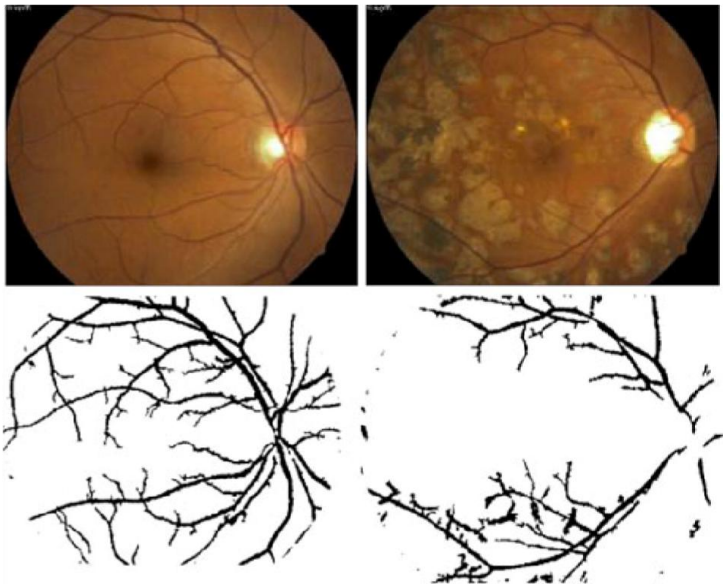

Fig. 3 Results of blood vessel detection for normal and PDR [4]

fundus images in hypertensive retinopathy was presented [23]. The features they have taken into account are vessel tortuosity, generalized and focal vessel narrowing, and presence of Gunn or Salus signs. A new system is proposed for the automatic extraction of the vascular structure in retinal images, based on a sparse tracking technique was proposed [28]. Blood vessel points in a cross section are found by means of a fuzzy C-means classifier. After tracking the vessels, identified segments were connected using greedy connection algorithm. Finally bifurcations and crossings were identified analyzing vessel end points with respect to the vessel structure. Blood vessel tracker algorithm was developed to determine the retinal vascular network captured using a digital camera [19]. The tracker algorithm detects optic disk, bright lesions such as cotton wools spots, and dark lesions such as haemorrhages. This algorithm identifies arteries and veins with an accuracy of 78.4% and 66.5% respectively. Vallabha et al. have proposed a method for automated detection and classification of vascular abnormalities in diabetic retinopathy. They detected vascular abnormalities using scale and orientation selective Gabor filter banks. The proposed method classifies retinal images as either mild or severe cases based on the Gabor filter outputs. The microaneurysms in retinal fluorescien angiograms was identified by first locating the fovea by sub sampling image by factor of four in each dimension [15]. Subsequently, the image was subjected to median filtering with a 5 by 5 mask to reduce high-frequency components. Then the image was correlated with a two-dimensional circularly symmetric triangular function with modelled gross shading of the macula. Blood vessel detection algorithm based on the regional recursive hierarchical decomposition using quad trees and post filtration of edges to extract blood vessels was studied [37]. This method was able to reduce false dismissals of predominately significant edges and faster in comparison to the existing approach with reduced storage requirements for the edge map. Li et al.

have used the arteriolar to venular diameter ratio of retinal blood vessels as an indicator of disease related changes in the retinal blood vessel tree [45]. Their experimental results indicate a 97.1% success rate in the identification of vessel starting points, and a 99.2% success rate in the tracking of retinal vessels. A new method of texture based vessel segmentation to overcome this problem was proposed [10]. The Fuzzy C-Means (FCM) clustering algorithm was used to classify the feature vectors into vessel or non-vessel based on the texture properties. They compared their method with hand labeled ground truth segmentation for five images and achieved 84.37% sensitivity and 99.61% specificity.

3.1 Microaneurysms detection

Microaneurysms detection is very important, because these structures constitute the earliest recognizable feature of DR. The first reports which link these structures to DR date back to 1879. Have analyzed the appearance and disappearance of microaneurysms in different phases of fluorescein angiography [34]. In a similar study both formation rate and disappearance of microaneurysms in early DR were analyzed [30]. The microaneurysms turnover were computed reliabibly from color fundus images [9]. They used a new method called MA-tracker to count microaneurysms. They showed that the microaneurysms remain stable over time, but only 29 % remain at the same place.

Figure 4 shows the results of microaneurysms detection for normal and PDR [4]. In example the green component, of the RGB fundus image, was chosen to obtain the microaneurysms. Similar to the exudates detection algorithm, first the prominent structures within retina images, such as blood vessel tree and optic disc are to be removed. After that a sophisticated sequence of image processing algorithms was used to determine the areas within the fundus images to get microaneurysms [4].

3.2 Normal Proliferative

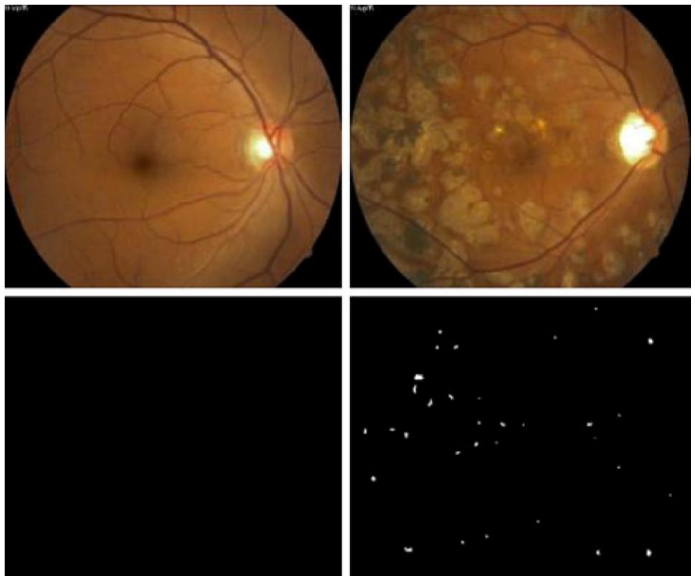

Fig. 4 Results of microaneurysms detection for normal, PDR [4]

The automated identification of diabetic retinopathy based on the presence of microaneurysms was studied [35]. The optometrists achieved 97 per cent sensitivity at 88 per cent specificity and the automated retinopathy detector achieved 85 per cent sensitivity at 90 per cent specificity.

IV. AUTOMATIC DETECTION OF DR STAGES

Over the last two decades there was a rapid development of Computer aided diagnosis (CAD) [25]. The idea of using computers to help in medical image diagnosis is in more practice. However, the quality of these CAD systems increased with more accurate sensor data, more processing power and better understanding of the underlying disease. Recently, Lee et al. have concluded that the performance of their computer vision system in diagnosing early retinal lesions is comparable with that of human experts [42]. In the next section we have reviewed different classification methods.

4.1 Classification methods

Colour features were used on Bayesian statistical classifier classify each pixel into lesion or non-lesion classes. They have achieved 100% accuracy in identifying all the retinal images with exudates, and 70% accuracy in classifying normal retinal images as normal. DR and normal retina were classified automatically using image processing and multilayer perceptron neural network. The system yielded a sensitivity of 80.21% and a specificity of 70.66%. Automated diagnosis of NPDR, based on three lesions: hemorrhages and microaneurysms, hard exudates, and cotton wool spots, was studied. The method was able to identify the NPDR stage correctly with an accuracy of 81.7 %. Exudates, haemorrhages, and microaneurysms were used for screening of DR subjects. The sensitivity and specificity of their software was 74.8% and 82.7 %, respectively in differentiating DR and normal subjects correctly.

Early detection of DR (presence of microaneurysms) was proposed based on decision support system by Kahai et al. [36]. Bayes optimality criteria was used to detect microaneurysms. Their method was able to identify the early stage of DR with a sensitivity of 100% and specificity of 67 %. Normal, mild, moderate, severe and prolific DR stages were automatically classified using both area and perimeter of the RGB components of the blood vessels together with a feed forward neural network. System average classification efficiency was 84% and sensitivity, specificity were 90% and 100% respectively. Nayak et al. have used exudates and blood vessel area along with texture parameters coupled with neural network to classify fundus images into normal, NPDR and PDR [48]. They obtained a detection accuracy of 93%, sensitivity and specificity of 90% and 100% respectively. Recently, bispectral invariant features were used as features for the support vector machine classifier to classify the fundus image in to normal, mild, moderate, severe and prolific DR classes by Acharya et al. [7]. They have demonstrated an average accuracy of 82% and sensitivity, specificity of 82% and 88% respectively. Normal, mild, moderate, severe and prolific classes of DR were classified automatically based on haemorrhages, microaneurysms, exudates and blood vessel areas with a support vector machine classifier [4]. The system was able to identify the unknown class accurately with an efficiency of more than 85% and a sensitivity of more than 82% and a specificity of 86 %. Nicolai et al. have designed an automated lesion system, which identified 90.1% of patients with DR and 81.3% of patients without DR, when applied in a screening population comprising of patients with untreated DR. The automated system demonstrated a sensitivity of 93.1% and a specificity of 71.6 %. Usher et al. have designed a support system for DR screenings. Their system showed a maximum sensitivity for the detection of any retinopathy on a per patient basis of 95.1%, accompanied by a specificity of 46.3%. The specificity could be increased as far as 78.9%, but this increase was accompanied by a fall in sensitivity to 70.8 %. At a setting with 94.8% sensitivity and 52.8% specificity, no cases of sight threatening retinopathy were missed. Have investigated both photography and optic disc topography mode of the retinal thickness analyzer. The system yielded a mean 93% sensitivity for PDR together with 100% specificity for DR cases. A software to grade the severity of 3 types of early lesions, hemorrhages and microaneurysms, hard exudates and cotton wool spots of DR was proposed to classify NPDR [43]. They were able to identify 82.6%, 82.6%, and 88.3% using the 430 images and 85.3%, 87.5%, and 93.1% using the 361 images, respectively, for hemorrhages and microaneurysms, hard exudates, and cotton wool spots. Philip et al. have assessed the efficiency of automated "disease/no disease" grading for DR within a systematic screening program. Detection of retinopathy was achieved by automated grading with 90.5% sensitivity and 67.4% specificity.

A system, designed by Estabridis et al., has detected features such as fovea, blood vessel network, optic disk, bright and dark lesions, which are associated with DR successfully [20]. It has achieved a classification accuracy of 90%.

Table 1 Comparison of different classification methods

Authors	No of classes	Method	Accuracy of classification	Sensitivity	Specificity
Lee et al. 2005 [43]	3	Hemorrhages, microaneurysms, hard exudates, cotton wool spots	Max: 88%	Not reported	Not reported
Estabridis and Figueiredo 2007[20]	2	Fovea, blood vessel network, optic disk, bright and dark lesions	90%	Not reported	Not reported
Li et al. 2008 [46]	2	Bright lesions, retinal vessel patterns	Not reported	81%	Not reported
Abràmoff et al. 2008 [2]	3	Optic disc, retinal vessels, hemorrhages, microaneurysms, vascular, abnormalities, exudates, cotton wool spots, drusen	Not reported	84%	64 %
Nayak et al. 2008 [48]	3	Blood vessels, exudates and texture	94%	90%	100 %
Acharya et al. 2008 [3]	5	Higher order spectra	82%	83%	89 %
Acharya et al. 2009 [5]	5	Blood vessel, exudates, microaneurysms, haemorrhages	86%	82%	86 %

Li et al. have proposed a method for screening DR and distinguishing PDR from NPDR automatically using color retinal images [46]. Their method showed a sensitivity 80.5%, positive predictive value 90.8%, true positive ratio 95.8% and false positive ratio 16.7% in detecting PDR and NPDR accurately. Have evaluated the performance of a system for automated detection of DR in digital retinal fundus images [2]. The system was constructed entirely from published algorithms and it was tested in a large, representative, screening population. They achieved a sensitivity of 84% and a specificity of 64 %. Higher order spectra features were used as input to a support vector machine classifier in order to classify fundus images into normal, mild DR, moderate DR, severe DR and PDR classes with an accuracy of 82%. Have

determined single lesions to grade clinical levels of DR and diabetic macular edema using both 1 and 3 non mydriatic digital color retinal images. Sensitivity and specificity for detecting referable levels of DR were 82% and 92%, respectively. Table 1 summarizes the results of the 15 automated DR classification systems. The table entries are chronologically ordered and the percentage values for accuracy of classification, sensitivity and specificity are rounded to the nearest integer.

V. CONCLUSIONS

DR where the retina is damaged due to fluid leaking from the blood vessels. Usually, the stage of DR is judged based on blood vessels, exudes, hemorrhages, microaneurysms and texture. In this review paper, we have discussed different methods for features extraction and automatic DR stage detection. An ophthalmologist uses an ophthalmoscope to visualize the blood vessels and his or her brain to detect the DR stages. Recently digital imaging became available as a tool for DR screening. It provides high quality permanent records of the retinal appearance, which can be used for monitoring of progression or response to treatment, and which can be reviewed by an ophthalmologist, digital images have the potential to be processed by automatic analysis systems. A combination of both accurate and early diagnosis as well as correct application of treatment can prevent blindness caused by DR in more than 50% of all cases. Therefore, regular screenings for DR of patients with diabetes is important. The grading of the resultant fundus images is an important cost factor. Automated DR detection can reduce the grading cost and thereby make the whole screening process less expensive. Some of the algorithms and systems reviewed in this paper are close to achieve DR identification in clinical practice.

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