Faculty of Engineering

Feature Extraction of Retinal Microvasculature of Retinal Images

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Grade: ____________

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Final Year Project Report	√
Masters	
PhD	

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This project is submitted as the partial fulfillment of the requirement for the accomplishment of the degree, Bachelor of Engineering (Hons) in Electronics (Computer)

Faculty of Engineering

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2017/2018

TO MY HONOURABLE SUPERVISOR DR. KURYATI BT KIPLI

AND

MY BELOVED BROTHER MOHAMMED AHSANUL HOQUE

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ABSTRACT

Image Processing, more generally digital image processing is one of the most widely used computer vision technology, especially in Biomedical engineering. Modern ophthalmology is directly dependent on this robust technology, digital image processing to find out the biomarkers analyzing the fundus eye images that are responsible for different kinds of life-threatening diseases like diabetic retinopathy, macular degeneration, hypertensive retinopathy, transient ischemic attack or sharp stroke and some other cardiovascular disease. The geometric features like vessel tortuosity, branching angles, vessel diameter and fractal dimension are considered as the biomarkers for the cardiovascular diseases mentioned above. Retinal vessel diameter widening has found as the early symptom of transient ischemic attack or sharp stroke. A succinct and meaningful review of the latest quantitative diagnostic methods that are developed employing the digital image analysis principles for measuring the remarkable features mainly the vessel diameter has been provided in the literature of this project. In this project, a completely new and computer-aided automatic method to measure the retinal vessel diameter employing the Euclidean Distance Transform technique has been developed. The proposed system measures the Euclidean Distance of the bright pixels exist on the Region of Interest (ROI). Further, the proposed system was evaluated on the High-Resolution Fundus Image Database (HRFID) and Retinal Vessel Image set for Estimation of Width (REVIEW) Database. The HRFID was used to evaluate the performance of the segmentation technique that was employed in this project and obtained 94.3% accuracy with 66.5% Sensitivity, 97.86% Specificity, 77.265 Positive Predictive Value (PPV) and 96.60% Negative Predictive Value (NPV). The Vascular Disease Image Set (VDIS) and Central Light Reflex Image Set (CLRIS) of REVIEW database were used to evaluate the overall system performance that measures the vessel diameter. The proposed system obtained 98.1% accuracy for the CLRIS and 97.7% accuracy for VDIS. With further evaluation, validation and enhancement of the method, it can be integrated into the clinical computer-aided diagnostic tool. The methodology and the evaluation results are explained in this report.

Keywords: Image Processing, Feature Extraction, AV nicking, Microaneurysm, Cotton Wool Spot, Hard Exudates, Focal Arteriolar narrowing, vessel width, Haemorrhages, Image Acquisition, Image Enhancement, Grey-Scale Image, Image Restoration, Segmentation, Edge Detection, Thresholding, Vessel Extraction, Image Registration.

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Chapter 1

Introduction

1.1 Introduction:

Image Processing is the method of applying mathematical operations in signal processing systems where image or video is fed as input and the output also be either image or a group of feature or parameters that are related to the image [1]. Digital imaging accomplishes functions on a digital image. It is being used in image enhancement, data compression, Machine vision and deals with difficulties from edge detection to pattern recognition and reconstruction [2], [3]. In biomedical engineering, digital image processing is being applied in researches and diagnosing the diseases, planning and supervising treatment for that diseases and monitoring the state of diseases simultaneously [4]. Digital image processing is playing an important role in medical sector to reduce the involvement of observers in avoiding unexpected errors and getting a more precise result [5].

For securing the expected results and creating more automated applications in the medical sector, researchers from all over the world are exploring this fertile field, image processing and contributing to the exciting advancements of image processing technology. One of the most important sub-field of biomedical engineering is the analysis of fundus retinal images. Analysis of the human fundus eye images has become the key point of diagnosing the life-threatening cardiovascular diseases like diabetic and hypertensive retinopathies that are related to the changes of the microvasculature of retinal blood vessels, because of the simple and non-invasive visualization of the microvascular structure of retinal blood vessels [6]–[8].

The fundus retinal images are directly captured from human eye that includes some other landmarks like microcirculation system of retina, macula, optic disc, fovea, microaneurysm and exudates [9]. This cost-effective, simple image acquisition system can be used in the large-scale screening programs and retinal image analysis developing mathematical and computational techniques to help the physicians to be introduced with some of the symptoms like the abnormalities in vessel tortuosity, vessel width, bifurcation angels, branching angels and vessel caliber that can be used for early detection of hypertensive and diabetic retinopathy, macular degeneration, acute stroke, neovascular glaucoma and some other cardiovascular disease [6], [8], [10]–[14].

There are several changes in the retinal microvasculature that are recognized as the pre-indicator of subsequent vascular incident like ischemic stroke or acute stroke [15] and it is found in many types of research that there is a clear relationship between the ocular funduscopic abnormalities and acute stroke even-though the blood pressure and other vascular risk factors are in control [16]. According to the study of [17] with a multiethnic cohort, retinal arteriolar narrowing and retinopathy of diabetic free people have an association with increased risk of acute stroke. But the Cardiovascular Health Study stated that there is no association between arteriolar diameter and stroke rather there is a close association between stroke and the largest retinal vein quartile and the smallest retinal vein quartile [18]. Rotterdam cohort study also came to a decision after a long-term observation that the retinal venular diameter is associated with any stroke or ischemic stroke [19].

[20] examined the association of hypertensive retinopathy with the risk of stroke in their population base study. Retinal microvascular abnormalities like microaneurysm, arterio-venous nicking, haemorrhages, vessel caliber are considered as associative to the stroke and indicative of death from stroke and Ischemic Heart Diseases(IHD) [6]. A population-based study collaborating with Beaver Dam Eye Study (BDES) of [6] revealed that Increased diameter ratio was associated with increased stroke mortality (P=0.02 unadjusted). [21] searched MEDLINE and EMBASE to find out the relation between microvascular changes of retinal microvasculature and prevalence or incident of stroke. [21] In their study 20659 patients were involved, 1178 patient of them had a stroke and they found the Odd Ratio (OR) of stroke and retinal arteriolar narrowing and AV nicking was 1.42 and 1.91 respectively which indicated that these abnormalities are slightly

associated with stroke. Microvascular lesions like microaneurysm and haemorrhages which were found as highly associated with stroke as their OR were 3.83 and 3.21 respectively and the OR between stroke and arteriole narrowing and venular network are 2.28 and 1.80 indicated the association of these abnormalities with stroke [21]. A cohort study of Asian Malay persons consisting of 3189 patients, free from prevalent stroke at baseline, revealed that 51 (1.93%) participants had an incident stroke event that could be predicted by analyzing the microvascular changes of retinal vasculature [22]. Prevalent and incident stroke have the association with retinopathy and venular widening [23]. Retinal vessel widening is also the predictor of hypertensive retinopathy which also has an association with stroke [24].

There are many techniques that have been developed using image processing principle to measure the vessel diameter of retinal microvasculature. Suppose some of the vessel diameter measuring techniques are based on Linear Discriminant Analysis (LDA), image gradient segmentation technique (ARG) for vessel edge detection, using active contour [25], [26], mask creation [25], graph-theoretic method [27], [28]. Multi-Step Regression Method (Higher order Gaussian modeling) [29], Adaptive Higuchi's Dimension [30] and so on. The aim of this project is to develop an automated algorithm to measure the diameter of a retinal blood vessel from fundus retinal image.

In the figure below, a line (bold) is shown that is perpendicular to the retinal arteriole which was used to measure the vessel diameter using operator dependent automated techniques. The dotted lines are also drawn parallelly and 2pixel apart from the bold line to measure the vessel diameter [31].

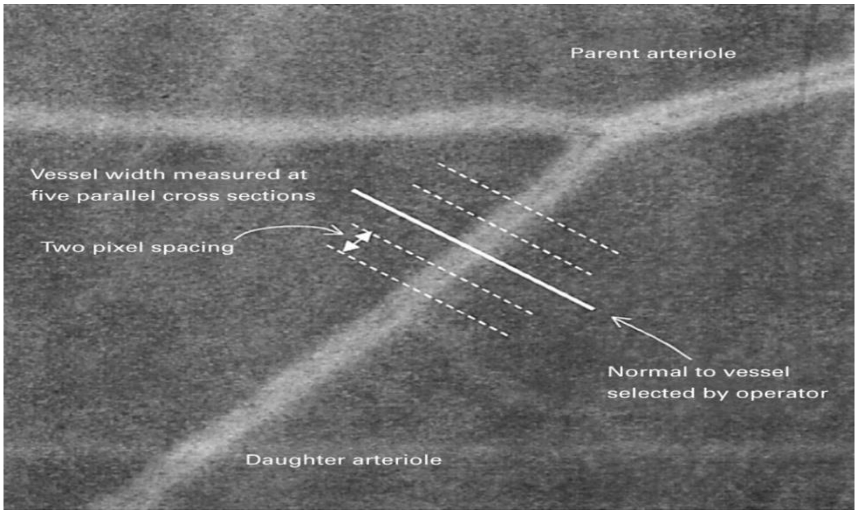

Figure 1. 1: Measurement of retinal blood vessel diameter [31.

There are several datasets for fundus retinal images that are publicly available for the researchers from all over the world. High-Resolution Fundus Image Database (HRFID) and Digital Retinal Images for Vessel Extraction (DRIVE) are two kinds of publicly open datasets that can be accessed by the researchers [10], [32]. Researchers from Digital Image Processing discipline can use images from this dataset as the raw materials for their experiment. REVIEW (Retinal Vessel Image set for Estimation of Width) is another publicly available standard dataset that includes various normal and pathological retinal images for the evaluation of the algorithm for retinal vessel diameter measurement. REVIEW dataset includes 16 images with 193 vessel segments that demonstrate the different types of pathologies and vessel types and this dataset consists of four subsets which are HRIS (High-Resolution Image Set), VDIS (Vascular Disease Image), CLRIS (Central Light Reflex Image Set) and KPIS (Kick Point Image) [33].

The retinal vessel widening is the pre-indicator of stroke that can be measured by employing the Digital Image Processing techniques. In this project, MATLAB software will be used to develop an automated vessel width measurement algorithm through image processing. The publicly available database, REVIEW will be used to evaluate the proposed algorithm.

1.2 Problem Statement:

Human retinal microvasculature shows several significant changes that are recognized as the pre-indicator of transient ischemic attack or sharp stroke. Analyzing fundus retinal image, the possibility of this risky disease can be predicted. One of the most important signs of happening stroke is retinal blood vessel widening. But the existing methods for the measurement of vessel widening are not fully automated, provide less accuracy in comparison with the manual measurement [27] and these are still in the development process. Development of automated vessel diameter measurement is critically important for modern ophthalmology.

The existing methods need the involvement of a good number of observers. This fact is responsible for making the diagnosing systems of the modern ophthalmology lengthier. The bulkiness of the observers also leads the diagnosing system to provide an inaccurate result. To overcome this misery fully automated computer-aided disease diagnosing system is the crying need in ophthalmology for detecting this dangerous and most uncertain cardiovascular diseases, stroke.

In the modern biomedical screening especially in the ophthalmic department, there are a limited number of human eye image analysis techniques. Due to this limitation, the outcome of the newly developed retinal image analysis algorithms cannot be compared with the wide range of outcome of previously developed methods. This scenario affects the outcome of the newly developed method in term of determining the accuracy and precision which leads the methods to be confusing. To come out from this situation, the dedication of the researchers to design automated retinal image analysis algorithm more extensively is very important.

1.3 Objectives:

The concern of this project is to deal with the problems stated above which are appeared as the major fact for the modern ophthalmology to predict the risky cardiovascular disease, stroke. The main focuses of this project are listed below.

I. To investigate existing Image Processing techniques for extracting features of the retinal image.
II. To determine the limitations and challenges of existing retinal vessel diameter measurement methods.
III. To develop a new algorithm for measuring retinal vessel diameter with high accuracy that can overcome the challenges.

1.4 Project Significance:

I. This project provides a platform to design an early indicator to predict the dangerous cardiovascular disease such as diabetes, hypertension, and stroke,

II. This automated diameter measurement system is important to eliminate the time-consuming manual and subjective process.

III. With further evaluation, validation and enhancement of the method, it can be integrated into the clinical computer-aided diagnostic tool

1.5 Project Scope:

The first scope of this project is the acquisition of fundus retinal images from REVIEW database. The main advantage of this database is that it provides various manually segmented normal and pathological retinal images. After the acquisition, the RGB images need to be converted to simplify the amount of information and maintain only the information related to the features of the image.

Image enhancement is performed to synthesize the digital images for making the output more acceptable for further analysis of that image. To fix the point of interest on vessel boundary of either side of the vessel for measuring the vessel diameter edge detection technique need to be employed. The line is the pre-step of measuring the perpendicular distance. First, need to fix two points in the edges of cylindrically shaped vessel body. Then based on these points need to trace two lines on either side of the vessel boundary that are parallel to each other. And finally, need to measure the perpendicular distance between the two-parallel line which is the diameter of the blood vessel.

The objectives of this project are achieved that provide the scope to utilize this in ophthalmic diagnosing. The outcome of this project proves the retinal vessel widening is an important biomarker for detecting stroke.

1.6 Outline of The Project:

There are five chapters in this project and that are Introduction, literature review, methodology, result and discussion, and finally conclusion and recommendation.

Chapter 1 includes the introduction, problem statement, objectives, and scope of the project.

Chapter 2 is designed with the literature review of the overall image processing techniques for detecting the retinal blood vessel abnormalities responsible for stroke. The existing image processing methods for the measurement of retinal blood vessel diameter and their limitations and challenges is emphasized more extensively here as vessel diameter is the focused feature of this is a project.

The project methodology and its flowchart and the brief of MATLAB functioned are described in chapter 3.

Chapter 4 is combined with project outcome and discussion.

The conclusion, challenges of the proposed algorithm and further improvement is explained in chapter 5.

Chapter 2

Literature Review

2.1 Introduction:

This review is focused mainly on the retinal vessel diameter measurement algorithms, applications of image processing technique, to provide an overview of the recent advancement in measuring the diameter of the retinal blood vessel. In biomedical engineering, the existing retinal image analysis methods are still dependent on a bulk of human observers. The blood vessel diameter measurement methods are also not fully automated. For medical diagnosing systems maximum precision is a must for detecting the diseases as it is one of the most sensitive issues. This review is a pre-step of our future work of shaping a novel, automated and computer-aided algorithm to measure the diameter of a retinal blood vessel with maximum accuracy.

In the following sections of this paper, we briefly discussed the abnormalities of retinal microvascular features, responsible for stroke and the circumstantial scenario of the existing methods for analyzing these abnormalities. Here we emphasized to manifest especially the retinal blood vessel diameter measurement techniques as it is one of the most important markers of prevalent and incident stroke. The basic principle of digital image processing and a general digital image processing procedure for extracting the features of the retinal image containing image acquisition, grey-scale image, image enhancement, restoration, segmentation, registration and vessel extraction subsection are described in this paper in a cabalistic manner. The arising challenges of present retinal image processing techniques for measuring the blood vessel diameter and the future scopes of this field are also explained in this paper.

2.2 Retinal vascularization:

The retina is a highly vascular tissue, which receives supply from two sources namely central and choroidal circulatory system (Figure 1). The central blood vessel supplies the inner retina which made ~30% of the retinal blood flow [34]. Central retinal artery (CRA) runs through the optic disc and enters the inner layer of the retina. CRA branches into superior- and inferior- arteries with diameters of 150µm [35]. Ultimately it forms a network of capillaries with diameters of 5µm [36]. On the other hand, blood from the retina drains into the central retinal vein (CRV). Approximately 70% of the retinal blood flow is supplied by the choroidal blood vessel which nourishes the outer retina and the photoreceptor–retinal pigment epithelium (RPE) complex located adjacent to Bruch's membrane [34]. Apart from nourishing the region, the choroidal circulatory system serves as a heat sink which removes generated metabolic heat due to light photons strike on the photopigments and the melanin of the RPE [37].

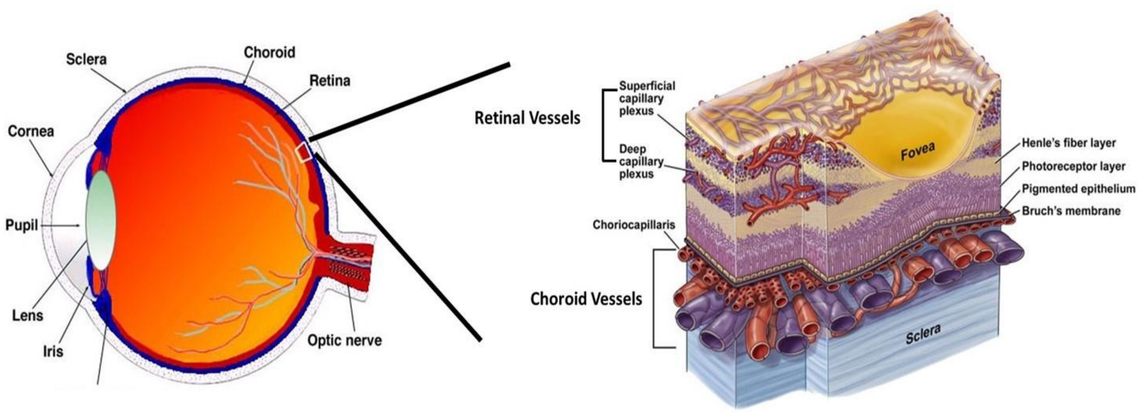

Figure 2.1: Schematic diagram of the retinal vasculature Adapted from [38].

2.3 Pathology of Retinal Vasculature:

There is a range of eye diseases particularly affecting retinal blood vessel. Amongst determinant factors of retinal vascular disorders are a physiological hardening of the artery walls in aging and existing vascular diseases such as high blood pressure and atherosclerosis. Most common retinal vascular disorders are hypertensive retinopathy, Retinal Vein Occlusion (RVO), Central Retinal Artery Occlusion (CRAO) and Diabetic Retinopathy. Monitoring of the retinal vasculature through retinal imaging and vascular caliber monitoring permit a direct assessment of the retinal vascular disorders.

2.4 Hypertensive Retinopathy:

Hypertensive retinopathy occurs when arterioles and venules of the retina are damaged, which eventually leads to blindness. Thus, several classification systems have been developed to facilitate early identification [39].

Hypertensive retinopathy initially affects the retinal blood vessels at all tributary levels, especially the arterial vessels. This process is known as sclerosis (thickening and stiffening of the artery), which can alter the angular course of the artery and may also affect the tributary angles. Furthermore, the artery and vein junction share a common adventitial sheath. Any sclerotic changes to the artery in this enclosed common 'compartment' space can further compress the weaker venular vessels, which can result in further changes to the angular course of the veins as well [40]. Such angular changes can be further studied to determine its significance in the prediction and assessment of disease process and progression.

2.5 Retinal Vein Occlusion (RVO):

Retinal vascular occlusive disorder (RVO), is commonly associated with various underlying systemic disorders including arterial hypertension, diabetes mellitus, dyslipidemia and systemic vasculitis. RVO may be found in varying blood vessel caliber. This includes central retinal vein occlusion (CRVO); media such as hemicentral retinal vein occlusion and small-caliber veins such as branch retinal vein occlusion (BRVO) [41].

Retinal vein occlusion can be divided into central and branch. The branch retinal vein occlusion can happen at the various tributary levels, especially the first and second tributaries. However, prior to a full-blown vein occlusion, a temporary phase known as impending retinal vein occlusion may occur. In this phase, the affected veins will become more engorged, dilated and tortuous, and the course and tributary angle of the affected veins will alter with this pathological process [42]. These angular changes can be further studied to determine its significance in the prediction and assessment of disease progression.

2.6 Central Retinal Artery Occlusion (CRAO):

Central Retinal Artery Occlusion (CRAO) is an ophthalmic emergency analogous to the acute stroke of the eye. Unfortunately, presentation of such cases to the appropriate medical attention is