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Learning from healthy and stable eyes: A new approach for detection of glaucomatous progression

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ABSTRACT

Glaucoma is a chronic neurodegenerative disease characterized by loss of retinal ganglion cells, resulting in distinctive changes in the optic nerve head (ONH) and retinal nerve fiber layer. Important advances in technology for non-invasive imaging of the eye have been made providing quantitative tools to measure structural changes in ONH topography, a crucial step in diagnosing and monitoring glaucoma. Three dimensional (3D) spectral domain optical coherence tomography (SD-OCT), an optical imaging technique, is now the standard of care for diagnosing and monitoring progression of numerous eye diseases.

Method: This paper aims to detect changes in multi-temporal 3D SD-OCT ONH images using a hierarchical fully Bayesian framework and then to differentiate between changes reflecting random variations or true changes due to glaucoma progression. To this end, we propose the use of kernel-based support vector data description (SVDD) classifier. SVDD is a well-known one-class classifier that allows us to map the data into a high-dimensional feature space where a hypersphere encloses most patterns belonging to the target class.

Results: The proposed glaucoma progression detection scheme using the whole 3D SD-OCT images detected glaucoma progression in a significant number of cases showing progression by conventional methods (78%), with high specificity in normal and non-progressing eyes (93% and 94% respectively).

Conclusion: The use of the dependency measurement in the SVDD framework increased the robustness of the proposed change-detection scheme with comparison to the classical support vector machine and SVDD methods. The validation using clinical data of the proposed approach has shown that the use of only healthy and non-progressing eyes to train the algorithm led to a high diagnostic accuracy for detecting glaucoma progression compared to other methods.

1. Introduction

Glaucoma is an optic neuropathy characterized by distinctive changes in the optic nerve head (ONH) and visual field. Glaucoma is often asymptomatic in its early stages and causes blindness if it remains without treatment. It results in progressive loss of retinal ganglion cells and their axons causing typical changes in the appearance of the retinal nerve fiber layer (RNFL) and the optic disk.

The detection of glaucoma change over time is of high interest in the diagnosis and management of glaucoma particularly for patients as the detection of progression could indicate uncontrolled disease and possible need for therapy advancement. Hence, it is important to develop clinically relevant methods for progression detection in order to avoid permanent damage to the optic nerve head.

In 1851, Helmholtz revolutionized the field of ophthalmology with the invention of the ophthalmoscope, which allowed physicians to examine the disc clinically and identify damages in the optic nerve head associated with glaucoma. This requires clinician identification of the outer and inner borders of the neuroretinal rim and visual estimation of the amount of rim tissue. However, the inner and the outer borders of the ONH neural tissue are not always visible by clinical examination techniques [1]. Furthermore, the clinical examination of the ONH remains subjective, qualitative and with limited reproducibility [2].

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In order to assist the expert in qualitative and quantitative analysis, automatic image processing methods have been proposed to facilitate the interpretation of the images obtained by objectively measuring the ONH structure and detecting changes between a reference image (baseline exam) and other images (follow-up exams).

In this context, important advances in technology for non-invasive imaging of the eye have been made providing quantitative tools to measure structural changes in ONH topography, an essential element in detecting glaucoma and monitoring its progression. In particular, the heidelberg retina tomograph (HRT), a confocal scanning laser technology, has been commonly used for glaucoma diagnosis since its commercialization 20 years ago [3]. A limited number of strategies have been proposed that quantitatively and qualitatively detect glaucomatous progression using HRT images. In [4], the topographic change analysis was proposed for assessing glaucomatous changes. This technique has been shown to classify progressing and stable eyes with reasonably good sensitivity and specificity. Another method called the proper orthogonal decomposition [5] indirectly utilizes the spatial relationship among voxels by controlling the family-wise Type I error rate. The Markov random field (MRF) model was used in [6] to model the inter/intra observations dependency allowing a better glaucoma progression detection rate. However, the HRT imaging technique is limited by its lower resolution (i.e. 300 μm axial resolution for the HRT3). Moreover, because HRT is limited to ONH surface topography, it cannot differentiate between retinal layers. It provides an indirect measure of RNFL thickness that is calculated as the difference between the retinal surface and a standard reference plane 50 μm below the surface of the retina temporal to the ONH.

In contrast, the 3D spectral domain optical coherence tomography (SD-OCT)can differentiate between retinal layers and provide quantitative estimates for change detection. SD-OCT is now the most commonly used instrument for imaging both the ONH and the RNFL thickness. Numerous studies have evaluated glaucoma detection using SD-OCT images. However, most of the studies use the RNFL measurements provided by the commercially available spectral-domain optical coherence tomographers for change detection [7]. Although those methods are successfully applied to SD-OCT images, its use is constrained by specific pre-requisite: it requires an accurate estimation of the RNFL layer thickness. In [8], authors showed that the instrument built-in segmentation software is relatively robust to the image quality and the noise may lower the accuracy of the RNFL layer thickness estimation.

In this paper we propose a hierarchical framework for glaucoma progression detection using 3D Spectralis (Heidelberg engineering) SD-OCT images. This paper is an extended version of the conference paper [9]. Specifically, we explain in more details the change detection algorithm and we add more experiments in the results section. Moreover, we propose the use of a new kernel-based classifier to improve the results of the fuzzy classifier. In contrast to previous works that use the RNFL thickness measurement, we consider the whole 3D volume for progression detection. Our framework is divided into two steps: (1) change detection step which consists of detecting changes between a baseline image and a follow-up image and (2) a classification step which consists of classifying the detected changes into random changes or true changes due to glaucoma progression. For the first step, we propose a fully Bayesian framework for change detection since these methods are relatively simple and offer efficient tools to include *a priori* knowledge through the *a posteriori* probability density function (PDF). In particular, we propose the use of the MRF model to exploit the statistical correlation of intensities among the neighborhood voxels [10]. In order to develop a noise robust algorithm, we propose consideration of the change detection problem as a missing data problem where we jointly estimate the noise hyperparameters and the change detection map. The widely used procedure to estimate the different problem parameters is the Expectation-Maximization (EM) algorithm [11]. However, since we used the MRF model with the change detection map as the prior for the change detection map, the optimization step is intractable. Hence, we propose the use of a Monte Carlo Markov chain (MCMC) technique [12].

Once the change detection map is estimated, we propose the use of kernel-based classifier for glaucoma progression detection. Kernel-based classifiers have several advantages compared with other approaches; they reduce the dimensionality of the data, increase the reliability and the robustness of the method in the presence of noise and allow flexible mappings between objects (inputs) represented by features vectors and class labels (outputs) [13]. As no prior knowledge on glaucoma progression is available, we are interested in the one class classifier where only the control data (healthy eyes and stable glaucoma eyes) are used to train the classifier. To this end, we have elected to use the support vector data description (SVDD) method [14] here. The SVDD one class-classifier method maps the data into a high-dimensional feature space. In this new space, a hypersphere that encloses most of the dataset belonging to the class of interest (the *target* class). Although basic kernel functions can be successfully applied for change detection [15–17], they do not exploit the additional constraints that are often available, such as the dependencies and the distribution of different features. We show in this paper that the classification should be more efficient if such information is integrated. To account for these characteristics in our change-detection scheme, we propose the use of a new kernel function that combines some properties of the old kernel functions with new information about the feature distribution and dependencies [17].

The paper is divided into three methodology sections. In Section 2, the proposed change detection scheme is presented. In Section 3, we describe the classification step. Then, in Section 4 results obtained by applying the proposed scheme to clinical data is presented. The diagnostic accuracy of this novel proposed approach is compared to two existing progression detection RNFL based approaches: the artificial neural network classifier (ANN) and the support vectors machine (SVM) classifier.

2. Change detection

2.1. Direct model

Let us consider the detection of changes in a pair of amplitude images. We denote by $I_0 = \{I_0(i)|i = 1, \ldots, M\}$ and $I_1 = \{I_1(i)|i = 1, \ldots, M\}$, where M is the number of the image voxels, two images acquired over the same eye at times t_0 and t_1, respectively ($t_1 > t_0$), and coregistered. In this work, we assume that the noise is additive, white and normally distributed.

The Spectralis SD-OCT instrument features three different options to enhance reproducibility and reduce the noise. A real time eye-tracking device (eye tracker) compensates for involuntary eye movements during the scanning process, a retest function assures that follow-up measurements are taken from the same area of the retina as the baseline examination and a Heidelberg noise reduction option that average automatically several images (10 images are the number recommended by the manufacturer) at the same location to increase image signal to noise ratio (SNR) and improve the quality of subsequent images. As recommended by the manufacturer, only images with a signal quality of equal or greater than 20 dB were used in this study. The mean and the standard deviation of different image qualities are 26 dB and 3, respectively (range 20–40 dB). In this study, five images have a SNR equals to 40 dB (1% of the whole number of images). We assume in these images that most of the noise was removed by the instrument. These images are then used to study the distribution of the retinal