ALTAIR: Supervised Methodology to Obtain Retinal Vessels Caliber

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ABSTRACT

A back of the eye examination allows performing a noninvasive evaluation of the retinal microcirculation, as well as of the vascular damage induced by multiple cardiovascular risk factors. The objective of this work is to study the existing needs to lead to the development and validation (reliability and validity) of a methodology able to extract all the information from the images of the back of the eye to solve the studied needs. Its development will subsequently allow analyzing its utility in various clinical environments. Currently there are different works that evaluate the thickness of the retinal veins and arteries, but they require either full intervention by an observer or no intervention at all, so when facing incorrect analysis (none of them achieves a 100 % accuracy in automatic analysis) erroneous results can be a serious problem when drawing conclusions. The proposed solution refers to the second group (automatic), but providing a supervisor the possibility to interfere with the analysis when any kind of error is produced, which ideally will not happen many times. Thanks to this the possible subjectivity that can be introduced by the supervisor does not affect the final result of the analysis.

1. Introduction

Fundus examination allows noninvasive assessment of retinal microcirculation and vascular damage induced by multiple cardiovascular risk factors. This test is performed by analyzing the images generated by a machine called retinograph. These kind of images have an orange tone which varies with skin color and age of the patient. But they also hide on them a lot of information to detect diseases.

A relationship between blood vessels and different diseases such as hypertension, left ventricular hypertrophy or stroke has been already found (Tanabe *et al*., 2010; Tikellis *et al*., 2008; Wong *et al*., 2004; Yatsuya *et al*., 2010; McGeechan *et al*., 2009).

Different methodologies to calculate the thickness of retinal arteries and veins have been developed, but most of them have some kind of deficiency. On the one hand, too much intervention by an expert supervisor is required by some of those methodologies, which may influence the tests results. On the other hand, there are other methodologies which are completely automatic and no intervention is required. In this case, some errors could be included because of the inherent lack of precision of this kind of analysis. These errors would be accumulated and would negatively affect the phase of knowledge extracting. Finally, there are other methodologies that do not extract all the information required to carry out a complete clinical study.

For this reason, the medical research team involved in this work, associated to the Research Unit of La Alamedilla Salamanca (Sacyl), wanted to develop a tool with a new methodology adapted to its needs.

This team has recently revealed that the measures of the vessels, especially venous caliber and arteriovenous index (AV Index or AVIx), behave like independent variables capable of predicting cardiovascular risks estimated with the Framingham scale (García-Ortiz *et al*., 2013), as well as renal microvascular injuries. This positive association between cardiovascular risk and venous caliber is related to the results published by (Wong *et al*., 2002; McGeechan *et al*., 2008). These results show an association between AV Index and the risk of coronary heart disease. Thus, the use of these parameters was considered necessary in prospective studies with more patients in order to clarify the discrepancies found in different jobs, and developing a new tool which can extract those parameters seems to be the best way to do it.

With the amount of information that the image of the retina can offer, not only regarding arteries and veins thickness, which is the way of getting the AV Index value, other relevant data or results can be obtained in order to assess other aspects.

Therefore, the proposed methodology should offer the medical research team enough parameters to meet their research needs. Clearly, the measurements taken by the proposed methodology must be reliable and validated before analyzing their usefulness in different clinical environments.

In addition, sharing the image analysis parameters may be possible in order to increase the population sample, which increases the reliability of the results.

The rest of the article is structured as follows. Section 2 introduces both retina elements and the existing tools and methodologies to analyze images with similar features. The proposed system is described in the section 3. Finally, section 4 presents the results, conclusions and the future research lines.

2. Retina and its Analysis Methodologies Overview

In this section, the reasons for carrying out fundus images analysis are presented. This is mainly because of their relation to certain diseases, which are also presented. For a complete analysis, the characteristics of these kind of images must be known, so their components are explained below.

Retina allows blood vessels to be directly visualized in a non-invasively manner. Different conclusions regarding the association between the obtained information and certain pathologies can be extracted from vessel identification and analysis. So the greatest potential of retinal analysis is the ability to perform automated diagnostics (Patton *et al*., 2006).

On the other hand, technological advances in the last two decades have made digital image processing to become more and more powerful. This make it possible to accurately extract the needed information in a really short time.

Thus, developing a platform that combines both different algorithmic and computer vision techniques applied to fundus analysis is the overall objective of this work. These techniques will be implemented to test the reliability and validity of the methodology. Then, the vessels information provided by the platform could be used. This extracted information should also be composed by those parameters which have been proved to be related to diseases, pathologies or risks, as in the case of the average thickness of veins and arteries.

To do so, a first functional version of the assistant tool to implement these investigated and proposed techniques has been developed. It is able to extract the necessary information, improving the one presented in (Chamoso *et al*., 2014).

Some of those pathologies that can be directly related to this kind of information, as published by different studies (Leibowitz *et al*., 1979; Wong *et al*., 2006; Dahlöf *et al*., 1992; Wong *et al*., 2002; Wong *et al*., 2001; Wong *et al*., 2004), are: diabetic retinopathy, macular degeneration, retinal detachment, retinitis pigmentosa, blood vessel disorders, arteriosclerotic retinopathy, hypertensive retinopathy, retinal vein obstruction, stroke, left ventricular hypertrophy, metabolic syndrome, atherosclerosis or artery coronary.

In order to perform the analysis, it is important to identify the fundus image components, which components correspond to certain parts of the retina. In addition to blood vessels, optic disc or papilla, macula and fovea can be found.

The **macula** is a spot located in the retina, particularly in the back side, whose diameter is approximately 5 mm. It is located in the temporal part of the eye and locating it allows knowing which one is the eye being analyzed (left one or right one).

The **Fovea** can be found within the macula, in the central area and it is located in the deepest place so its color is darker. Its diameter is usually about 1.5 mm.

Another part is the **optical disc**. It is also known as optic papilla. It is the part of the retina where the optic nerve arises and it represents the access point for the blood vessels of the retina.

Once these elements that facilitate the analysis are known, artificial or computer vision should be explained. Computer vision is a field of artificial intelligence that includes some methods to acquire, process, analyze and understand images and, in general, high-dimensional data of the real world in order to produce numeric or symbolic information (Klette, 2014). The complete organization of an artificial vision system is:

- **Image acquisition**: in this case, the digital image is generated by a retinograph.
- **Preprocessing**: different techniques can be applied before applying artificial vision in order to process specific information. In general, this step is required to ensure certain implicit assumptions. Noise reduction is a good preprocessing example. It is usually used to remove false information introduced by the sensor used to take the image. Contrast enhancement techniques to ensure relevant information is detectable are also common.
- **Feature extraction**: this step consists in extracting features from the image in different complexity levels from the image data. Lines, ridges, peaks and localized points of interest such as corners or spots are typical examples of such features.
- **Detection or segmentation**: at some point in the processing, decisions about the image points or regions that are relevant for further analysis are taken, such as the selection of a specific set of interest or the segmentation of some of the image areas containing a specific object of interest.
- **High-level processing**: verifying that extracted data satisfy the specific cases.
- **Decision-making**: final decisions required by the application, such as the approval or rejection in automated inspection applications.

2.1. Tools and Techniques

Techniques and characteristics of similar existing platforms are presented in this section. Then, a summary of the techniques applied to every part of these and other existing tools are presented.

Despite the increase of the power of computer vision in recent years, fundus image analysis is not a new technique as it was already used more than 15 years ago.

One of the earliest research was the one performed by (Chapman *et al*., 200), where algorithms based on adaptive filtering techniques used to emphasize the vessels were presented.

Morphological methods have been also applied successfully, which have been proved very effective in extracting features from images whose form is kwon a priori, as in this case. They have been successfully used in works such as (Zana *et al*., 1997; Zana *et al*., 1999; Matsopoulos *et al*., 1999) for segmentation of the vasculature, being especially useful for the detection of micro-aneurysms.

More recently, (Sanchez *et al*., 2008) presented a new automatic preprocessing image algorithm for detecting retinal exudates, something very similar to the detection discussed in this paper, but less complete.

In (Ege *et al*., 2000) a design of the steps required for the detection of diabetic retinopathy is proposed. They considered a first block of 'Image preprocessing', followed by 'Shape estimation', then a step of 'Feature extraction' and finally a step for 'Classification'.

In (Martinez-Perez *et al*., 2007) different techniques are presented when trying to measure the blood vessels for diseases such as diabetes, hypertension or premature retinopathy.

There is a precedent in the team involved in this research. Studies based on a software called 'AVIndex' and their results has been published in (García-Ortiz *et al*., 2012). They have requested the extension of such software in order to complete their studies, since the extracted information is now scarce.

When reviewing computer vision techniques applied on similar tools to the one presented, three common phases have been considered: 'Preprocessing' (Table 1), 'Localization of optic disk' (Table 2) and 'Segmentation of vasculature' (Table 3). 19 articles have been examined on the first one, 38 articles have been examined on the 'Localization of optic disk' phase and a total of 62 articles has been examined on the segmentation phase as shown in (Winder *et al*., 2009).

Preprocessing	
Algorithm	**Number of articles**
Local contrast enhancement / normalization	7
Corrected (non-uniform) illumination	5
Noise reduction / removal	3
Color normalization	2
Histogram analysis	2

Table 1. Summary of the techniques used in the preprocessing stage image

Localization of the optic disc	
Algorithm	**Number of articles**
Position of vessels	6
Snakes / deformable models	5
Principal Components Analysis	5
Watershed Transform	5
Pixel intensity	3
Image (adaptive) thresholding	3
Pyramidal decomposition	2
Edge detection	2
Morphology	2
Hough transform	2
Point distribution model	1
Hierarchical filter scheme	1
Maximum contrast	1

Table 2. Summary of the techniques used at the stage of optical disk location

Segmentation of the vasculature	
Algorithm	**Number of articles**
Vessel tracking	17
Matched filter	12
Morphological analysis	6
PCA/Neural network	4
Watershed transform / thresholding	3
Gaussian filters	3
Localization via vessel structure	3
Classification / NN	3
Edge detection	2
Wavelet transform	2
Miscellaneous	7

Table 3. Summary of the techniques used at the stage of segmentation of the vasculature

3. ALTAIR Platform

In this section, the methodology, techniques and structure proposed for analyzing eye background images is proposed. The system is capable of extracting all the information required by the involved clinical team in order to continue with their studies.

A platform schema is presented for a clearer understanding of the proposed system. In Figure 1, five main sequential blocks can be found inside a circle. Inside these main blocks, some tasks (inside the rectangles) are performed in order to continue to the next main block.

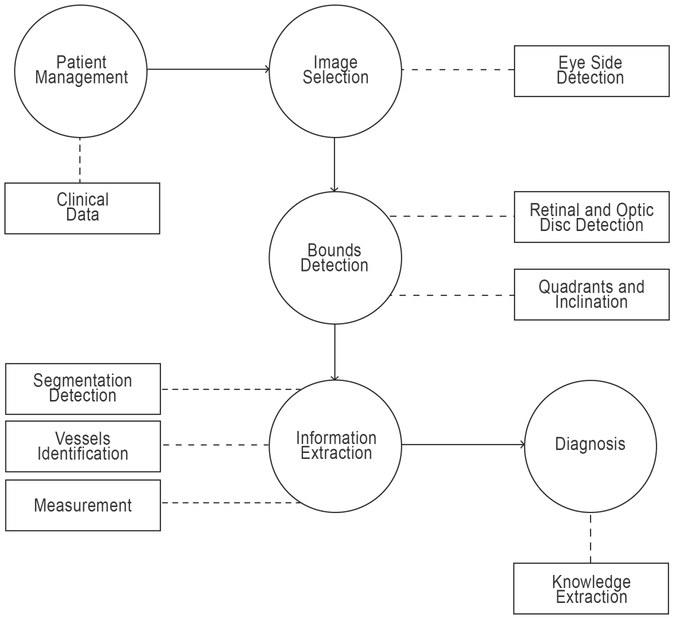

Figure 1. Platform schema

The first main block on the diagram is '**Patient Management**'. It allows associating patients and their previous clinical data (obtained by other proceedings) with fundus images. This is useful in the knowledge extraction task of 'Diagnosis' block.

Every patient can be associated with as much fundus images as taken in the second block, '**Image Selection**'. This block represents the first phase of the computer vision analysis. In this step, the position of the macula is located. This position determines the eye side (left or right). Adaptive thresholding and pixel intensity techniques are applied on this task.

Because of the well-known characteristics of the processed images, that knowledge can be used to facilitate the analysis. Thus, when detecting the retina size, the approximate optic disc size will be known. The third block, '**Bounds detection**', consists in locating the optic disk, taking into consideration the retina size. Then, the first step is locating the retina edge and then, the optic disc can be located by applying pixel intensity, adaptive thresholding, morphological filters and Hough transform algorithms following the methodology proposed in (Sekhat *et al*., 2008). These morphological operations are as below:

$f(x, y)$ is a grayscale image function defined on grid Z^2 and B is a binary structuring element.

Dilation:

$$(f \oplus B)(x, y) = \max\{f(x - s, y - t) | (s, t) \in B\}$$

Erosion:

$$(f \ominus B)(x, y) = \min\{f(x + s, y + t) | (s, t) \in B\}$$

Opening:

$$f \circ B = (f \ominus B) \oplus B$$

Closing:

$$f \circ B = (f \oplus B) \ominus B$$

Reconstruction:

$$\rho f(g) = v_{n \geq 1} \partial_f^{(n)}(g)$$

In the above, v stands for the point-wise maximum and $\partial_f^{(n)}(g) = (g \oplus nB) \wedge f$, where nB is the self-dilation of $B(n-1)$ times and $\wedge$ denotes the point-wise minimum.

The boundary of the optic disk and its center are found by applying the Hough transform to the gradient image. The circular Hough transform is almost identical to the Hough transform for lines, but it uses the parametric form for a circle:

$$(x-a)^2 + (y-b)^2 = r^2$$

where (a, b) is the center of the circle of radious r that passes through (x, y).

The next block is '**Information Extraction**'. It encapsulates the most important tasks of the images analysis. Segmentation, identification and measurement tasks are carried on this block. Pixel intensity and Gaussian filters algorithms are applied in order to increase de contrast between the vessels structure and the retina background, adaptive thresholding techniques are used to establish the point taken into consideration to separate vessels from the background and morphologic analysis to reject all the fake positives. Once the vasculature segmentation is done, the next step is the identification of vessels. This step classifies the kind of blood vessel: vein or artery. Pixel intensity, adaptive thresholding and morphologic filters are applied along with a classifier which considers inputs associated to the color of the vessels and their closest background. In the last task from this block parameter such as vessels area, length or thickness are extracted and grouped by type (vein and artery).

The last block is focused on the '**Diagnosis**' stage, which has not been started yet. It is associated to the clinical research as a result from the analysis of the parameters exported by the developed tool. In this phase, Case-Based Reasoning (CBR) techniques will be applied as proposed by (Díaz *et al*., 2006).

Table 4 summarizes the techniques applied on every stage of the tool where visual analysis is used.

Macula	**Optic Disc**	**Segmentation**	**Identification**
Pixel intensity	Pixel intensity	Pixel intensity	Pixel intensity
Adaptive thresholding	Adaptive thresholding	Adaptive thresholding	Adaptive thresholding
	Morphologic filter	Gaussian filters	Classifier
	Hough transform	Morphologic analysis	Morphologic analysis

Table 4. Applied techniques

4. Results and conclusions

The proposed solution provides a supervised automated tool for analyzing fundus images in an average time of about 10 seconds per image. As a supervised tool, it is possible to act manually in case the supervisor wants to correct any error that may appear in the process. This image processing time is lower than the time that the software previously used by the clinical research team involved in this development (AVIndex). That software analysis was limited to the area between the edge of the optical disk and twice its radius as the new one goes up to three times its radius. Figure 2 shows the average time (in seconds) for every step in the new platform (left) and its overall time compared to the previous tool (right).

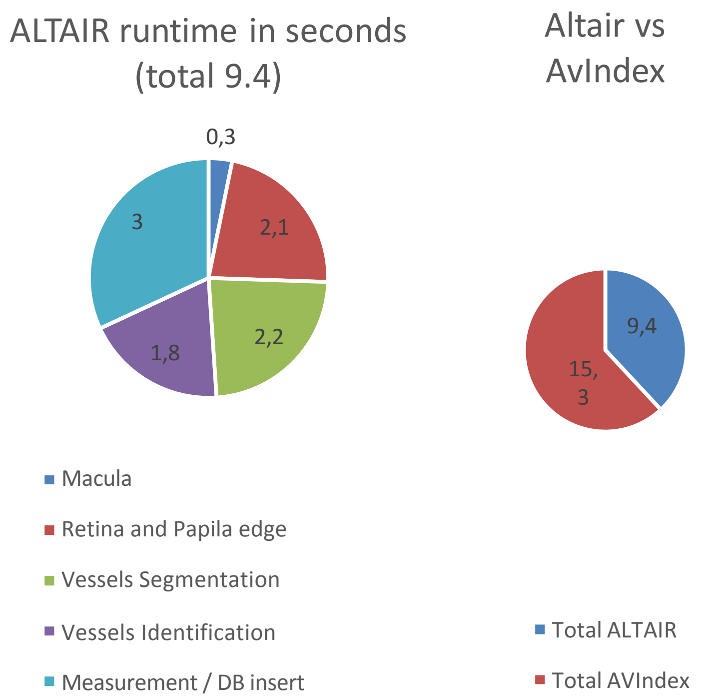

Figure 2. Average time of every step (left) and total time compared with the previous tool (right)

To test the performance of the methodology, 50 images have been tested by the tool. 490 main vessels were identified manually and the results of each step can be seen in Table 5:

	Macula location	Retina bounds	Optic Disk	Segmentation	Identification
Right	50	50	44	396	326
Wrong	0	0	6	94	70
% success	100%	100%	88%	80%	72%*

Table 5. Success rate of every step of the tool

(*) In the case of identification, only detected vessels are considered when accounting for the success rate.

Figure 3 shows the result of the whole process over the analyzed image. Vessels have been detected and identified classifying them as veins (blue) or arteries (red). Then, their parameters have been measured as can be found on the left side of the tool.

Figure 3. Screenshot with the results (last step of the tool)

Additionally, the tool is provided with a configuration tool where the parameter of the relationship between image size and the actual size of the retina can be defined. This allows the software to operate independently of the fundus camera used to take the images.

This development is a first version to validate the results generated by the tool in order to propose the used methodology as a model to follow when making fundus images analysis. Today, there is no one validated.

From that moment, the exported parameters will be scanned for those signs that may be associated to any of the diseases that have been shown to relate.

Regarding the visual analysis, the challenge of improving the success rate shown by the applied set of algorithms is presented. In addition, a solution to the problem at intersections, where a vessel can be hidden by other one, has to be found. Future versions will attempt to provide a solution to these problems to try to extract as much information as possible.

The software is going to be completed, redesigning its architecture and building a virtual organization based system. This will allow agents to work collaboratively in online or cloud environments to be able to have a larger database and provide more information to the clinical test.

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