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New algorithms to characterize and classify ophthalmic images

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ABSTRACT

Unprecedented advances in machine learning have led to a variety of algorithms for the remote evaluation of biomedical images, allowing for cost-effective early detection of diseases. In particular, a lot of efforts are focused on the development of reliable image analysis tools for the early diagnosis of eye diseases. Here we present several new methods for ophthalmic image analysis. We propose a machine learning algorithm for ordering images of the anterior chamber (optical coherence tomography, OCT), which extracts features that discriminate between healthy subjects and patients with angle-closure. We also present an algorithm to detect the OCT images that contain artifacts, and we show that removing these images from the data base improves the performance of the ordering algorithm. Finally, we present algorithms for the analysis of retina fundus images, which are able to segment the vessel network in the retina and extract features from the topological tree-like network structure. We show that these features discriminate between healthy subjects and those with glaucoma or diabetic retinopathy.

Keywords: ophthalmic image analysis, retina fundus image analysis, optical coherence tomography, machine learning, outlier mining

1. INTRODUCTION

Photonics, artificial intelligence and big data are transforming the field of medical imaging, and in particular, the field of ophthalmic imaging.¹⁻⁷ New optical imaging modalities and image analysis tools now allow for the accurate remote eye evaluation, causing unprecedented advances in the early diagnoses of eye disorders, treatment decisions and treatment follow-ups.

Optical coherence tomography (OCT) is a tomographic high-resolution imaging modality that, when used to inspect the anterior segment (AS-OCT), allows the visualization and measurement of the anterior chamber angle, needed for the diagnosis of glaucoma (open-angle or closed-angle glaucoma). Another popular imaging modality is the retinal fundus imaging, which allows to visualize the main structures in the central and peripheral retina, optic disc and macula, whose features may indicate the presence of diseases such as diabetic retinopathy or glaucoma. Importantly, the retina is a noninvasive window for studying brain deceases such as Alzheimer or dementia, because changes in retinal microvasculature may reflect similar changes in cerebral microvasculature.⁸

Here we first present novel algorithms to analyze a database of AS-OCT images: we demonstrate machine learning algorithms to order the images of an AS-OCT image database according to the degree of angle-closure,⁹ and also, to identify the images in the database that contain artifacts.¹⁰ In the second part we present novel algorithms for the analysis of color retinal fundus images.¹¹ These algorithms segment the images and return features of the retinal blood vessel network structure that quantify changes in patients diagnosed with glaucoma or with diabetic retinopathy.

2. ALGORITHMS FOR ANTERIOR SEGMENT OCT IMAGE ANALYSIS

2.1 AS-OCT image database

The database consists of 1213 AS-OCT images of the eyes of healthy and non-healthy patients of the Instituto de Microcirugia Ocular (IMO) in Barcelona.¹² The images were acquired using a Visante OCT instrument

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Figure 1. Examples of the four categories of anterior chamber OCT images, classified by glaucoma experts: closed (top), narrow (middle-top), open (middle-bottom), and wide open (bottom).

(Carl Zeiss Meditec) using the “Anterior segment” scan and the “Enhanced anterior segment” scan. The image resolution is 256-by-1024 pixels, which corresponds to an area of 16 mm-by-8 mm. Image pre-processing (homogenization, filtering, centering and aligning) is described in Ref.⁹ The AC-OCT images were classified in four categories by two ophthalmologists experts in glaucoma: close, narrow, open, and wide open. Examples are shown in Fig. 1.

2.2 Unsupervised machine learning algorithms

The machine learning algorithms start with the distance matrix, D_{ij} , between images i and j (after processing each image by filtering, centering and aligning), which is defined pixel-to-pixel. Two distance measures were tested (Hellinger and Euclidean), and similar results were obtained.

The first algorithm uses the matrix D_{ij} as input to well-known nonlinear dimensionality reduction algorithms (Isomap¹³ or t-SNE¹⁴), which return two features that allow ordering the images in a 2D plane. The second algorithm, described in Ref.¹⁰ uses Isomap to learn the low-dimensional manifold in which the images are embedded, and assigns to each image an outlier score by comparing the geodesic distances with the distances in the low-dimensional space.

2.3 Results and discussion

Figure 2 shows the Image Map obtained from the two features returned by Isomap. The images are ordered such that wide-angle (close-angle) images are located on the left (on the right) side of the map. As shown in Fig. 3, the features are in good correlation with the classification in four categories done manually by expert ophthalmologists.

Figure 4 shows that the performance of the algorithm, measured by the correlation coefficient between the feature returned by the ordering algorithm and the feature provided by manual expert annotation (mean angle),

Figure 2. Image Map obtained from the two features returned by the nonlinear dimensionality reduction algorithm Isomap.

Figure 3. Comparison between the features returned by the machine learning algorithm and the manual classification.

improves when the images that contain artifacts (outliers detected by the outlier detection algorithms proposed in Ref.¹⁰) are removed from the database. The different lines show results with different methods of outlier identification and the colored region indicates results when the images removed are randomly selected. In this latter case, as expected, there is no significant change in the performance of the algorithm.

3. RETINAL FUNDUS IMAGE ANALYSIS

In this section we present new tools for the analysis of color retinal fundus images. First, we use an automatic unsupervised segmentation algorithm to extract a weighted tree-like graph from the retina blood vessel structure.¹⁵ The nodes represent branching (bifurcation) points and endpoints; the links represent vessel segments that connect pairs of nodes. An example is shown in Fig. 5. The link between two nodes i and j has an associated weight, $w_{ij} = l_{ij}^l W_{ij}^a$, where W_{ij} is the width and l_{ij} is the length of the segment that connects i and j ,

Figure 4. Performance of the ordering algorithm as a function of the number of outliers that are removed from the database. For some methods a sharp improvement (marked with a circle) is observed when removing a particular image.

and l and a are adjustable exponents. Then, we use a graph-dissimilarity measure¹⁶ and Isomap¹³ to quantify structural differences between the graphs extracted from the groups of healthy and non-healthy patients. We also use fractal analysis to characterize the extracted graphs.¹⁷

Applying these techniques to three retina fundus image databases (HRF,¹⁸ Messidor¹⁹ and a database from patients of IMO¹²) we found significant differences between the healthy and non-healthy groups (p-values lower than 0.005 or 0.001 depending on the method and on the database).¹¹ An example obtained with the manual segmentation of the HRF database is shown in Fig. 6. The results are sensitive to the segmentation method and to the resolution of the images. When analyzing images with low resolution, the differences found among the groups are not as statistically significant, which suggests that the differences found correspond to differences in the thinnest vessels of the network.

4. CONCLUSIONS

To summarize, new algorithms have been proposed to analyze, order and classify ophthalmic images (anterior segment OCT and retinal fundus images) according to relevant features. The OCT algorithm doesn't need training and it does not rely on specific landmarks; thus, it can analyze images in which relevant landmarks are not visible or not easy to locate. In addition, outlier finding algorithms allow to identify and remove from the image database the images that contain artifacts, improving the performance of the ordering algorithm.

In high-resolution fundus images, the analysis of the structure of the retinal vascular network was found to be a good discriminator for healthy and non-healthy patients. However, in order to use the graph-based features as reliable indicators of the development of retinal diseases, further progress is needed in the development of accurate and fully automated segmentation methods.

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Figure 5. Example of a raw fundus image (a) and the result of the pre-processing (b), segmentation (c) and graph identification (d) algorithms.

Figure 6. IsoMap features obtained from the manual segmentation of the HRF database.

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