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An automatic algorithm measuring the retinal intercapillary area to assess diabetic retinopathy

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Introduction

Diabetic retinopathy (DR), a complication of diabetes mellitus (DM), is a leading cause of blindness worldwide [1]. Since early stage DR is usually asymptomatic there is an acute need for early disease detection and monitoring. Thus far, automatic quantitative analysis has focused on measurements of the total non-perfused area [2] and capillary density [3]. Analysis of the intercapillary areas of the perifoveum using manual segmentation has also been demonstrated [4]. The purpose of this study is to develop a robust, sensitive, and fully automatic algorithm to quantify diabetes related capillary dropout using optical coherence tomography (OCT) angiography (OCTA).

Materials and Methods

SS-OCT and SS-OCTA imaging was performed using a research prototype ultrahigh-speed SS-OCT system [5]. The system uses a 400 kHz vertical cavity surface emitting laser (VCSEL) centered at 1050 nm. The imaging range was approximately 2.1 mm in tissue, and the axial and transverse resolutions in tissue were ~8-9 µm and ~15 µm, FWHM, respectively. OCT and OCTA imaging was performed over 3 mm × 3 mm fields of view, resulting in volumes of 500x500 A-scans. The algorithm is displayed in **Figure 1**.

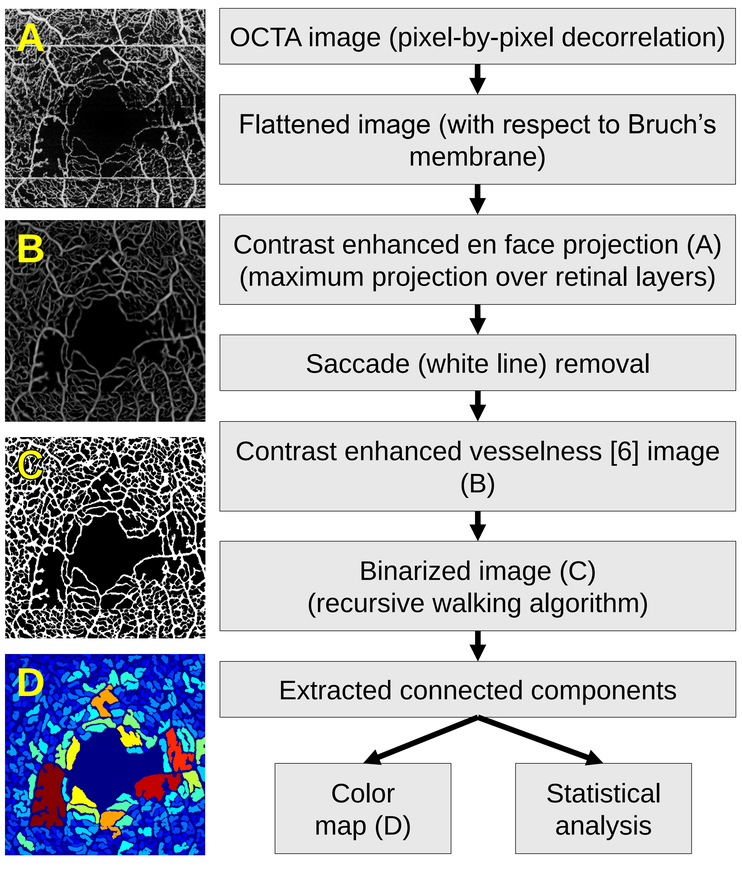

Figure 1: Processing steps of the algorithm

Results and Discussion

Eyes from a normal controls, DM patients without DR, NPDR patients, and PDR patients, were analyzed using the described algorithm (**Table 1**)

	Normal	*DM without DR*	*NPDR*	*PDR*
Mean Age (± std)	36.0 ± 11.7	62.4 ± 5.9	59.0 ± 7.1	45.6 ± 15.8
Patients Analyzed (Male : Female)	5 (1 : 4)	7 (3 : 4)	9 (6 : 3)	5 (2 : 3)

Table 1: Subject characteristics

4 of the 26 eyes analyzed were excluded: 3 due to regions of very low OCTA signal in the image, leading false large intercapillary areas and 1 due to high noise in the region of the FAZ, leading to wrongly detected vessels. Example output images are shown in **Figure 2**.

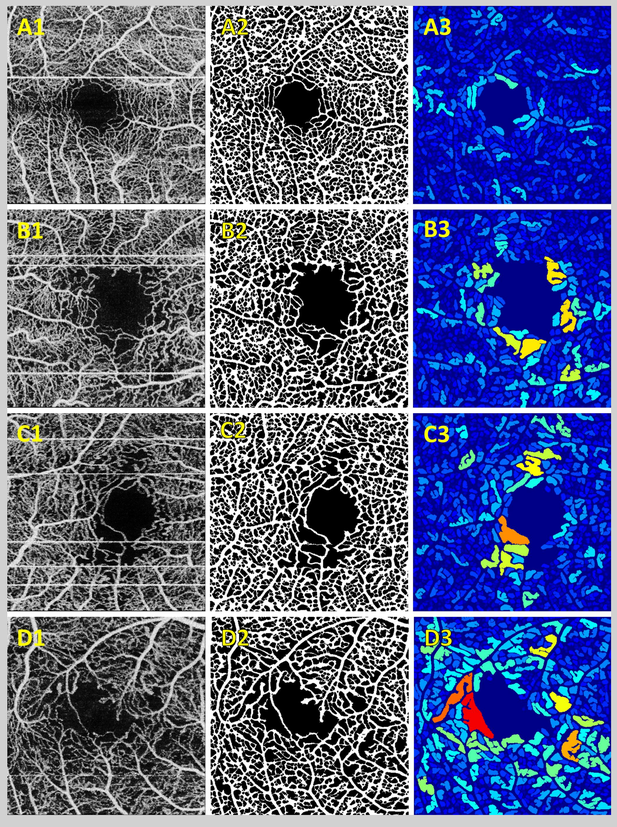

Figure 2: Representative examples of algorithm output. (A) normal control; (B) DM patient without DR; (C) NPDR patient; (D) PDR patient. (A-D).1 Contrast enhanced input en face OCTA projections. (A-D).2 Binarized vessel maps. (A-D).3 Intercapillary area maps.

For the quantitative analysis of intercapillary area, the mean of the largest 10 and 20 areas, either including or excluding the FAZ, contained within a 0.75 mm radius centered on the FAZ, were computed. The cohort statistics are summarized in **Figure 3** and **Table 2**. The results are in accordance with previous work, however the presented method is fully automatic and more sensitive to smaller changes than density and total non-perfused area based methods as explained in **Figure 4**.

	20 with FAZ	*20 without FAZ*	*10 with FAZ*	*10 without FAZ*
CV	0.2%-6.7%	0.3%-11.0%	0.2%-8.8%	0.2%-16.2%

Table 2: Repeatability computed as coefficient of variation (CV) for the 5 eyes (1 normal, 2 NPDR, and 2 PDR) having two independent OCTA acquisitions

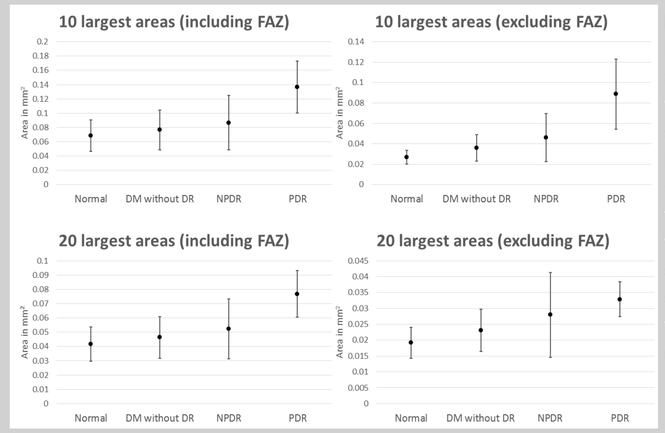

Figure 3: Intercapillary area statistics for each cohort. Points correspond to mean value and error bars correspond to standard deviations.

Further remarks about the study:

- Analyzation of only 3x3mm field of views (larger areas proportionally lower A-scan sampling density, making individual vessels hard to resolve and automatic segmentation difficult in pathology)
- Motion correction could further improve results (in this study no correction for vessel discontinuity due to patient motion)

Limitations of the study:

- Small cohort size and lack of age-matched normals
- Evaluation of data only from a single prototype system

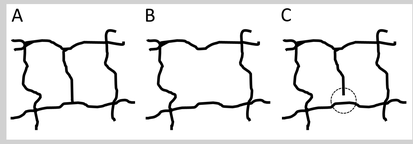

Figure 4: Pictorial explanation of the advantages of intercapillary area based techniques. (A) Hypothetical healthy vascular structure, showing two intercapillary areas. (B) The center capillary is lost, creating a single intercapillary area of roughly double the size. Thus, the largest intercapillary area would double; however, the vessel density does not change by a commensurate amount. (C) The increased sensitivity comes at a cost: if there is an error in segmentation, seen here as a small discontinuity inside the dashed circle, the intercapillary area doubles, while the vessel density remains virtually unaffected.

Conclusions

The means of the 10 and 20 largest intercapillary areas, either including or excluding the FAZ, are useful metrics for identifying disease status in patients with DM and DR.

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