Platform Image Processing Applied to the Study of Retinal Vessels

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Abstract. Recent studies have found retinal vessel caliber to be related to the risk of hypertension, left ventricular hypertrophy, metabolic syndrome, stroke and others coronary artery diseases. The vascular system in the human retina is easily perceived in its natural living state by the use of a retinal camera. Nowadays, there is general experimental agreement on the analysis of the patterns of the retinal blood vessels in the normal human retina. The development of automated tools designed to improve performance and decrease interobserver variability, therefore, appears necessary. This paper presents a study focused on developing a technological platform specialized in assessing retinal vessel caliber and describing the relationship of the results obtained to cardiovascular risk.

Keywords: arteriolar–venular ratio, arterial stiffness, cardiovascular disease, AI algorithms, pattern recognition, image analysis, expert knowledge.

1 Introduction and Background

Retinal images have an orange form, varying with the skin color and age of the patient. Fundoscopy provides important information, as it enables detecting diseases of the eyes, which is also the only area of the body where small blood vessels can be studied with relative ease. There are many systemic diseases (hypertension, diabetes, atherosclerosis, left ventricular hypertrophy, metabolic syndrome, stroke, and coronary artery disease) that affect vessels of this size in a relatively slow and silent way. It is, however, frequently impossible to directly assess the extent of this damage during a physical examination, as the affected organs, e.g. kidneys, are well hidden. Evaluation of the retina provides an opportunity to directly visualize these functions. Based on this information, expert clinicians can make educated guesses as to what is occurring elsewhere in the body. Image processing techniques are growing in prominence in all fields of medical science. Automatic detection of parameters from retinal images is an important problem since they are associated with the risk of diseases such as those named above [29][31][33]. The cataloging of key features such as the optic disc, fovea and the retinal vessels as reference matches is a requirement to systems being able to achieve more complex responsibilities that identify pathological

J. Sáez-Rodríguez et al. (eds.), *8th International Conference on Practical Appl. of Comput. Biol. & Bioinform. (PACBB 2014)*, Advances in Intelligent Systems and Computing 294,
DOI: 10.1007/978-3-319-07581-5_3,

entities. There are a lot of techniques for identifying these structures in retinal photographs. The most studied areas in this field can be classified into three groups [21]: (i) The *location of the optic disc*, which is necessary for measuring distances in retinal images, and for identifying changes within the optic disc region due to disease. Techniques such as analysis of intensity pixels with a high grey-scale value [18][11] or principal component analysis (PCA) [19] are used for locating the disk. Other authors [16] use the Hough transform (a general technique for identifying the locations and orientations of certain types of shapes within a digital image [16]) to locate the optic disc. A ''fuzzy convergence'' algorithm is another technique used for this purpose [12]. (ii) The *detection of the fovea*, habitually chosen as the position of maximum correlation between a model template and the intensity image [19]. (iii) The *segmentation of the vasculature form retinal images*, that is, the representation of the blood vessels and their connections by segments or similar structures. There are many techniques to accomplish this, the most significant of which are: (i) matched filters, which typically have a Gaussian or a Gaussian derivative profile [3] [13] [20] [14]; (ii) vessel tracking, whereby vessel center locations are automatically sought over each cross-section of a vessel along the vessels longitudinal axis, having been given a starting and end point [28]; (iii) neural networks, which employ mathematical ''weights'' to decide the probability of input data belonging to a particular output [1]; and (iv) morphological processing, which uses characteristics of the vasculature shape that are known a priori, such as being piecewise linear and connected [12].

Present scientific literature includes much research focused on automating the analysis of retinal images [25] [15] [4][10][12]. In this paper, we propose a novel image processing platform to study the structural properties of vessels, arteries and veins that are observed with a red-free fundus camera in the normal human eye. The platform, called Altair "*Automatic image analyzer to assess retinal vessel caliber*" [30], employs analytical methods and AI (Artificial Intelligence) algorithms to detect retinal parameters of interest. The sequence of algorithms represents a new methodology to determine the properties of retinal veins and arteries. The platform does not require user initialization, it is robust to the changes in the appearance of retinal fundus images typically encountered in clinical environments, and it is intended as a unified tool to link all the methods needed to automate all processes of measurement on the retinas. Section 2 introduces the platform and its most important characteristics, showing some of the relevant techniques and results. Finally, some conclusions and results are presented in section 3.

2 Description of the Platform

The platform facilitates the study of structural properties of vessels, arteries and veins that are observed with a red-free fundus camera in the normal human eye. The retina is the only human location where blood vessels can be directly visualized non-invasively by the use of a retinal camera. Figure 1 displays a retinal image in which branching blood vessels are shown. The bigger, darker ones are the veins and the smaller, brighter red structures the arteries. Changes in the appearance of the arteries as well as alterations in the arterial-venous crossing pattern (av index) occur with atherosclerosis

and hypertension. These vessels are more obvious in the superior and inferior aspects of the retina, with relative sparing of the temporal and medial regions. to the use of the platform allows expert clinicians to observe the parameters measured by regions or quadrants to discriminate the information that they do not consider relevant.

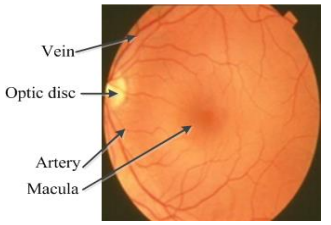

Fig. 1. A retinograph usually takes three images of each eye; this image corresponds to the photograph with the disc on one side. The nose is on the left side.

Different analytical methods and AI algorithms are used to determine the scaling properties of real objects, yielding different measures of the fractal dimension, length and area of retinal veins and arteries. The main objective is to relate the level of cardiovascular risk in patients to everything that can be observed in the retinas. In this work we are interested in obtaining as much information as possible from the images obtained, and have focused on the following: (i) Index Artery / Vein: represents a relationship between the thickness of arteries and veins. (ii) Area occupied by the veins and arteries. (iii) Distribution of the capillary: according to the blood distribution, the color distribution of the capillaries varies.

Based on the values for area, length and position of the vascular system in healthy patients, we expect to determine ranges of normalcy within the population for their subsequent application to subjects affected by various diseases.

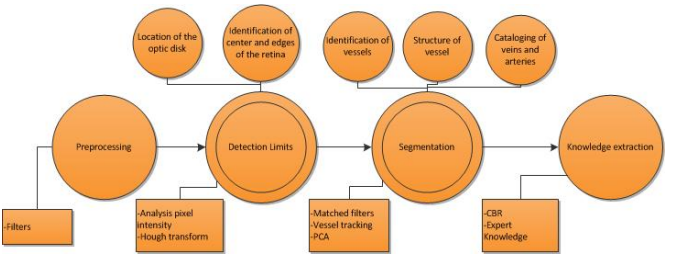

Fig. 2. Outline of the platform

The next subsections describe the main phases through which the retinal image passes within the platform. Figure 2 shows the diagram that represents these phases. The circles represent modules in the platform; some of them are divided and contain different submodules. The original image passes through each one of the modules (preprocessing, detection, segmentation and extraction of knowledge) which use different techniques and algorithms to obtain the desired image information. The main techniques are represented in the squares. This sequence of steps is a methodology that is explained in the following section, also showing examples of the results obtained.

2.1 Phases

The methodology used to obtain the functionality of the platform may be divided into two phases. Firstly, a phase called "digitization of the retina", in which the different parts of the eye image are identified. Here a data structure is created, which makes it possible to represent and process the retina without requiring the original image. This phase includes modules of preprocessing, detection and segmentation. Secondly, a phase of "measurements" in which we work with retinas that have been previously identified. This phase includes extraction of knowledge and manual correction, or expert knowledge, if necessary.

This paper focuses on the first phase, which is in charge of creating and identifying all the elements of interest of the retina. To carry out these phases, the following steps are necessary.

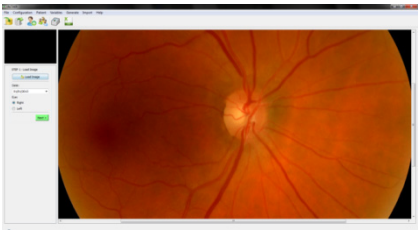

Fig. 3. Load image and find macula. First step in the platform.

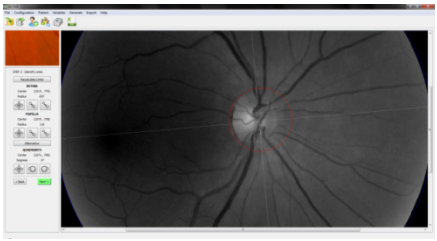

Fig. 4. Identify the papilla in the retinal image

2.1.1 Preprocessing

During the testing, a retinography was performed using a Topcon TRC NW 200 nonmydriatic retinal camera (Topcon Europe B.C., Capelle a/d Ijssel, The Netherlands), obtaining nasal and temporal images centered on the disk (Figure 1). The nasal image with the centered disk is loaded into the platform software through the preprocessing module (Figure 3). The preprocessing or filtering module reduces noise, improves contrast, sharpens edges or corrects blurriness. Moreover, the platform is able to automatically detect the type of image (left or right eye) and find the macula by using dynamic thresholds, binary filters and comparing both sides. Some of these actions can be carried out at the hardware level, which is to say with the features included with the camera.

2.1.2 Detection Limits

This module is in charge of locating the disk and identifying the center, edges and regions of the retina (Figure 4). The aim is to construct a data structure that identifies each part of the retina based on the matrices of colors representing the images obtained (Figure 1). In this phase, image processing techniques were used to detect intensity based on the boundaries of the structures [12][4]. The identification of the papilla is important since it serves as the starting point for the detection and identification of the different blood vessels.

This phase identifies the boundaries and the retinal papilla from an RGB image of the retina. The following values are returned: C_r is the center of the retina, which identifies the vector with coordinates *x, y* of the center of the retina. C_p is the center of the disc, which identifies the vector with the coordinates *x, y* of the center of the papilla. R_r, is the radius of the retina. R_p, is the radius of the papilla. As an example, a sequence of output values in this phase is shown in the following table and figure:

Table 1. Sequence of output values in detection modules (pixel)

C_r	C_p	R_r	R_p
1012,44 ; 774,13	**1035,98 ; 734,11**	**692,68**	**111,76**
	1104,87 ; 562,52		108,92
	915,38 ; 736,77		122,15
	900,27 ; 658,74		101,95

In order to identify the limits, and in particular to identify the circumferences, it became necessary to carry out a process of image segmentation. Segmentation is the process that divides an image into regions or objects whose pixels have similar attributes. Each segmented region typically has a physical significance within the image. It is one of the most important processes in an automated vision system because it makes it possible to extract the objects from the image for subsequent description and recognition. Segmentation techniques can be divided into three main groups: techniques based on the detection of edges or borders [16], thresholding techniques [18], and techniques based on clustering of pixels [11]. After analyzing the possibilities, we chose one of the techniques from the first group that provided the best results and that, in this case, uses an optimization of the Hough transform [16]. This technique is very robust against noise and the existence of gaps in the border of the object. It is used to detect different shapes in digital images. When applying the Hough transform to an image, it is first necessary to obtain a binary image of the pixels that form part of the limits of the object (applying edge detection). The aim of the Hough transform is to find aligned points that may exist in the image to form a desired shape. For example, to identify line points that satisfy the equation of the line: ($\rho = x \cdot cos\ \theta + sen\ \theta$, in polar coordinate). In our case, we looked for points that verify the equation of the circle: (i) in polar coordinate system: $r^2 - 2sr \cdot cos\ (\theta - \alpha) + s^2 = c^2$, where (s, α) is the center and c the radius; (ii) in Cartesian coordinate system: $(x-a)^2 + (y-b)^2 = r^2$, where (a,b) is the center and r the radius.

The algorithm is not computationally heavy, as it does not check all radius, or all possible centers, only the candidate values. The candidate centers are those defined in a near portion of the retina, and the radius is approximately one sixth the radius of the retina. To measure the approximate diameter of the retina, the algorithm calculates the average color of the image column: diameter of the retina is the length that has a non-zero value (black).

Identifying the papilla is a necessary step because it provides a starting point for other stages of segmentation and serves as a reference point for some typical

measurements. Typically the correct result is the circumference of the higher value in the accumulator (over 70% of cases). In almost 100% of the cases, the correct identification can be found among the 3 greatest values found by the accumulator. In this phase it is divided into image regions (squares), for further handling by experts.

2.1.3 Segmentation of the Vasculature from Retinal Images

The ultimate goal is to identify each blood vessel as a series of points that define the path of the vessel. Each of these points will be assigned a certain thickness. Moreover, it will be necessary to distinguish whether a particular blood vessel is a vein or an artery. AI algorithms responsible for identifying veins and arteries must perform a series of sweeps in search of "key points". Algorithms based on matched filters[3] [13] [20] [14], vessel tracking [25] and PCA [19], among others, are used for obtaining the proximity points between objects (veins, arteries, capillaries), the structures retinal structures or assemblies, branching patterns, etc. These algorithms work with transformations of the original image of the retina obtained from the previous step. Three steps are necessary within this module: (i) identification of vessels; (ii) definition of the structure of vessel; (iii) cataloging of veins and arteries.

- Identification of vessels: In this step the blood vessels are identified in the image by thresholding techniques. Their purpose is to remove pixels where the structuring element does not enter, in this case the blood vessels. The image on the retina is blurred to keep an image similar to the background. This image is used as a threshold so that the pixels of the original image will be treated as vessels if their intensity reaches 90% of the background intensity.
- Structure of vessel: This phase defines the tree forming blood vessels. Various techniques are used in conjunction with the following steps:
- Cataloging of veins and arteries: To detect whether a vessel is vein or artery, the main branch is taken of the vessel. The platform carries out an automatic differentiation between veins and arteries by comparing the detected vessels and the nearest background colors (R and G layers). It is possible to make manual changes if necessary for vessels that have been incorrectly identified.

The following images show the output of this phase. At the end of this stage the entire arterio-venous tree is stored in a structured way, making it possible to know not only if a vessel passes through a point or not, but through which point each vessel passes, which one is the parent vessel, etc.

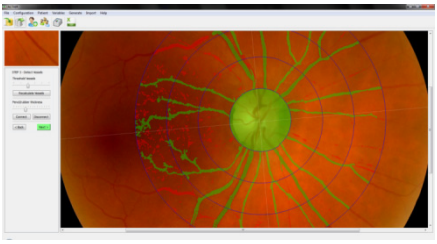

Fig. 5. Structure of the vessels

Fig. 6. Arteries and veins detection

2.1.4 Knowledge Extraction

The system provides statistical methods to facilitate the analysis of the data, and allows analyzing the relationship between vein thickness, artery thickness, AV index, artery area and vascular area with different pathologies. The analysis of different pathologies is performed in an assisted way and, so that it is not necessary to use additional software. Besides, the system incorporates traditional statistical functionality to analyze continuous variables. The ANOVA parametric test [6] and the Kruskal-Wallis non-parametric test [24] are provided to analyze the influence of a continuous variable with respect to a categorical variable.

The system does not define categorical variables, but it allows creating intervals from continuous variables. Chi squared [17] is provided to perform dependency analysis methods. When the expected frequencies are less than 5, the result may not be correct so a Yates correction is applied to try to mitigate this effect. Finally, a Fisher exact test [32] is applied when working with a small size sample and it is not possible to guarantee that 80% of the data in a contingency table have a value greater than 5.

A case based reasoning system is incorporated to make predictions about categorical variables from the system variables. The system allows grouping the cases by applying EM [2]. EM was selected because it allows an automatic establishment of the number of clusters. The most similar cluster to the new case is recovered during retrieve phase of the CBR cycle by applying the nearest neighbor technique. If the memory of cases was not structured in clusters, then there is a single cluster. During the retrieve phase, the system retrieves not only the most similar cluster, but also the classifier associated with the cluster. More especifically, C4.5 algorithm [22] is used because it makes easy to interpret the results over alternatives SVM , Bayesian networks, bagging, etc. In the reuse phase, a C4.5 decision tree is used to perform the classification of the patient according to the variable taken into consideration. Then, in the review phase, the system obtains information about the decision tree and the kappa index in order to interpret and analyze the efficiency of the classifier. Finally, in the retain phase, the user determines if the new case should be stored. If that is the case, the clusters and trees are rebuilt.

3 Results and Conclusions

In this work, we have assessed the performance of our platform using retinal images [30] acquired from Primary Care Research Unit La Alamedilla, SACYL, IBSAL, Salamanca, Spain. The images were obtained using a TopCon TRC-NW6S Non-Mydriatic Retinal Camera.

Figure 7 shows the tests performed using 10 retinal images. No difference was found between values in terms of age, sex, cardiovascular risk factors, or drug use. The figure shows: Area veins and arteries, AV index (AV), Veins P (VP) = number of veins around the papilla, Veins A (VA)= number of veins that cross the corona outlined with radius=2*R_p. R_p is the radio of the papilla, Veins B (VB)= number of veins that cross the corona outlined with radius=3*R_p, same values for arteries.

The values for the arteries are the same. It is possible to observe the measurement of the values for veins and arteries (thickness, area) are similar between different retinas (in this case no retinal images of sick patients were introduced).

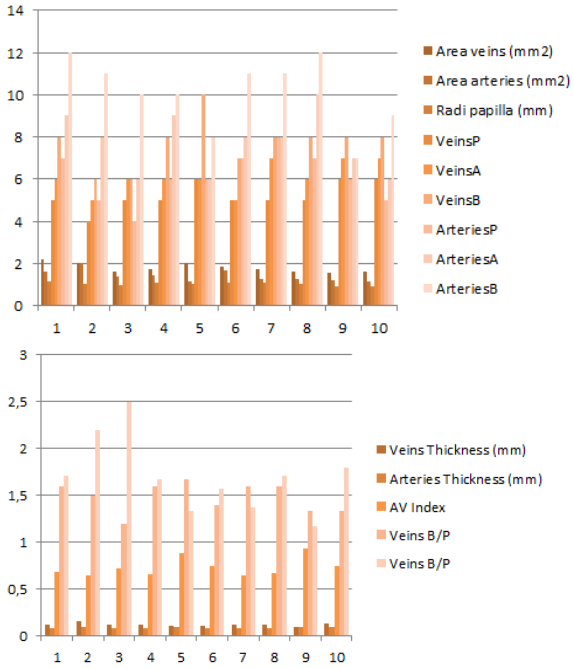

Fig. 7. Relations between the parameters obtained by the platform

Parameters like the veins in the papilla and AV index are the most fluctuating. Due to the lack of a common database and a reliable way to measure performance, it is difficult to compare our platform to those previously reported in the literature. Although some authors report algorithms and methods [25] [15] [4][10] [12] that performed in a manner similar to that of our platform, these results may not be comparable, since these methods are tested separately and were assessed using different databases. Since automation has been valid and verified, our next step is to compare the values obtained with significant medical values in our database including the case based reasoning system proposed in previous section.

The platform is intended to be used as a unified tool to link all the methods needed to automate all processes of measurement on the retinas. It uses the latest computer techniques both statistical and medical. In a research context, the platform offers the potential to examine a large number of images with time and cost savings and offer more objective measurements than current observer-driven techniques. Advantages in a clinical context include the potential to perform large numbers of automated screening for conditions such as risk of hypertension, left ventricular hypertrophy, metabolic syndrome, stroke, and coronary artery disease, which in turn reduces the workload required from medical staff. As a future line of study in this point, the next step would be to analyze the significance of the measurements obtained with regard to their meaning in a medical context. That is, to describe the relationship of the results obtained to the risk of cardiovascular disease estimated with the Framingham or similar scale and markers of cardiovascular target organ damage.

Acknowledgements. This work has been carried out by the project *Sociedades Humano-Agente: Inmersión, Adaptación y Simulación*. TIN2012-36586-C03-03. Ministerio de Economía y Competitividad (Spain). Project co-financed with FEDER funds.

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