Expert Systems with Applications 42 (2015) 7221–7234

Contents lists available at ScienceDirect

Expert Systems with Applications

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

QUARTZ: Quantitative Analysis of Retinal Vessel Topology and size – An automated system for quantification of retinal vessels morphology

M.M. Fraz [a,*], R.A. Welikala [b], A.R. Rudnicka [c], C.G. Owen [c], D.P. Strachan [c], S.A. Barman [b]

[a] School of Electrical Engineering and Computer Science, National University of Sciences and Technology, Islamabad, Pakistan
[b] Faculty of Science Engineering and Computing, Kingston University London, United Kingdom
[c] Population Health Research Institute, St. George's, University of London, United Kingdom

ARTICLE INFO

Article history:
Available online 19 May 2015

Keywords:
Retinal image processing
Automated analysis
Retinal vessel morphology
Vessel quantification
Feature extraction
Epidemiological studies
Screening programs
Large population studies

ABSTRACT

Retinal vessels are easily and non-invasively imaged using fundus cameras. Growing evidence including longitudinal evidence, suggests morphological changes in retinal vessels are early physio-markers of cardio-metabolic risk and outcome (as well as other disease processes). However, data from large population based studies are needed to examine the nature of these morphological associations. Several retinal image analysis (RIA) systems have been developed. While these provide a number of retinal vessel indices, they are often restricted in the area of analysis, and have limited automation, including the ability to distinguish between arterioles and venules. With the aim of developing reliable, automated, efficient retinal image analysis (RIA) software, generating a rich quantification of retinal vasculature in large volumes of fundus images, we present QUARTZ (Quantitative Analysis of Retinal Vessel Topology and size), a novel automated system for processing and analysing retinal images. QUARTZ consists of modules for vessel segmentation, width measurement and angular change at each vessel centreline pixel with sub-pixel accuracy, computing local vessel orientation, optic disc localisation, arteriole/venule classification, tortuosity measurement, and exporting the quantitative measurements in various output file formats. The performance metrics of the algorithms incorporated in QUARTZ are validated on a number of publically available retinal databases (including DRIVE, STARE, CHASE_DB1, INSPIRE-AVR, and DIARETDB1). QUARTZ performs well in terms of segmentation accuracy, calibre measurement, optic disc and arteriole/venule recognition. The system provides a rich quantification of retinal vessel morphology, which has potential medical applications in identifying those at high risk, so that prophylactic measure can be initiated before onset of overt disease.

1. Introduction

Medical imaging has revolutionised healthcare procedures, allowing professionals to detect and diagnose disease at the earliest and most treatable stages, thus improving patient outcomes with appropriate and effective care. An accurate diagnosis in medical imaging depends on the successful acquisition of the image as well as on the successful interpretation of the image. The advances in image capture hardware and the unrelenting development in computational efficiency, coupled with increasingly sophisticated image analysis and machine learning techniques, have provided the platform for acquiring minute details of biological tissues in regions such as the retina, and interpretation of the image to aid a physician in detecting possibly subtle abnormalities. With the development of digital imaging and computational efficiency, medical image processing, analysis and modelling techniques are increasingly used in all fields of medical sciences, particularly in ophthalmology and retinal image analysis.

The blood vessel structure in retinal images is unique in the sense that it is the only part of the blood circulation system that can be directly observed non-invasively and can be easily imaged using Fundus cameras. The morphological characteristics of retinal vessels are associated with cardiovascular and systemic disease. Cardiovascular disease (CVD) accounts for almost a third of deaths in both men and women, responsible for nearly 200,000 deaths in the UK per year (Statistics, 2012). Coronary heart disease (CHD), stroke and heart failure account for most of these deaths with CHD making the largest contribution. CVD is responsible for a substantial burden of morbidity and disability, accentuated by an ageing population and rising survival rates following myocardial

* Corresponding author.
E-mail addresses: moazam.fraz@seecs.edu.pk (M.M. Fraz), Roshan.Welikala@kingston.ac.uk (R.A. Welikala), arudnick@sgul.ac.uk (A.R. Rudnicka), s.barman@kingston.ac.uk (S.A. Barman).

http://dx.doi.org/10.1016/j.eswa.2015.05.022
0957-4174/

infarction. Diabetes is a strong risk factor for CVD both in middle and later life (Seshasai, Kaptoge, & Thompson, 2011). The UK prevalence of diabetes, particularly type 2 diabetes (T2D) has more than doubled over 30 years (González, Johansson, Wallander, & Rodríguez, 2009; Thomas et al., 2009). Diabetic precursors (particularly insulin resistance), as well as other blood markers, are important determinants of cardiovascular and metabolic risk (Seshasai et al., 2011). These precursors, along with other patient characteristics/phenotypes, are used in primary prevention to estimate future risk of cardiovascular disease, providing indications for medical/lifestyle interventions to alter disease trajectory (Collins & Altman, 2010). Early detection and prevention of disease outcome is key, especially as morbidity and mortality are so much higher in those with CVD compared to those without. In addition to vessel features pathognomonic of overt disease (e.g., micro-aneurysms and diabetes, artery–vein nicking and hypertension), accurate measurement/monitoring of vascular morphology may be an important marker of early vascular disease, which may be important in risk prediction. Abnormalities of retinal vessels have been prospectively associated with CVD outcomes in adult life, including coronary heart disease (CHD), stroke and cardiovascular mortality (Wong et al., 2002). In particular, narrowing of retinal arterioles has been related to CHD, and cardiovascular mortality (Wong et al., 2002). Changes in retinal vessel calibre in later life have also been associated with established risk factors for cardiovascular disease. Narrow arterioles have been linked with the presence of hypertension and raised blood pressure (Ikram et al., 2006; Leung et al., 2003). Changes in retinal vessel calibre in later life have also been associated with other established risk factors for cardiovascular disease; narrow arterioles being linked to obesity and higher HDL cholesterol (Cheung et al., 2007; Ikram et al., 2004). Wider arterioles have been associated with higher levels of blood glucose, total cholesterol, triglycerides and inflammatory markers (Wong et al., 2006). Associations of venular width with blood pressure have been less conclusive. Wider venules seem to be associated with diabetes, elevated glycosylated haemoglobin, lower levels of high density lipoprotein, inflammatory markers, smoking and obesity (Wang et al., 2006; Wong et al., 2006).

Some of these associations with vessel morphology (particularly with obesity and blood pressure) have been observed in childhood, and retinal vessel tortuosity has been associated with a number of established cardiovascular risk markers in the first decade of life (Owen et al., 2011). This suggests life course patterning of vascular development and that retinal vessel morphology may be an important early marker of vascular health. Hence, accurate assessment of retinal vessel morphology (in both arterioles and venules) may be an important physio-marker of vascular health, which might predict those at high risk of disease in middle and later life (Abràmoff, Garvin, & Sonka, 2010).

Screening programs and large population based studies produce a large number of images to deal with, which brings specific challenges. The inter-expert variability which in-turn is the repeatability between the experts is a desirable feature. Different conclusions could be reached by two experts when they are provided with the same set of images. This may be due to the varying image conditions, difficulty related to the data analysed, observer training for this particular task or even the subjective difference in perception. Moreover, the manual segmentation, Arteriole/venule (A/V) labelling, width marking and optic disc localisation is a tedious and slow task. This inevitably results in performance decline over time for the human grader that is the challenge of intra-expert variability. Finally, with the objective of finding epidemiological associations in the images acquired from the large screening programs and population based studies, it is impossible to derive the quantitative measures of vessel morphology for each of the vessel segments in all of the retinal images. These quantitative measures may include the width measurement and the local orientation angle at each centreline pixel, the tortuosity of the vessel segment, A/V classification, the branching index of the vessel and many more.

1.1. Motivation

Epidemiological objective of retinal imaging include the following:

- To deliver automatic and semi-automatic image analysis for generating quantitative measures from retinal vessel morphology by establishing a common repeatable procedure, therefore increasing the reliability and performance of the analysis.
- Help to extract the quantitative measures from a large number of images acquired which can be used to find epidemiological associations.

Therefore an automated system is required which can process and analyse the large amount of data; and extract useful quantitative information from vessel morphology which helps epidemiologists and other medical experts in identifying those at high risk of disease (Trucco et al., 2013).

There are some software systems that have been released recently for automatic and semi-automatic analysis for retinal images. This includes Retinopathy Image Search and Analysis (RISA) (Mirsharif, Tajeripour, & Pourreza) system that uses a content-based image retrieval method to perform rapid analysis and diagnosis of diabetic retinopathy from digital retinal imagery through a telemedicine model. The RoPtool (Rothaus, Jiang, & Rhiem, 2009) and RoPnet (Dashtbozorg, Mendonca, & Campilho, 2013) which are designed for the evaluation and analysis of retinopathy of prematurity in infancy. ROPnet (Dashtbozorg et al., 2013) is an interactive tool for semi-automatic tracking of retinal vessels and computation of tortuosity index in narrow-field images, whereas RoPtool (Rothaus et al., 2009) traces retinal blood vessels and calculates width (expressed as dilation index) and tortuosity (expressed as tortuosity index). CAIAR program (Owen et al., 2009) developed in python and Pearl, is designed for measuring retinal vessel width and has been used to calculate tortuosity in the retinal images of school children.

Several software packages to analyse adult retinal images have been developed, including the System for the Integration of Retinal Image Understanding Services (SIRUS), Interactive Vessel Analysis (IVAN), the Vascular Assessment and Measurement Platform for Images of the Retina system (VAMPIRE), and the Singapore 'I' Vessel Assessment program (SIVA). SIVA (Vázquez et al., 2013) developed by the Singapore Eye Research Institute is designed for extraction of the retinal vascular structure and derives quantitative measures from retinal images to describe the retinal vessels' characteristics. IVAN (Grisan & Ruggeri, 2003) is another software tool used for obtaining clinical indexes of AVR, but the time for the analysis of a single image is approximately 20 min, too long to allow its use in screening studies or to become a standard in clinical practise (Huang, Zhang, & Huang, 2012). SIRIUS (Ortega et al., 2010) is a web-based system for retinal image analysis which provides a collaborative framework for experts. SIRIUS consists of a web based client user interface, a web application server for service delivery and the service module for the analysis of retinal microcirculation using a semi-automatic methodology for the computation of the arteriolar-to-venular ratio (AVR). The RIVERS (Retinal Image Vessel Extraction and Registration System) project (Tsai et al., 2008) can also be considered as an initiative in this direction. Automated Retinal Image Analyser (ARIA) software is designed to facilitate fast, accurate and repeatable measurements of retinal vessel diameters in a variety of retinal image types. VAMPIRE (Perez-Rovira et al., 2011) (Vascular Assessment and