On the Relevance of 3D Retinal Vascular Network from OCT Data

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Abstract

Abnormal patterns of the retinal vascular system have been associated with several heart and cerebral diseases. However, these correlations were obtained using 2D imaging of the eye fundus, disregarding information on the third component (depth) of the vascular system. In this paper, we show that the depth component is relevant and should not be disregarded in this analysis. In this way, the relevance of the analysis of the retinal vascular network as a biometrical marker for the general health status of the individual can be increased.

1 Introduction

The retinal vascular system is usually imaged using color fundus photography (CFP) or fluorescein angiography (FA), both providing only a 2D projection of the retinal vascular system. Moreover, FA is an invasive technique as it relies in the administration of a fluorescent dye, that provoques adverse reactions in about 5% of the cases [9]. From the retinal vascular system as imaged by these modalities, one can retrieve several metrics, such as tortuosity, length, diameter and angle of bifurcation among others [1]. It is clear that if these metrics are obtained from 2D projections, thus disregarding the depth component, there is loss of information. Nonetheless, correlations between these metrics and heart [16] and cerebral diseases [8, 11] have been shown, as well as in the cases of diabetes and hypertension [15].

Optical coherence tomography (OCT) is an *in vivo* imaging modality of the human eye fundus. Making use of low coherent light interferometry, it provides 3D volumetric data of light backscattering of the human eye fundus, allowing to image the human retina non-invasively. OCT has been mainly used in a clinical sense to diagnose macular edema, or in other words, to establish a thickness map of the retina. However, in a series of recent works by our research group [5, 6, 13] there was significant progress in recovering the 3D positioning of the retinal vascular network. This possibility makes use of the fact that blood absorbs light at the wavelengths used in OCT [3, 4], therefore provoking a shadow in the depth-wise direction below a blood vessel in the 3D OCT data.

Recent work shows that about 70% of the retinal vascular system recovered from FA can be recovered from OCT data [6]. Moreover, ongoing research shows that it is possible to recover the 3D position of the retinal vascular system from OCT [5, 13].

Kiss et al. [7] already mentioned the importance of getting 3D information on the retinal vascular system, but disclose no further information. In this way, it is relevant to know whether the depth component of the position of the vascular system can change significantly the metrics used and therefore the correlations with disease status. If this is the case, the use of 3D metrics might strengthen correlations between the retinal vascular system and the corresponding disease status of the subject.

In this paper we test the significance of the correlations between widely used tortuosity metrics in 2D and 3D, for the same subject. We will consider correlations between metrics in 2D and 3D and between metrics in 2D and in the depth component alone. The latter indicates whether tortuosity in 2D and in the depth component are dependent. If so, there should be no relevance on the 3D segmentation for correlation purposes. However, if the tortuosity on the 2D projection and the depth component alone are not correlated, the new information on the tortuosity in depth might originate new correlations with disease status.

The paper is organized as follows. In section 2, a brief overview of the 3D segmentation method for the retinal vascular network is given. In section 3, we present the tortuosity metrics used and formulate the statistical problem that one wants to answer, that is, if the 2D and 3D metrics are significantly correlated. In section 4 we present the main results and in section 5 we summarize the main conclusions and make some references to future work.

2 Vascular Network Segmentation

We will only provide a briefly overview on the segmentation in 2D and 3D. Details can be found in [5].

We first consider the appropriate projection of 3D volumetric OCT data to obtain 2D projections of the vascular system. To achieve this, we make use of the depth-wise shadow caused by the vessel in the OCT signal, in order to get several images with good

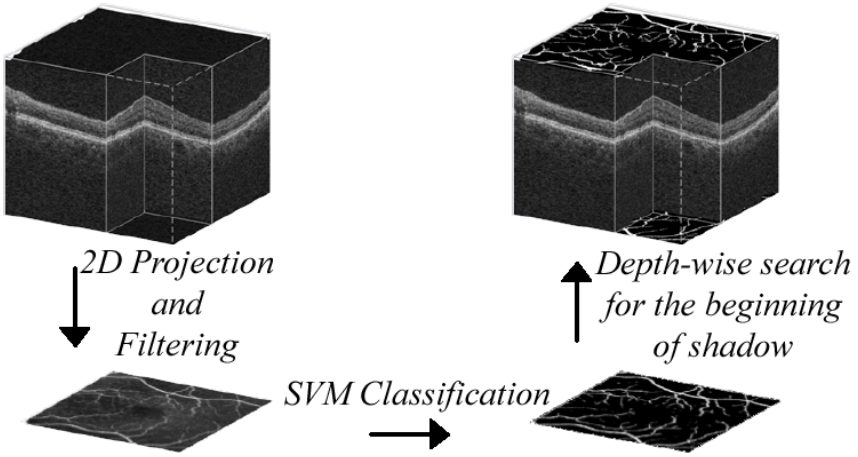

Figure 1: Scheme of the 3D retinal vascular system segmentation process from OCT data.

contrast between vessel and non-vessel pixels. These images are then processed with several filters, namely intensity, gradient and Hessian based ones, among others. Local Phase features are also computed.

This set of images is used to obtain a binary segmented imaged by means of Support Vector Machine (SVM) classification as detailed in [5].

Having the 2D projection of the vessels, the depth component is obtained by depth-wise search of the beginning of the vessel shadow in OCT data. A scheme of this procedure can be seen in figure 1

3 Tortuosity metrics and correlation

From the vessel segmentation, one retrieves a binary image where true and false pixels correspond to the presence or absence, respectively, of a vessel.

The vessels centerlines were retrieved. Tortuosity metrics were computed for all vessel segments defined as the path between two endpoints, an endpoint and a branchpoint, or two branchpoints. Note that an endpoint is a vessel point with at most one vessel point in its 3x3 neighborhood, while a branchpoint has at least three (these may include bifurcation or crossovers).

The fundus image is convoluted with a bank of log-Gabor filters, each having its unique pair direction-scale. Then each vessel segment was categorized into thin, medium and large, depending on the average scale with maximum filter response along the segment.

Three different metrics were used to assess vessel tortuosity: the distance metric

(DM), the sum of angles metric (SOAM), and the inflection count metric (ICM). To our knowledge these are the main vessel tortuosity metrics used in the literature (see for instance [2, 10, 14], among others).

The DM is the most common approach when evaluating vessel tortuosity. It is the ratio between total length of the vessel and the linear distance between its ends. However, this metric has shown that it cannot completely describe vessel tortuosity. For instance, it cannot distinguish a curve, from a vessel that has abrupt direction changes.

The SOAM can be described as the integrated total curvature normalized by the path length. The ICM is the total number of inflection points multiplied with DM. These metrics were computed as described in [2]. Instead of using just the adjacent points P_{k-1} and P_{k+1} at each point P_k, the four points $P_{k-s}, P_k, P_{k+s}, P_{k+2s}$ were considered, where s is the spacing between the points.

Since a pixel representation is used to describe the blood vessels (a discrete representation), undesirable noise can be introduced into metrics such as SOAM and ICM. For instance, a diagonal vessel with respect to the sampling direction of the OCT, can be represented as ragged line. As so, the vessel representation must be smoothed prior to the metric computation. Instead of computing these metrics on the vessel path itself, for each point Pk, a polynomial (maximum order 3) least square fit with of the path $P_{k-s}, P_k, P_{k+s}, P_{k+2s}$ was computed independently for coordinates x, y and z.

In a first approach, the comparison was performed between the 2D and 3D metrics. Though this is not completely the case for our surprise, it was expected that no major differences were found. This expectation can be explained due to the nature of the retina itself. Retina presents an macular thickness that oscillates between about 141 micrometers in the foveal area and about 267 micrometers in outer macular areas [12], while the scans were retrieved from an area of 6000x6000 micrometers (x and y directions). This can mean that depth changes in vessel position are lost by their small scale. As so, in a second approach, 2D projection tortuosity was compared to the tortuosity in depth.

To achieve our purpose, we started by dividing the recovered vessels for each subject, according to its diameter. Therefore we considered three classes of vessels: thin, medium and large (see Figure 2), depending on the diameter of the vessel in pixels and the OCT protocol used in the acquisition of the image.

In each of these classes we establish the correlation R between the values of the three metrics (DM, ICM, SOAM) in 2D and 3D, in order to test whether the correspondence is linear. From there, one can establish whether the linear regression is significant, that is, considering the linear regression line

$$\hat{y} = \beta_0 x + \beta_1$$

we considered the hypothesis test

$$\begin{cases} \text{H0: } \beta_0 = 0 \\ \text{H1: } \beta_0 \neq 0. \end{cases}$$

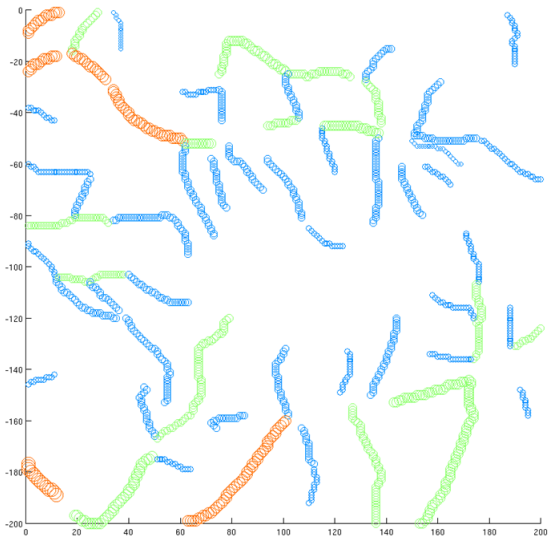

Figure 2: The recovered network by vessel diameter: thin (blue), medium (green) and large (orange) vessels. Small branches were eliminated from the segmentation.

It can be shown that this is equivalent to a t-student test given by

$$\frac{R}{\sqrt{\frac{1-R^2}{n-2}}} \sim t_{1-\alpha/2,n-2} \tag{1}$$

where n is the dimension of the sample. From there, if the p-value was lower than the level of significance α, there was a significant linear relation between the values in 2D and 3D, while in the other case there was not statistical evidence of a linear relation. The latter means that there is a possible alteration on the correlations between 2D and 3D metrics and disease status.

4 Results

We considered 15 OCT volumes from healthy and early stage diabetic patients. We also considered a significance level of $\alpha = 0.05$.

We started by comparing the results between the tortuosity metrics in 2D and 3D. In table 1 we present the obtained correlations R and p-values for the hypothesis test (1). It is clear that for DM in small vessel the null hypothesis is accepted, that is, there is no statistical evidence that the relation is linear. In fact, this shows that the most widely used tortuosity metric (DM) is significantly different in 2D and 3D in what concerns the retinal vascular system. The difference is higher in smaller vessels, since they tend to be more tortuous in depth.

Table 1: Table of correlations between 2D and 3D tortuosity metrics and the respective p-values for the hypothesis test (1).

Diameter	Correlation R			p-value		
	DM	SOAM	ICM	DM	SOAM	ICM
thin	-0.459	0.957	0.612	**0.085**	$<$0.001	0.015
medium	0.238	0.991	0.960	**0.394**	$<$0.001	$<$0.001
large	0.535	0.949	0.993	0.040	$<$0.001	$<$0.001

Taking into consideration the relatively small retinal thickness, we compared the still significant tortuosity metrics (SOAM, ICM) using 2D and only the depth-wise data. The results are shown in table 2. In this case it is clear that the SOAM also becomes nonlinear, therefore opening the possibility of using the depth-wise tortuosity alone to correlate with disease status.

Table 2: Table of correlations between 2D and depth-wise (only) tortuosity metrics and the respective p-values for the hypothesis test (1).

Diameter	Correlation R		p-value	
	SOAM	ICM	SOAM	ICM
thin	0.228	0.596	**0.413**	0.019
medium	0.485	0.818	**0.067**	$<$0.001
large	0.829	0.967	$<$0.001	$<$0.001

5 Conclusions and future perspectives

We intended to show that tortuosity metrics in 2D (that is, disregarding the depth component) do not relate linearly with tortuosity metrics considering the depth-wise component, in what concerns the retinal vascular system.

In this preliminary study, we show that the most widely used tortuosity metric (DM) for measuring vessel tortuosity is the one where the linear relation between 2D and 3D metrics is not significant. This shows that the use of 3D tortuosity metrics to correlate with disease status might have a significant impact in the correlation values, when compared with the ones obtained using 2D metrics.

In this sense, the next step is to conclude if this change comes into the benefit of diagnose, that is, if the correlations with disease status turn stronger using 3D metrics rather than 2D metrics. This will be subject of future work.

Acknowledgments

This work was partially supported by the Portuguese Foundation for Science and Technology (Fundação para a Ciência e a Tecnologia) under the research project PTDC/SAU-ENB/111139/2009 and program COMPETE (FCOMP-01-0124-FEDER-015712).

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