Computerized Medical Imaging and Graphics 44 (2015) 41–53

Contents lists available at ScienceDirect

Computerized Medical Imaging and Graphics

journal homepage: www.elsevier.com/locate/compmedimag

A method to assist in the diagnosis of early diabetic retinopathy: Image processing applied to detection of microaneurysms in fundus images

Roberto Rosas-Romero[a,*], Jorge Martínez-Carballido[b], Jonathan Hernández-Capistrán[b], Laura J. Uribe-Valencia[b]

[a] Universidad de las Américas-Puebla, Puebla, Mexico
[b] Instituto Nacional de Astrofísica, Óptica y Electrónica, Puebla, Mexico

ARTICLE INFO

Article history:
Received 12 June 2014
Received in revised form 12 March 2015
Accepted 2 July 2015

Keywords:
Morphological processing
Eye fundus image
Principal component analysis
Radon transform

ABSTRACT

Diabetes increases the risk of developing any deterioration in the blood vessels that supply the retina, an ailment known as *Diabetic Retinopathy* (DR). Since this disease is asymptomatic, it can only be diagnosed by an ophthalmologist. However, the growth of the number of ophthalmologists is lower than the growth of the population with diabetes so that preventive and early diagnosis is difficult due to the lack of opportunity in terms of time and cost. Preliminary, affordable and accessible ophthalmological diagnosis will give the opportunity to perform routine preventive examinations, indicating the need to consult an ophthalmologist during a stage of non proliferation. During this stage, there is a lesion on the retina known as *microaneurysm* (MA), which is one of the first clinically observable lesions that indicate the disease. In recent years, different *image processing* algorithms, which allow the detection of the DR, have been developed; however, the issue is still open since acceptable levels of *sensitivity* and *specificity* have not yet been reached, preventing its use as a pre-diagnostic tool. Consequently, this work proposes a new approach for MA detection based on (1) reduction of non-uniform illumination; (2) normalization of image grayscale content to improve dependence of images from different contexts; (3) application of the *bottom-hat transform* to leave reddish regions intact while suppressing bright objects; (4) binarization of the image of interest with the result that objects corresponding to MAs, blood vessels, and other reddish objects (*Regions of Interest*—ROIs) are completely separated from the background; (5) application of the *hit-or-miss Transformation* on the binary image to remove blood vessels from the ROIs; (6) two features are extracted from a candidate to distinguish real MAs from FPs, where one feature discriminates round shaped candidates (MAs) from elongated shaped ones (vessels) through application of *Principal Component Analysis* (PCA); (7) the second feature is a count of the number of times that the radon transform of the candidate ROI, evaluated at the set of discrete angle values $\{0^\circ, 1^\circ, 2^\circ, \ldots, 180^\circ\}$, is characterized by a valley between two peaks. The proposed approach is tested on the public databases DiaretDB1 and Retinopathy Online Challenge (ROC) competition. The proposed MA detection method achieves sensitivity, specificity and precision of 92.32%, 93.87% and 95.93% for the diaretDB1 database and 88.06%, 97.47% and 92.19% for the ROC database. Theory, results, challenges and performance related to the proposed MA detecting method are presented.

1. Introduction

According to the International Diabetes Federation (IDF), 366 million people were diagnosed with diabetes in 2011. It is expected that the number will increase to 522 million in 2030. In addition, 183 million people (50%) with diabetes are not diagnosed [1]. Due to the prolific increase in diabetes, based on current estimates, a minimum of 3 million people will need to be evaluated every day by the year 2030 (35 tests per second).

Diabetes can increase the risk of contracting any type of eye disease, but the main cause of blindness associated with diabetes is *diabetic retinopathy* (DR) [2]. DR causes damage to the blood vessels within the retina. Commonly, it affects both eyes and can lead to progressive vision loss if it is not treated. More than 75% of all

* Corresponding author. Tel.: +52 2222292677.
E-mail address: roberto.rosas@udlap.mx (R. Rosas-Romero).

http://dx.doi.org/10.1016/j.compmedimag.2015.07.001

people, who have had diabetes for more than 20 years, will have some form of DR, according to [3]. From the USA National Diabetes Report [33], during 2005–2008, of diabetic adults aged 40 years or older, 28% people had DR that may result in vision loss, and 4.4% people had advanced DR that could lead to severe vision loss.

These complications can be prevented if tests are performed appropriately and regularly at least once per year. The vast majority of patients, who develop DR, have no symptoms until the last stage of the disease, where it could be too late for effective treatment. Therefore, detection and early medical intervention is critical. In terms of cure rates in first world countries, we will expect a 15% reduction of the diagnosed DR with vision loss. At third-world countries, we could expect 30% reduction of the diagnosed DR with vision loss, given the time, cost and irregular visits to the ophthalmologist.

To diagnose DR, a retinography is performed, which consists in capturing images of the inside of the eye (retina) by dilating the pupil (mydriatic) or without dilation. Usually, ophthalmologists recognize DR based on features, such as the areas of the blood vessels, exudates, *microaneurysms* (MAs), hemorrhages and texture [4]. Hemorrhages and MAs are the first observable injuries that indicate a diabetic retinopathy and they are known as red lesions.

According to a study, conducted and published in [5,6], half of 205,000 ophthalmologists that exist globally are located in six countries (China, USA, Russia, Japan, Brazil and India). It is also mentioned that there are 23 countries that have less than one ophthalmologist for each million inhabitants; 30 with less than four; 48 countries with less than 25 for every million people; 74 with less than 100 and only 18 countries have more than 100 ophthalmologists for every million citizens. For the case of underdeveloped countries, the economic level is still a disadvantage that avoids the generation of professionals in this field. For the case of developed countries, the level of population which exceeds 60 years of age doubles the rate of professionals that arise each year. In addition, it is expected that the number of ophthalmologists will grow only 2% while the increase in the population with diabetes will be 54% [2] for 2030. Furthermore, the examination time takes from 15 to 30 min in each eye, as well as an additional delay because of the need of dilatation of the pupil for a fundus eye exam.

For the aforementioned reasons the development of an automatic system of pre-diagnosis is necessary to perform a rapid assessment of the retina and to indicate if there is any type of lesion that should be treated by a specialist. In addition, the algorithm of detection and classification of lesions must be simple to facilitate its subsequent mass deployment. The simplification of the pre-diagnosis, early and preliminary diagnosis will benefit from algorithms that require less computing resources.

Statement of the problem: In short, the only way to diagnose non-Proliferative Diabetic Retinopathy is through the study of eye background images. In addition, the growth in the number of ophthalmologists is much lower than the growth of diabetics. For this reason, this work focuses on the development of an algorithm, which is capable of detecting red lesions which are visible on background eye images. Also, the algorithm is based on techniques of morphology and principal component analysis with a small number of features. These arguments encourage the future implementation of devices for autonomous diagnostic that will help to reduce the number of people who go to an ophthalmologist without apparent diabetic retinopathy.

The rest paper is organized as follows. Section 2 reviews the relevant and recent related work in detection of lesions in color fundus images. Section 3 gives a detailed overview of the proposed algorithm for detection of candidates to MAs. The proposed classification stage to discriminate between real MAs and false positives is explained in Section 4. Section 5 provides the experimental results obtained by following the proposed approach as well as comparisons. Conclusions are presented in Section 6.

2. Review of related work

According to [8,9], the detection of lesions on color background images is performed in two major stages, (1) *Extraction of candidates* to MAs and (2) *Classification* of candidates as MAs or normal regions.

Most of the current algorithms perform processing using only the green channel of the RGB image. The first stage requires a preprocessing to reduce noise and improve contrast. Then red areas (darker regions in one-channel images) on the image are extracted and segmented to obtain *candidates* for red lesions (*regions of interest*—ROI), followed by segmentation for removal of blood vessels to reduce the number of *false positives* that may appear during the stage of candidate extraction. After detection of *candidates* for red lesions, different *features* are extracted and selected on those regions. In the second stage, a classification algorithm is applied to categorize these *features* within *candidates* for red lesions (abnormal) and *non-candidates* (normal). The general process for detection of red lesions is shown in Fig. 1.

Different methods for preprocessing have been applied for detection of red lesions such as CLAHE (Contrast Limited Adaptive Histogram Equalization), lighting and brightness correction, normalization, shadow correction, etc. The extraction of candidates is usually based on morphological processing techniques, region growing algorithms, Wavelet transform, Radon transform, Curvelets, among others. All these techniques are commonly applied to grayscale images; however, we noted that injuries can be distinguished by color, size and shape. In order to have a basis of comparison, *Receiver Operating Characteristic* (ROC) graphics have been used in recent years with minor modifications.

Objectives, results and disadvantages of important related articles are discussed below. Not all research projects, mentioned below, used a standard database that works as the basis for comparison; however, some databases that can be used to standardize research results have been developed in the past years.

Some methods rely on the use of *fluorescein angiography* (FA) where a fluorescent dye is injected into the bloodstream to highlight blood vessels in the back of the eye so that they can be photographed. After the test, the pupils may remain dilated for up to 12 h. and urine is darker and orange in color for a few days. Possible reactions due to the test are nausea, vomiting, swelling of the larynx, hives, difficult breathing, fainting and cardiac arrest. Thus, the use of FAs represents a disadvantage.

Detection of MAs in FAs using morphological methods is performed in [10]. In this work, a sensitivity is not reported. The disadvantages of this method are the use of FAs, few images, and very slow processing time. Spencer et al. proposed a method in [11] for detection of MAs in digital images using adaptive filters. It has the disadvantages of using FAs, and the requirement of image amplification by a factor of at least four times to obtain good results. Detection of MAs in FAs is also presented in [12]. This method is divided into three stages. In the first stage, lighting and tone correction are used. In the second stage, adaptive filters, top-hat bilinear transformation, gray-level thresholding, and a region growing algorithm are used. Finally, in the third stage, an analysis of candidates is executed. A sensitivity of 82% was reached, it failed to detect 13 MAs on 13 images. Its disadvantages are the use of FAs, conflict with threshold levels, and high computation time. In the work by Cree et al. [13], the sensitivity is 82%, there is not human intervention and there is an improvement in speed; however, FAs are used and there is conflict with threshold levels. In [14], each candidate is classified according to its intensity and size by the application of a set of rules derived from 102 training images. A sensitivity of 81%