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Color fundus image registration techniques and applications for automated analysis of diabetic retinopathy progression: A review

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ABSTRACT

Diabetic retinopathy (DR) is one of the leading cause of visual impairments in the working age population in the developed world. It is a complication of both types of diabetes mellitus, which affects the light perception part of the retina; and without timely treatment patients could lose their sight and eventually become blind. Automated methods for the detection and progression analysis of DR are considered as potential health-care need to stop disease propagation and to ensure improved management for DR. Aiming for the detection and progression analysis of DR, color fundus photography is considered as one of the best candidates for non-invasive imaging of the eye fundus. A list of methods has already been developed to analyse DR related changes in the retina using color fundus photographs. In this manuscript we review those automated methods. In order to accurately compare the evolution of DR over time, retinal images that are typically collected on an annual or biennial basis must be perfectly superimposed. However, in reality, for two separate photographic-eye examinations the patient is never in exactly the same position and also the camera may vary. Therefore, a registration method is applied prior to evolution computation. Knowing registration as a fundamental preprocessing step for longitudinal (over time) analysis, we also reviewed state-of-the art methods for the registration of color fundus images.

The review summarizes the achievement so far and also identifies potential study areas for further improvement and future research toward more efficient and accurate DR progression analysis.

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1. Introduction

Diabetic retinopathy (DR) is a microvascular complication of diabetes, causing abnormalities in the retina and is a leading cause of blindness in the developed world [1,2]. Diabetic retinopathy typically begins as small changes in the retinal capillaries. The first detectable abnormalities are microaneurysms which are local distensions of the retinal capillary and which cause intraretinal haemorrhages when ruptured [3]. When the first appearance of mircroaneurysms are observed in the retina the disease severity is classified as mild non-proliferative diabetic retinopathy. Over time due to the increased permeability of the capillary walls more and more mircroaneurysms along with haemorrhages are formed and the next state of the diabetic retinopathy called moderate non-proliferative diabetic. As the retinopathy advances, the blood vessels become obstructed which causes microinfarcts called soft exudates in the retina. When a significant number of intraretinal haemorrhages (more than 20 in each of the 4 quadrants) or venous beading (in 2+ quadrants), or intraretinal microvascular abnormalities (IRMA) (in 1+ quadrants) are encountered, the state of the retinopathy is defined as severe non-proliferative diabetic retinopathy [4]. The severe non-proliferative diabetic retinopathy can quickly turn into proliferative diabetic retinopathy [4], while neovascularisations or preretinal haemorrhages present, and may cause sudden loss in visual acuity or even a permanent blindness due to vitreous haemorrhage or tractional detachment of the central retina [3].

Early detection and progression analysis of diabetic retinopathy can enable timely treatment by minimizing further deterioration. One of the best candidates for non-invasive imaging of the eye fundus is clearly digital color fundus photography because of the availability of retinal cameras along with data format that are easily manageable by computer-assisted procedure [5]. Clinical signs observable by color fundus photographs include mircroaneurysms, haemorrhages, exudates and intra-retinal micro-vascular abnormalities [2,103]. Timely diagnosis and evidence-based treatment of diabetic patients are important for preventing vision loss. However, the current society faces the conflict of increasing number of diabetics and decreasing number of ophthalmologists [6]. Thus automatic methods are of great importance as they help to significantly reduce the work load from ophthalmologists and image graders in clinic [7].

Fig. 1 shows an exemplary retinal image with DR features. While DR can be detected from a single time stamp image, to identify progression it is essential to collect sequential series of images, and these images must be compared. Prior to comparison, images that are collected over time need to be aligned. Thus longitudinal registration is a fundamental step for computer-aided DR progression analysis [2,5,8–10].

While DR detection and progression analysis are related they are somewhat difference in the sense that the later allows longitudinal (over time) analysis facilitating retinal change detection to monitor DR development and progression. In comparison to DR detection which has been an active research area over the last few decades and has been addressed by several research groups [7,11–17], progression analysis has recently been focused and the number of publications are still limited. This paper reviews automated methods that are used for DR progression analysis. Considering image registration as a fundamental pre-processing step for the progression analysis we also review longitudinal retinal image registration methods.

We performed comprehensive literature search on PubMed database, Web of Science database, Google scholar database to identify all the pertinent peer-reviewed articles published till July 2018. The keywords used for search included registration of retinal images, automated analysis of retinal changes, longitudinal registration of color fundus photographs, temporal color fundus image registration, automated diagnosis of retinal changes, automated diagnosis of diabetic retinopathy, color fundus photographs.

The rest of the paper is organized as follows: First, we provide an overview of retinal image registration framework in section II. In section III, we review the longitudinal registration methods that are used to align retinal images collected over time. Automated change analysis algorithms are reviewed in section IV. Section V presents the discussions and section VI presents the conclusion.

2. Image registration framework

Image registration establishes a correspondence between the reference image, I_r and the floating image, I_f by a parametric transformation $T_P(.)$ in line with a similarity (or cost) function $S(.)$. This can be generalized as a maximization problem [24,90]:

$$T_P{}^*(.) = arg\,\max_{T_P(.)} S(I_r, T_P(I_f))$$

where $T_P{}^*(.)$ gives the best registration parameter settings.

Similarity (cost) functions quantify the correspondences between the reference and floating images. Well-known examples of similarity functions are the sum of squared differences and ratio-image uniformity [18], cross-correlation [19], phase correlation [20] and mutual information [21–23].

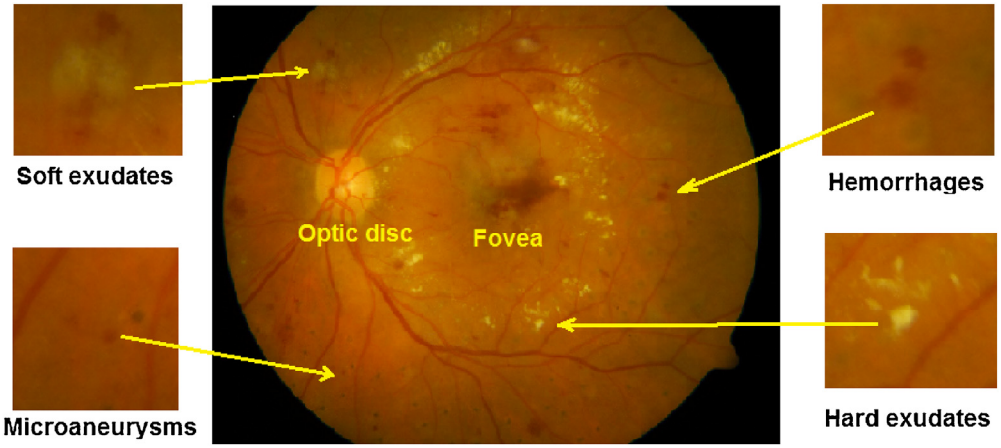

Fig. 1. Typical diabetic retinopathy features on a color fundus image.