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Original research

Impact of correct anatomical slab segmentation on foveal avascular zone measurements by optical coherence tomography angiography in healthy adults

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Abstract

Purpose: To evaluate the impact of correct anatomical slab segmentation on foveal avascular zone (FAZ) dimensions in the superficial capillary plexus (SCP) and deep capillary plexus (DCP) using optical coherence tomography angiography (OCTA).
Methods: Participants with healthy retinas were recruited, and 5 × 5 mm OCTA images were acquired using the Canon HS-100 Angio eXpert module. FAZ size was measured in automatically (AS, manufacturer-based) and manually (MS, anatomical-based) segmented OCTA slabs by two experienced graders. FAZ dimensions, inter-rater agreement, and correlation to demographic and retinal parameters were evaluated.
Results: A total of 38 eyes from 20 healthy adult subjects were included in this cross-sectional study. While in AS slabs, the FAZ in the SCP was smaller than in the DCP, in MS images, it was the opposite. MS had a relevant impact on inter-rater agreement of FAZ measurements in the SCP. The FAZ area in both plexus correlated inversely with the central retinal thickness (CRT), irrespective of the segmentation applied. Furthermore, an enlargement of FAZ size in the DCP with increasing age was found. Finally, the FAZ in female participants was significantly larger than in their male counterparts, regardless of the evaluated plexus and chosen segmentation.
Conclusions: Correct anatomical slab segmentation has a significant impact on FAZ size measurements. Not adjusting the segmentation boundaries represents a significant source of error for measuring FAZ area and confounds comparisons across studies as well as OCTA devices.

Keywords: Foveal avascular zone; Optical coherence tomography; Optical coherence tomography angiography; Slab segmentation

Introduction

The foveal avascular zone (FAZ), the capillary-free area within the macula, plays an important role for central vision.[1] Changes in the FAZ size can indicate alterations of the microcirculation state of the fovea.[2] This biomarker might even have prognostic significance as enlargement of the FAZ, which can be seen in ischemic diseases such as diabetic retinopathy or retinal vein occlusion, and has been shown to be associated with poor visual outcome.[3–5] Therefore, the adequate and precise measurement of FAZ dimensions is of clinical interest.

During the last 50 years, fundus fluorescein angiography (FA) has been the most popular method to evaluate the retinal capillary perfusion and to obtain FAZ measurements.[6] However, FA is an invasive operation and requires intravenous administration of the contrast agent fluorescein, for which adverse reactions have been reported. Hence, follow-up

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examinations to monitor and compare FAZ over time are difficult to obtain.

The introduction of optical coherence tomography (OCT) after the turn of the millennium has revolutionized retinal imaging.[7] OCT has become an established non-invasive technique for providing rapidly performed, high-resolution, cross-sectional images of the posterior pole. As OCT devices became faster over time, it is now possible to create flow maps of the retinal microvasculature non-invasively by discrimination of static and non-static (erythrocyte motion) signals. This technological extension is known as OCT angiography (OCTA).[8]

By now, several devices are commercially available and have been evaluated for image quality, speed, and reproducibility, which are all important characteristics. Moreover, these devices have been assessed with regard to correct segmentation of the different capillary plexus within the retina.[9] Herein, we investigated the impact of correct anatomical slab segmentation on FAZ dimensions in the superficial capillary plexus (SCP) as well as deep capillary plexus (DCP) in eyes of healthy adults.

Methods

A cross-sectional study was conducted during the period from March 2017 until May 2017 to measure the FAZ area in healthy adults. The setup of our study was in accordance with the Declaration of Helsinki. Approval by the Institutional Review Board (IRB) at the University of Lübeck (vote reference number 17-008) was given. Informed consent was obtained individually by each participant. Ethnically, all participants were Caucasian and underwent a thorough ophthalmologic examination including best corrected visual acuity (BCVA) in Snellen, slit-lamp biomicroscopy, and OCTA.

Only healthy participants with a BCVA of at least 20/25 and age-appropriate, normal ocular findings without prior ophthalmic surgery were included in our study. Furthermore, the maximal permissible spherical and cylindrical aberration was ±2 and ±1 diopters (D), respectively.

OCTA was performed using the Canon HS-100 (Angio eXpert, OCTA Version 2.0, Tokyo, Japan) without prior pupil dilatation, and 5 × 5 mm macular scans of both eyes were acquired. The device functions at a rate of 70.000 A-scans per second and offers an axial optical resolution of 3 µm. The scanning laser ophthalmoscopy (SLO)-assisted tracking allows better image quality with reduced motion artifacts.

After acquisition, all images were automatically segmented (AS) according to the manufacturer's default settings as well as manually segmented (MS) according to the anatomical-based recommendations published by Spaide and Curcio in all B-scans (Table 1 and Fig. 1).[9]

The FAZ area was manually measured in mm^2 by two experienced graders (F.R. and M.K.) in every OCTA image (MS and AS) using the built-in measurement tool of the device. The outline of the innermost macular arcades was manually marked, and the integrated software automatically calculated the enclosed area. The graders were allowed to adjust the brightness and contrast of the images to optimize the measurements.

Table 1
Automated and manual segmentation strategies including segmentation values.

	Reference	Vascular plexus	Slab boundary	Anatomic basis	Offset[a] (µm)
Automatically segmented (AS)	Angio eXpert V2.0	Superficial	Top	ILM	
			Bottom	GCL	+50
		Deep	Bottom	IPL	
			Bottom	OPL	
Manually segmented (MS)	Spaide and Curcio	Superficial	Top	ILM	
			Middle	IPL	
		Deep	Bottom	IPL	−10
			Top	OPL	+10

GCL: Ganglion cell layer; ILM: Internal limiting membrane; IPL: Inner plexiform layer; OPL: Outer plexiform layer.
[a] Offset is the number of µm below (+) or above (−) stated anatomic structure.

Data were analyzed using IBM SPSS (Version 24.0, Chicago, IL, USA). The Shapiro-Wilk test was used to check for normality of all obtained data. Inter-rater agreement between OCTA graders was evaluated using concordance correlation coefficient (CCC). Finally, we correlated the various FAZ measurements among each other as well as the foveal thickness by Spearman's correlation analysis. Age- and gender-specific differences were analyzed by linear regression and Mann-Whitney *U* test. Results with $P < 0.05$ were considered statistically significant.

Results

A total of 38 eyes from 20 healthy adult subjects were included in this cross-sectional study. These eyes had no relevant artefacts for measurement of FAZ. However, two eyes had to be excluded due to motion artefacts which did not allow adequate measurement of the FAZ. Demographics as well as central retinal thickness (CRT) measurements are reported in Table 2.

FAZ measurements for the respective plexus and segmentation are listed in Table 3. Based on the Shapiro-Wilk test, our data did not show a normal distribution. Therefore, non-parametric analyses were performed.

In AS measurements, the FAZ in the deep plexus was significantly larger than in the superficial one ($P = 0.027$), whereas in MS measurements, it was the reverse ($P < 0.001$). While the FAZ in the superficial plexus was quantified significantly larger in MS measurements than in the AS ones ($P < 0.001$), the FAZ in the deep plexus was measured significantly smaller ($P = 0.010$).

Evaluating FAZ measurements of both graders with regard to inter-rater reliability by CCC analysis showed that the agreement was the highest for the AS measurements of the FAZ in the superficial plexus and the lowest for the MS measurements of the FAZ in the superficial plexus (Table 4).

Correlating the FAZ measurements among each other, we noted a very strong positive correlation between FAZ AS-Superficial and AS-Deep ($r = 0.88$; $P < 0.01$) as well as a

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