

AUTHORS

AUTHORS (LAST NAME, FIRST NAME): Schottenhamml, Julia^{1, 2}; Moulton, Eric M.¹; Novais, Eduardo A.^{4, 3}; Kraus, Martin F.²; Lee, ByungKun¹; Choi, WooJhon¹; Ploner, Stefan B.²; Husvagt, Lennart²; Lu, Chen D.¹; Yiu, Patrick¹; Rosenfeld, Philip J.⁵; Duker, Jay S.³; Maier, Andreas K.²; Waheed, Nadia³; Fujimoto, James G.¹

INSTITUTIONS (ALL):

1. Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, MA, United States.
2. Pattern Recognition Lab, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, Germany.
3. New England Eye Center, Tufts Medical Center, Boston, MA, United States.
4. Department of Ophthalmology, Federal University of Sao Paulo, Sao Paulo, Brazil.
5. Department of Ophthalmology, University of Miami Miller School of Medicine, Miami, FL, United States.

Commercial Relationships Disclosure (Abstract): Julia Schottenhamml: Commercial Relationship: Code N (No Commercial Relationship) | Eric Moulton: Commercial Relationship: Code N (No Commercial Relationship) | Eduardo Novais: Commercial Relationship: Code N (No Commercial Relationship) | Martin Kraus: Commercial Relationship(s);Optovue, Inc.:Code C (Consultant) ;Optovue, Inc.:Code P (Patent) | ByungKun Lee: Commercial Relationship: Code N (No Commercial Relationship) | WooJhon Choi: Commercial Relationship: Code N (No Commercial Relationship) | Stefan Ploner: Commercial Relationship: Code N (No Commercial Relationship) | Lennart Husvagt: Commercial Relationship: Code N (No Commercial Relationship) | Chen Lu: Commercial Relationship: Code N (No Commercial Relationship) | Patrick Yiu: Commercial Relationship: Code N (No Commercial Relationship) | Philip Rosenfeld: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code R (Recipient) ;Carl Zeiss Meditec, Inc.:Code F (Financial Support) ;Carl Zeiss Meditec, Inc.:Code C (Consultant) | Jay Duker: Commercial Relationship(s);Optovue, Inc.:Code F (Financial Support) ;Topcon Medical Systems, Inc.:Code F (Financial Support) ;Topcon Medical Systems, Inc.:Code C (Consultant) ;Carl Zeiss Meditec, Inc.:Code F (Financial Support) ;Carl Zeiss Meditec, Inc.:Code C (Consultant) ;Optovue, Inc.:Code C (Consultant) | Andreas Maier: Commercial Relationship: Code N (No Commercial Relationship) | Nadia Waheed: Commercial Relationship(s);MVRF:Code F (Financial Support) ;Genentech:Code C (Consultant) ;Ocudyne:Code C (Consultant) ;Carl Zeiss Meditec, Inc.:Code R (Recipient) ;Janssen:Code C (Consultant) ;Regeneron:Code C (Consultant) ;Optovue, Inc.:Code R (Recipient) ;Nidek:Code R (Recipient) | James Fujimoto: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code P (Patent) ;Optovue, Inc.:Code P (Patent) ;Optovue, Inc.:Code I (Personal Financial Interest)

Study Group: (none)

ABSTRACT

TITLE: OCT-OCTA Segmentation: a Novel Framework and an Application to Segment Bruch's Membrane in the Presence of Drusen

ABSTRACT BODY:

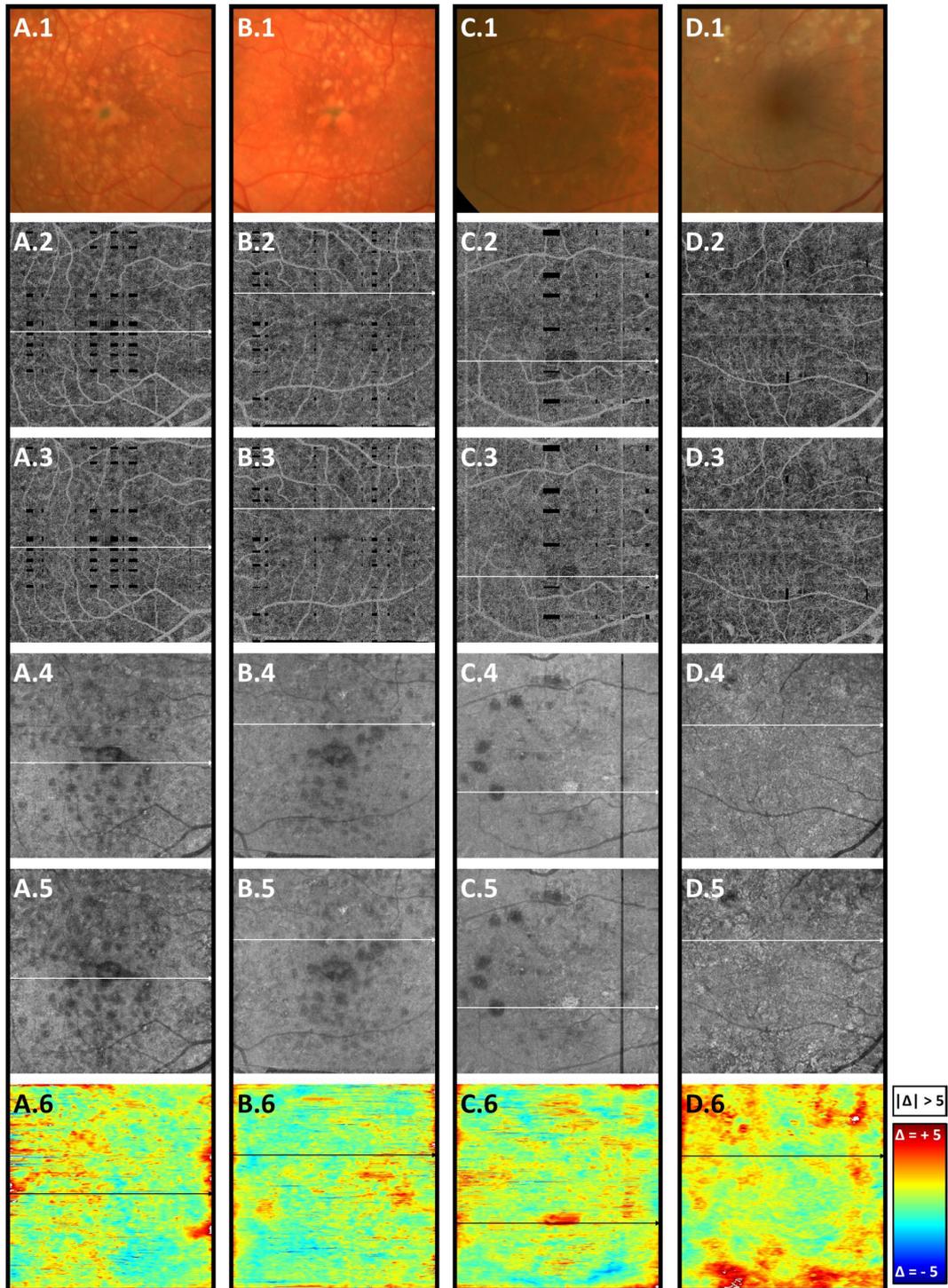
Purpose: We present a novel framework for segmenting optical coherence tomography (OCT) and OCT angiography (OCTA) that jointly uses structural and angiographic information. We term this new paradigm "OCT-OCTA segmentation," and demonstrate its utility by segmenting Bruch's membrane (BM) in the presence of drusen.

Methods: We developed an automatic OCT-OCTA graph-cut algorithm for BM segmentation. Our algorithm's performance was quantitatively validated by comparing it with manual segmentation in 7 eyes (6 patients; 73.8±5.7 y/o) with drusen. The algorithm was also qualitatively assessed in healthy eyes (n=13), eyes with diabetic retinopathy (n=21), early/intermediate age-related macular degeneration (AMD) (n=14), exudative AMD (n=5), geographic atrophy (GA) (n=6), and polypoidal choroidal vasculopathy (n=7).

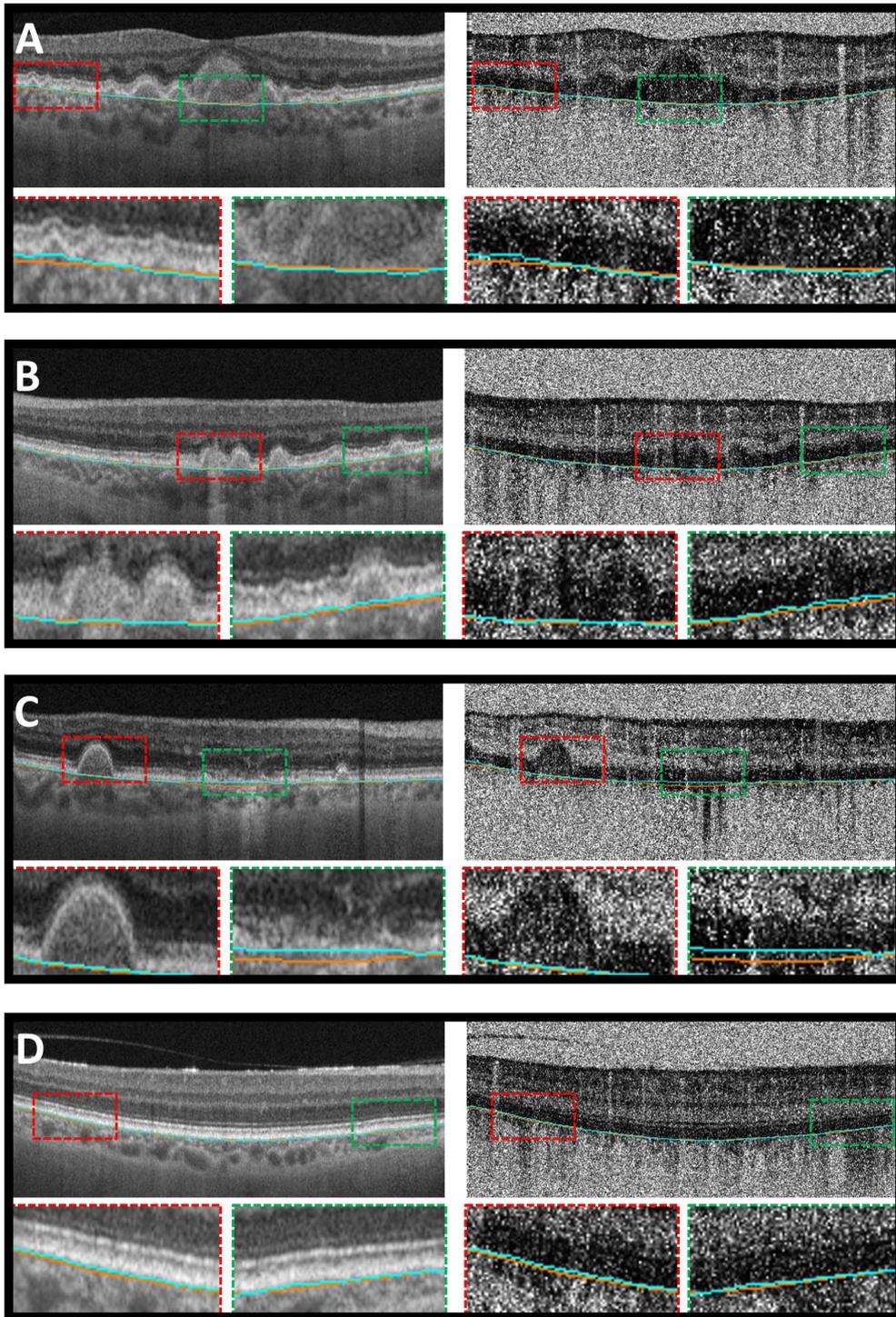
Results: The absolute pixel-wise error between the manual and automatic segmentations had the following values: mean: 4.5±0.89µm; 1st Quartile: 1.9±1.35µm; 2nd Quartile: 3.9±1.90µm; and 3rd Quartile: 6.3±2.67. This corresponds to a mean absolute error smaller than the optical axial resolution of our OCT system (~8-9µm). In all other tested eyes, qualitative visual inspection showed BM contours that were deemed suitably accurate for use in forming en face

OCT(A) projections. The algorithm's poorest results occurred in GA patients with large areas of atrophy.

Conclusions: By leveraging both structural and angiographic information we showed that OCT-OCTA segmentation is likely to be a widely useful framework for segmenting ocular structures.



En face segmentation analysis, where each column corresponds to a different nGA/DAGA eye. 1st row: color fundus photo; 2nd, 3rd rows: en face OCTA slice taken at the manual and automatic segmentations, respectively; 4th, 5th row: en face OCT slices taken the manual and automatic segmentations, respectively. 6th row: heat map of the segmentation error (legend, bottom right; units of pixels; 1 pixel = 4.5 μ m). All OCT(A) fields are 6x6mm.



OCT(A) B-scan analysis of manual (teal) and automatic (orange) segmentations; A-D are taken from the white lines in Figure 1. Each row shows both OCT data (left) and OCTA data (right). Enlargements, indicated by red and green boxes, are also shown.

DETAILS

PRESENTATION TYPE: #1 Paper, #2 Poster

CURRENT REVIEWING CODE: 2510 imaging: image processing and analysis methodologies - MOI

CURRENT SECTION: Multidisciplinary Ophthalmic Imaging Cross-sectional Group

Clinical Trial Registration (Abstract): No

Other Registry Site (Abstract): (none)

Registration Number (Abstract): (none)

Date Trial was Registered (MM/DD/YYYY) (Abstract): (none)

Date Trial Began (MM/DD/YYYY) (Abstract): (none)

Grant Support (Abstract): Yes

Support Detail (Abstract): NIH Grant 5-R01-EY011289-28, AFOSR Grant FA9550-15-1-0473, AFOSR Grant FA9550-10-1-0551

TRAVEL GRANTS and AWARDS APPLICATIONS

AWARDS: ARVO and ARVO Foundation Travel Grants|ARVO Members-in-Training Outstanding Poster Award

AFFIRMATIONS

Affirmations: Affirmation to reveal essential structure, novel compound elements, or identify new gene compounds.

Affirmations: Affirmation of copyright transfer from each author to ARVO, or certification of public domain abstract.

Affirmations: Affirmation of compliance with ARVO policy on registering clinical trials.

Affirmations: Affirmation to pay Annual Meeting's full registration fee.

Affirmations: Affirmation that abstract data/conclusions have not been published; not redundant with other submissions from same investigators.

Affirmations: Affirmation of compliance with ARVO's Statement for Use of Animals.

Affirmations: Affirmation of compliance with ARVO's Statement for Use of Human Subjects and/or Declaration of Helsinki.

Affirmations: Affirmation to present same work as abstract submission.

Affirmations: Affirmation that submission of this abstract has been approved by the Principal Investigator.

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

Julia J. Schottenhamml^{1,2}, Eric M. Moul¹, Stefan B. Ploner^{1,2}, ByungKun Lee¹, Chen D. Lu¹, Lennart Husvagt², Nadia K. Waheed³, Jay S. Duker³, Joachim Hornegger², James G. Fujimoto¹

¹Research Laboratory of Electronics and Department of Electrical Engineering and Computer Science, Massachusetts Institute of Technology, Cambridge, MA; ²Pattern Recognition Lab, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany; ³New England Eye Center and Tufts Medical Center, Tufts University, Boston, MA, United States

Commercial Relationships Disclosure: JJS: No Commercial Relationships || EMM: No Commercial Relationships || SBP: No Commercial Relationships || BL: No Commercial Relationships || CDL: No Commercial Relationships || LH: No Commercial Relationships || NKW: Iconic Therapeutics: Code C (Consultant); ThromboGenics: Code C (Consultant); Carl Zeiss Meditec Inc.: Code R (Recipient); Optovue Inc.: Code R (Recipient) || JSD: Carl Zeiss Meditec Inc.: Code F (Financial Support); Optovue Inc.: Code F (Financial Support); Carl Zeiss Meditec Inc.: Code C (Consultant); Optovue Inc.: Code C (Consultant) || Joachim Hornegger: Royalties from property owned by MIT and licensed to Optovue: Code P (Patent) || James Fujimoto: Optovue Inc.: Code I (Personal Financial Interest); Carl Zeiss Meditec Inc.: Code P (Patent); Optovue Inc.: Code P (Patent).



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 x 3 mm fields of view, resulting in volumes of 500x500 A-scans. The algorithm is displayed in Figure 1.

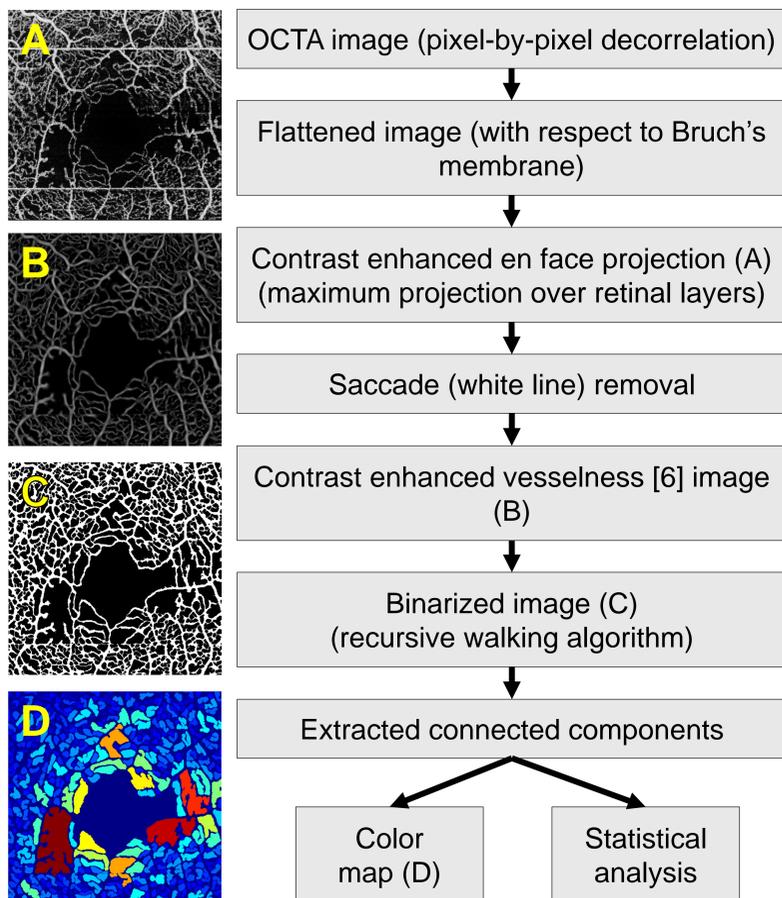


Figure 1: Processing steps of the algorithm

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 (\pm std)	36.0 \pm 11.7	62.4 \pm 5.9	59.0 \pm 7.1	45.6 \pm 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.

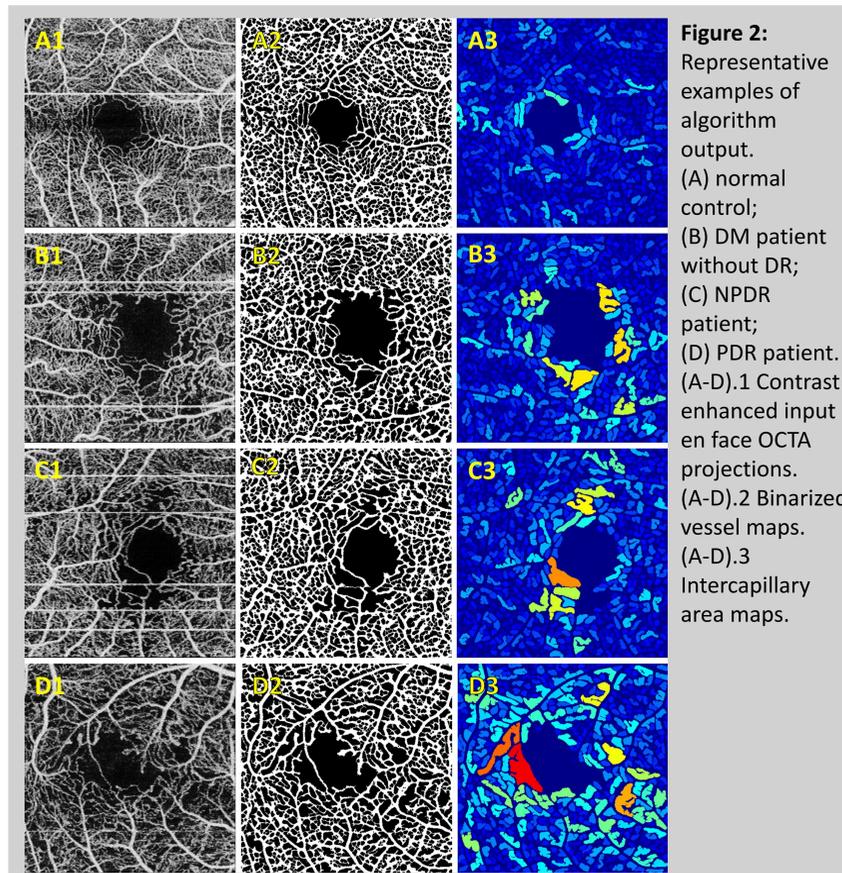


Figure 2: Representative examples of algorithm output. (A) normal control; (B) DM patient without DR; (C) NPDR patient; (D) PDR patient. (A-D).1 Contrast enhanced input en face OCTA projections. (A-D).2 Binarized vessel maps. (A-D).3 Intercapillary area maps.

For the quantitative analysis of intercapillary area, the mean of the largest 10 and 20 areas, either including or excluding the FAZ, 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

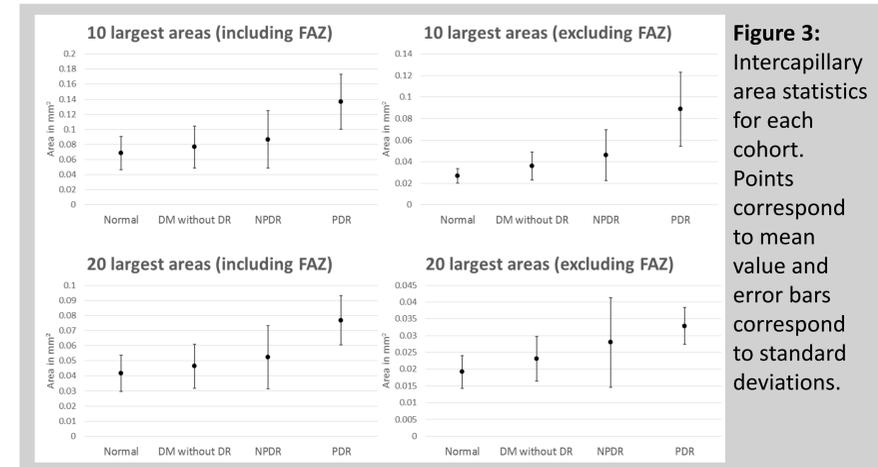


Figure 3: Intercapillary area statistics for each cohort. Points correspond to mean value and error bars correspond to standard deviations.

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

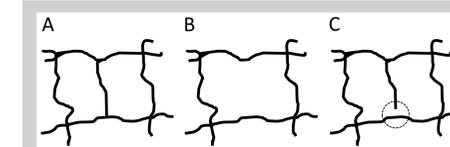


Figure 4: Pictorial explanation of the advantages of intercapillary area based techniques. (A) Hypothetical healthy vascular structure, showing two intercapillary areas. (B) The center capillary is lost, creating a single intercapillary area of roughly double the size. Thus, the largest intercapillary 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.

References

- [1] Engelgau MM, Geiss LS, Saaddine JB, Boyle JP, Benjamin SM, Gregg EW, et al. The Evolving Diabetes Burden in the United States. *Ann Intern Med.* 2004;140:945-950. doi:10.7326/0003-4819-140-11-200406010-00035[2] Hwang TS, Gao SS, Liu L, et al. Automated quantification of capillary nonperfusion using optical coherence tomography angiography in diabetic retinopathy. *JAMA Ophthalmology* 2016;134:367-73.
- [3] Agemy SA, Scripsema NK, Shah CM, et al. RETINAL VASCULAR PERFUSION DENSITY MAPPING USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN NORMALS AND DIABETIC RETINOPATHY PATIENTS. *RETINA* 2015;35:2353-63.
- [4] Salz DA, de Carlo TE, Adhi M, et al. SElect features of diabetic retinopathy on swept-source optical coherence tomographic angiography compared with fluorescein angiography and normal eyes. *JAMA Ophthalmology* 2016.
- [5] Choi W, Potsaid B, Jayaraman V, et al. Phase-sensitive swept-source optical coherence tomography imaging of the human retina with a vertical cavity surface-emitting laser light source. *Optics Letters* 2013;38:338-40.
- [6] Frangi AF, Niessen WJ, Vincken KL, et al. Multiscale vessel enhancement filtering. In: Wells WM, Colchester A, Delp S, eds. *Medical Image Computing and Computer-Assisted Intervention - MICCAI'98: First International Conference Cambridge, MA, USA, October 11-13, 1998 Proceedings.* Berlin, Heidelberg: Springer Berlin Heidelberg, 1998:130-7.

Acknowledgements

We acknowledge support from National Institutes of Health contract R01-EY011289-29A, R44-EY022864, R01-CA075289-16, FA9550-15-1-0473 and FA9550-12-1-0499.

Contact

✉ julia.schottenhamml@fau.de