Automatic Screening and Classification of Diabetic Retinopathy Eye Fundus Images

By

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June 2016

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A thesis submitted in partial fulfilment of the University's requirements for the Degree of Doctor of Philosophy

ABSTRACT

Diabetic Retinopathy (DR) is a disorder of the retinal vasculature. It develops to some degree in nearly all patients with long-standing diabetes mellitus and can result in blindness. Screening of DR is essential for both early detection and early treatment. This thesis aims to investigate automatic methods for diabetic retinopathy detection and subsequently develop an effective system for the detection and screening of diabetic retinopathy.

The presented diabetic retinopathy research involves three development stages. Firstly, the thesis presents the development of a preliminary classification and screening system for diabetic retinopathy using eye fundus images. The research will then focus on the detection of the earliest signs of diabetic retinopathy, which are the microaneurysms. The detection of microaneurysms at an early stage is vital and is the first step in preventing diabetic retinopathy. Finally, the thesis will present decision support systems for the detection of diabetic retinopathy and maculopathy in eye fundus images. The detection of maculopathy, which are yellow lesions near the macula, is essential as it will eventually cause the loss of vision if the affected macula is not treated in time.

An accurate retinal screening, therefore, is required to assist the retinal screeners to classify the retinal images effectively. Highly efficient and accurate image processing techniques must thus be used in order to produce an effective screening of diabetic retinopathy. In addition to the proposed diabetic retinopathy detection systems, this thesis will present a new dataset, and will highlight the dataset collection, the expert diagnosis process and the advantages of the new dataset, compared to other public eye fundus images datasets available. The new dataset will be useful to researchers and practitioners working in the retinal imaging area and would widely encourage comparative studies in the field of diabetic retinopathy research. It is envisaged that the proposed decision support system for clinical screening would greatly contribute to and assist the management and the detection of diabetic retinopathy. It is also hoped that the developed automatic detection techniques will assist clinicians to diagnose diabetic retinopathy at an early stage.

ACKNOWLEDGEMENTS

First of all, I would like to express my gratitude to my Director of Studies, Dr. Vasile Palade, for his time, guidance and support for me during my studies. I am also grateful to my supervisors, Dr. James Shuttleworth and Prof. Chrisina Jayne. I would like to thank them for being a great supervisory team.

My gratitude also goes to my previous supervisory team, Dr. Rajeev Bali and Prof. Raouf Naguib. Under their supervision, I learnt a lot from their vast knowledge and experience.

The deepest gratitude and thanks go to the Universiti Teknikal Malaysia Melaka and Ministry of Higher Education Malaysia for sponsoring this PhD research. I am also thankful to the Ministry of Health Malaysia and the Melaka Hospital, Malaysia for providing access and approve the research and data collection.

Special thanks go to Dr. Raja Norliza Raja Omar and the staff at the Eye Clinic, Department of Ophthalmology, Melaka Hospital, Malaysia for the medical guidance, supports and for making my research data collection possible.

Thanks go to my wonderful parents, my siblings, other members of my family and my friends for their countless support.

Finally, I would like to thank everyone who was involved directly or indirectly throughout this research.

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DM	Diabetes Mellitus
DR	Diabetic Retinopathy
DME	Diabetic Macula Edema
MOHM	Ministry of Health Malaysia
NPDR	Non-proliferative Diabetic Retinopathy
PDR	Proliferative Diabetic Retinopathy
WHO	World Health Organization
NHMS	National Health and Morbidity Survey
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
IRMAs	Intraretinal Microvascular Anomalies
NED	National Eye Database
SVM	Support Vector Machines
HOS	Higher Order Spectra
DWT	Discrete Wavelet Transform
ANN	Artificial Neural Network
D-FNN	Dynamic Fuzzy Neural Network
RBFNN	Radial Basis Function Neural Network
PNN	Probabilistic Neural Network
kNN	k-Nearest Neighbours
CNN	Convolutional Neural Networks

LIST OF PUBLISHED PAPERS ON THIS RESEARCH

Journal:

Rahim, S, S., Jayne, C., Palade, V., and Shuttleworth, J. (2015) 'Automatic Detection of Microaneurysms in Colour Fundus Images for Diabetic Retinopathy Screening'. *Journal of Neural Computing and Applications* 521, 1-16

Rahim, S. S., Palade, V., Shuttleworth, J., and Jayne, C. (2016) 'Automatic Screening and Classification of Diabetic Retinopathy and Maculopathy Using Fuzzy Image Processing'. in Zhong, N., and Peng, H. (ed.) *Brain Informatics* 40708, 1-19

Conference Papers:

Rahim, S. S., Palade, V., Shuttleworth, J., and Jayne, C. (2014) 'Automatic Screening and Classification of Diabetic Retinopathy Fundus Images'. in Mladenov, V. et al. (ed.) *Proceedings of 15th International Conference on Engineering Applications of Neural Networks, EANN 2014, Communications in Computer and Information Science* 459. held 5-7 September 2014 at Sofia, Bulgaria. Switzerland: Springer, 113-122

Rahim, S. S., Palade, V., Shuttleworth, J., Jayne, C., and Raja Omar, R. N. (2015) 'Automatic Detection of Microaneurysms for Diabetic Retinopathy Screening Using Fuzzy Image Processing'. in Iliadis, L., and Jayne, C. (ed.) *Proceedings of 16th International Conference on Engineering Applications of Neural Networks, EANN 2015, Communications in Computer and Information Science* 517. held 25-28 September 2015 at Rhodes, Greece. Switzerland: Springer, 69-79

Rahim, S. S., Palade, V., Jayne, C., Holzinger, A., and Shuttleworth, J. (2015) 'Detection of Diabetic Retinopathy and Maculopathy in Eye Fundus Images Using Fuzzy Image Processing'. in Guo, Y. et al. (ed.) *Proceedings of 8th International Conference on Brain Informatics and Health, BIH 2015, LNAI 9250*. held 30 August-2 September 2015 at London, UK. Switzerland: Springer, 379-388

1 INTRODUCTION

Diabetic Retinopathy (DR) is one of the diabetes complications and is an important cause of visual disability and blindness. It is vital to have a regular eye examination for initial detection and early treatment. This thesis is about the development of a medical decision support system for automatic diabetic retinopathy screening and classification in eye fundus images.

The scope of this research focuses on the Asian country of Malaysia. The research was sponsored by the Ministry of Higher Education in Malaysia and the Universiti Teknikal Malaysia Melaka (UTeM). In addition, the research also received support, particularly in the contribution of expertise, from the Department of Ophthalmology at the Melaka Hospital, Malaysia, under the Ministry of Health for Malaysia.

In order to develop an accurate and efficient diabetic retinopathy screening system, the capabilities of image processing techniques are investigated in this research work. Several highly efficient image processing techniques are implemented and tested to evaluate the system performance. The main image processing techniques used in this research involve fuzzy image processing on eye fundus images, which has not been previously investigated. A more reliable screening system can be produced with fuzzy image processing capability and therefore enable the achievement of the screening general aim, which is the earlier detection of sight threatening problems to ensure prompt treatment for the prevention of vision loss.

This chapter introduces diabetic retinopathy and its screening. It focuses on Malaysia and highlights some challenges faced by the Malaysian healthcare system in dealing with diabetic retinopathy screening. Section 1.2 presents the research aims and objectives. Section 1.3 explains the research motivation, alongside the contributions of the thesis. Finally, Section 1.4 presents the overview of the chapters of this thesis.

1.1 Diabetic Retinopathy Screening and the Challenges Faced by the Malaysian Government

Diabetic Retinopathy (DR) is a diabetes mellitus complication, which also include stroke, cardiovascular disease, diabetic nephropathy and diabetic neuropathy. The retinal capillaries damage occurs in diabetes mellitus. Diabetic retinopathy can be visualised only in the retina (Taylor and Batey, 2012), which is a layer of tissue. Diabetic retinopathy happens through lasting of small blood vessels damage in the retina, which eventually results in blindness. Hence, an effective screening of diabetic retinopathy is important for early treatment, as well as an effective management of risk factor to prevent diabetic complications.

The prevalence of diabetes globally presented by the World Health Organization (WHO), reported in 2014 was estimated to be 9% among adults aged 18 and above (2012a). Diabetes contributes to about one percent of global blindness (2012b). Globally, 4.8% of the 37 million blindness cases is caused by the diabetic retinopathy and approximately 366 million will be affected by diabetes mellitus worldwide in the year 2030 (World Health Organization, 2005). In addition, diabetes has also been predicted to be the seventh leading cause of death by the year 2030 (Mathers and Loncar, 2006). The initial National Health and Morbidity Survey I (NHMS I) for Malaysia was conducted in 1986. The survey reveals a prevalence of diabetes mellitus is 6.3%. In the year 1996, the percentage in NHMS II had increased to 8.3% and, the newest NHMS III 2006 report shows that the total diabetes mellitus prevalence is 14.9% (Letchuman et al., 2010).

Diabetes Mellitus (DM) is a complex disease resulting in severe complications in various parts of the body. Nevertheless, good control of DM will avoid or delay various complications, including diabetic retinopathy. The length of DM is associated with the diabetic retinopathy incidence, and it has been reported that more than 75% of diabetes patients have some diabetic retinopathy form after 20 years of the disease (World Health Organization, 2005). Thus, screening and early treatment can avoid significant loss of vision. Such efforts to control this enduring disease as well as the early complications detection such as diabetic retinopathy should be strengthened, because diabetic retinopathy is an asymptomatic condition in its initial stage (Taylor and Batey,

2012; Ministry of Health Malaysia, Malaysian Society of Ophthalmology and Academy of Medicine Malaysia, 2011). It is also stated that diabetics are twenty-five times more likely to develop blindness compared to the general population (Health Technology Assessment Unit, Medical Development Division, Ministry of Health Malaysia, 2002). Considering these complications and the rising numbers of diabetic patients in Malaysia, a programme of diabetic retinopathy screening in the country must be complete, covering all people with DM in Malaysia. To achieve this, significant resources will be required for the management of the condition including human resources, to increase the current workload within the field of disease diagnostics.

Diabetic retinopathy can only be identified through medical eye examination since it is asymptomatic in its initial stage. The diabetes management at the facilities of the Ministry of Health Malaysia (MOHM) is presently being performed in health clinics, in addition in polyclinics, specialised clinics as well as hospital wards. In Malaysia, screening is currently performed by general practitioners, clinicians in hospital based diabetes centres, ophthalmologists, optometrists or a technician and a medically trained photographic interpreter, in the case of photography (Health Technology Assessment Unit, Medical Development Division, Ministry of Health Malaysia, 2002). There are many modalities of screening available to detect and classify diabetic retinopathy. One of the most common techniques used is ophthalmoscopy. Non-mydriatic digital fundus photography is also popular (Ministry of Health Malaysia, Malaysian Society of Ophthalmology and Academy of Medicine Malaysia, 2011).

Different screening modalities performed by different practitioners will produce a wide variation of sensitivity and specificity. The screening tools include the following: the direct and indirect ophthalmoscope, the slit lamp biomicroscope, the mydriatic fundus camera and the non-mydriatic fundus camera. The non-mydratic fundus camera has high sensitivity and specificity among other advantages. For example pupillary dilatation is not required, especially if the room is adequately darkened, promoting compliance, efficiency and safety (Ministry of Health Malaysia, Malaysian Society of Ophthalmology and Academy of Medicine Malaysia, 2011). Trained primary care clinicians are needed for screening of diabetic retinopathy to increase the accuracy of

interpretation and grading. Proper training among all healthcare personnel therefore is essential. Specialised personnel for retinal screening and grading need specific training and regular performance assessment. Moreover, the Clinical Practice Guidelines Screening for Diabetic Retinopathy requires that the module of training should comprise clinical skills and knowledge, computer imaging and skills, in addition operational concerns and training of fundus grading (Ministry of Health Malaysia, Malaysian Society of Ophthalmology and Academy of Medicine Malaysia, 2011).

Diabetes Mellitus is a growing problem among increasing numbers of diabetics every year. Subsequently, there are several challenges faced by the Ministry of Health Malaysia in diabetic retinopathy handling cases (Ministry of Health Malaysia, 2012a), including:

i. Inadequate diabetic eye screening programs

In order to perform successful eye screening, a team of trained healthcare personnel is required. Fewer screening teams, especially in rural hospitals, have significantly decreased the number of the eye screening programs. At the moment, screening programs are exclusively performed at primary health care centres (selected health clinic with fundus camera), hospital or clinics with eye care providers such as ophthalmology and optometry clinics. According to a relatively recent report on diabetic retinopathy screening by the Unit of Health Technology Assessment, only 24 out of the 114 Ministry of Health hospitals have a department of ophthalmology, while ophthalmologists aim to visits other hospitals regularly (Health Technology Assessment Unit, Medical Development Division, Ministry of Health Malaysia, 2002).

ii. Inadequate resources to complete the task

The main resources needed for the screening are trained staff and fundus cameras. All healthcare personnel involved in screening require proper training before they can join the programs. There is a need for training on

how to screen the images and how to improve the accuracy of interpretation and grading, in addition in terms of sensitivity and specificity.

The screening tools and techniques used in the program are the other important factors to be considered. There are many available screening modalities used for diabetic retinopathy screening. Ophthalmoscopy is a popular screening method, but non-mydriatic digital camera is also widely prescribed due to its high sensitivity and specificity. The fundus camera however is limited throughout Malaysian hospitals and health clinics. In the year of 2011, the total number of fundus camera available at health clinics under the Ministry of Health was only 107 (Ministry of Health Malaysia, Malaysian Society of Ophthalmology, Academy of Medicine Malaysia, 2011). This lack of vital screening resources will invariably result in longer waiting lists for initial screenings and referrals to ophthalmologist. This will ultimately lead to more serious eye complications.

iii. Poor patient information or awareness

One of the barriers in handling diabetic retinopathy is the patient factor. A lack of awareness of the possible eye complications from diabetes mellitus is one of the factors that have decreased the frequency of diabetic retinopathy screening. Moreover, other factors which impede the level of diabetic retinopathy awareness amongst Malaysians are eye care services poor access and dissimilar cultural beliefs. As such, patients should be aware that regular eye examinations are important.

1.2 Research Aims and Objectives

The aim of this research is to investigate automatic methods for diabetic retinopathy detection that can contribute towards improving diabetic retinopathy management and, subsequently, to develop an efficient system for diabetic retinopathy screening. Basically, the proposed diabetic retinopathy research consists of three types of systems. Firstly, the thesis will present the development of a basic system for the screening and classification of diabetic retinopathy using eye fundus images, which is a system for

general detection for diabetic retinopathy screening and will classify images into two respective cases: Normal and Diabetic Retinopathy. The research will then focus on the microaneurysms detection which are the earliest diabetic retinopathy signs.

Different image processing techniques, including fuzzy image processing, are implemented in a variety of detection systems for microaneurysms which classify images into two main categories. The first categorisation classifies them into detected and non-detected cases. The second categorisation is based on Normal (No DR) and Diabetic Retinopathy cases. In addition, the thesis presents the fuzzy-based image processing decision support systems for diabetic retinopathy and maculopathy detection in eye fundus images. The proposed systems classify the images into two types of classification, in order to generate a diversity of results and system performance analysis, which are the two above cases (Normal and Diabetic Retinopathy) and an additional ten cases which follow the ophthalmologists' practice and provide more details. The second classification involves No Diabetic Retinopathy and the other nine detailed classes of the DR cases: Mild DR without maculopathy, Mild DR with maculopathy, Moderate DR without maculopathy, Moderate DR with maculopathy, Severe DR without maculopathy, Severe DR with maculopathy, Proliferative DR without maculopathy, Proliferative DR with maculopathy and Advanced Diabetic Eye Disease (ADED).

In order to assist screeners to classify the retinal images effectively and with high confidence, an accurate retinal screening system is necessary. Therefore, to develop a diabetic retinopathy screening grading and classification system, effective techniques of image processing must be used. This research project examines the use of the fundus images for detecting the diabetic retinopathy features presence in the eyes. This is a particularly challenging problem and this thesis proposes novel use of image processing techniques in order to automatically detect the stages of retinopathy. To achieve this aim, highly efficient and accurate image processing techniques must be used to produce an effective screening of diabetic retinopathy.

Despite the existence of a range of image processing techniques, the need for highly effective and specialised image processing techniques in this case cannot be over emphasised. Factors such as the fundus images suffering from noise and latency are often encountered, necessitating calibration and filtering before the images can be used reliably. In addition, the quality of the image depends on the skills applied by the paramedic in capturing the eye fundus images, as well as on other factors including the quality of the equipment and possible distractions from the environment. Due to these facts, all healthcare staff requires proper training before they are qualified and equipped for diabetic retinopathy screening. This is important as it can help increase the likelihood of accurate interpretation and grading. In addition to the lengthy and rigorous training of healthcare personnel before qualification, a growing challenge faced by the healthcare sector is the fact that diabetes mellitus is on the increase, with higher numbers of diabetics each year. It has also been highlighted by governments and other relevant stakeholders that the diabetic eye screening program is inadequate, as are the resources to complete the task, in addition to poor patient information or awareness (Ministry of Health Diabetic Retinopathy Screening Team, 2012b).

Further to the range of complications associated with images captured by the fundus camera, there is also the need for an experienced paramedic to diagnose whether the patient has any conditions (i.e., diabetic retinopathy). This screening phase is carried out manually by the paramedic who looks for any changes (abnormalities) on the retinal image, making the whole diagnostic process highly convoluted and protracted.

Based on the aforementioned reasons, in order to pursue this study primary research outcome, which is the development of a computer-based imaging tool, a method must be created in order to effectively detect important features on the fundus images and efficiently classify patients into the correct retinopathy stages. This automatic diabetic retinopathy grading will facilitate a reduction in the burden of manual grading for the screening team, and help alleviate the pressure on the limited eye screening centres in Malaysia (Ministry of Health Malaysia, Malaysian Society of Ophthalmology and Academy of Medicine Malaysia, 2011). As a result of early detection, it would also help ophthalmologists to treat patients before their conditions worsen and, most importantly,

increase the chance of protecting the patient's vision. Moreover, an automatic diabetic retinopathy system would diagnose it in a faster and more efficient way. In addition, as suggested by the available literature, the initial detection of retinopathy, the existing retinopathy monitoring with consistent fundus examinations and effective laser treatment at suitable times, are among the key measures to prevent visual loss from diabetic retinopathy (Health Technology Assessment Unit, Medical Development Division, Ministry of Health Malaysia, 2002).

The main objectives of the research described in this thesis are as follows:

i. To develop an automatic screening and classification systems for diabetic retinopathy using fundus images in order to detect diabetic retinopathy at an early stage.
ii. To propose novel use of image processing and machine learning techniques for early detection of the signs of diabetic retinopathy.

The research introduced novel use of image processing techniques for the automated detection of retinopathy stages, including the combination of various pre-processing techniques as well as fuzzy image processing techniques, such as fuzzy histogram equalisation, fuzzy filtering and fuzzy edge detection. In addition, the research proposed the use of Circular Hough Transform and various machine learning classifiers.

1.3 Motivation and Contributions of the Thesis

Eye screening is important for the early detection and treatment of diabetic retinopathy. Regular screening can help detect patients with diabetes at an early stage thus, earlier identification of any retinopathy can allow changes in blood pressure or blood glucose to be managed efficiently to slow the rate of progression of the disease. The importance of the proposed research is to overcome the current problems faced in the diabetic retinopathy screening process, such as:

i. Manual diagnosis by the ophthalmologist

Currently, clinicians use non-mydratic fundus cameras to capture retinal images. Based on the image produced from the fundus camera, the experienced screening team will diagnose whether or not patients have any conditions (including diabetic retinopathy). The diagnosis is carried out manually by screeners who assess any changes (abnormalities) on the retinal image. This process is both laborious and prone to error. Therefore, a computer-based imaging tool is needed to effectively detect the signs of diabetic retinopathy, allowing ophthalmologists to gain a suitable window in which to treat patients, before serious damage occurs, thus increasing the chance of protecting the patient's vision. It will also help decrease the workload for healthcare personnel in the diabetic retinopathy screening process.

ii. Time taken and limitations of screening resources

The proposed automatic diabetic retinopathy system would help save time, costs and ultimately the vision of patients. With appropriate automation (i.e., decision support systems) in place, preventative actions to protect vision can then be taken earlier and therefore can help reduce the number of diabetic retinopathy problems, in addition to the risk of blindness. A decision support system for clinical diagnosis would contribute greatly in assisting with the management and detection of diabetic retinopathy. An automatic system will assist an ophthalmologist (or optometrist) to detect diabetic retinopathy (and its detailed classification) in a more efficient and faster way compared with manual analysis, which is more time-consuming. As a result, the proposed system will indirectly assist in the process of recommended follow-up schedules for each category of diabetic retinopathy based on the system detection. Furthermore, the development of the proposed system will contribute to overcoming the diabetic retinopathy screening limitations inherent in the present manual screening procedure, especially given the problems of inadequately trained staff and the use of the fundus camera, as highlighted in Section 1.1.

iii. Developing effective techniques of image processing for the diabetic retinopathy detection

Diabetic retinopathy screening is a popular research area and many researchers focus on and contribute to the advancement of this study area. Most researchers focus on finding and proposing an accurate technique or method for detecting certain features of diabetic retinopathy through exploring the eye fundus images. Although there have been immense advancements in this area of research, there are still lacunae or spaces for improvement. The proposed techniques in this research will most notably benefit the realm of image processing in a number of areas or ways that include the provision of an accurate method for effectively detecting features of diabetic retinopathy.

Based on the general objectives in Section 1.2 above, in particular the second objective, the highlighted contributions of this thesis include: implementing image processing techniques combination for the general diabetic retinopathy screening detection (Rahim et al., 2014), investigating image processing techniques combination for the diabetic retinopathy features detection, focusing on microaneurysms, an important early feature of diabetic retinopathy (Rahim et al., 2015a; 2015b) and the evaluation of image processing techniques combination for the diabetic retinopathy and diabetic maculopathy detection (Rahim et al., 2015c; 2016). In addition, the contributions of this thesis include employing the novel use of fuzzy image processing techniques for the pre-processing stage of medical images, i.e., eye fundus images for diabetic retinopathy screening (Rahim et al., 2015a; 2015b; 2015c; 2016), as well as implementing a new online dataset containing normal and diabetic retinopathy fundus images (Rahim et al., 2015b; 2015c; 2016) and finally, testing a new method for macula region localisation in order to detect maculopathy (Rahim et al., 2016).

To summarise, diabetes mellitus is a main health problem. One of the diabetes mellitus health effects is diabetic retinopathy, which causes blindness. Therefore, an effective