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# Optical Coherence Tomography Angiography in High Myopia

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## Abstract

**Background:** The axial length of 25.5 mm or greater in high myopic eyes is commonly implicated in stretching and traction on the retina and choroid which lead to multiple complications: retinal tears and degeneration, posterior staphyloma, lacquer cracks, and choroidal new vascularization.

**Aim:** To evaluate changes in the retinal vascular plexuses in high myopia in adults using optical coherence tomographic angiography.

**Patients and methods:** This is a prospective, cross-sectional, descriptive study that was conducted on 40 patients with high myopia. Patients had optical coherence tomography angiography (OCTA) done by Topcon DRI-OCT. Measurements were corrected for magnification errors according to Littmann's method and Bennet's formula, based on measured axial length. The main outcomes of the study were the area of the foveal avascular zone (FAZ) of the superficial capillary plexus (SCP) and the deep capillary plexus (DCP).

**Results:** 40 eyes in 23 patients, 14 males, and 9 females, were included. Results showed that area of FAZ in SCP was wider than FAZ in the DCP. The area of the FAZ in the SCP and DCP layers had no correlation to the patient's age, axial length, intraocular pressure, and best-corrected visual acuity. While the FAZ in SCP had a positive correlation to the FAZ area in the DCP and a negative correlation to UCVA. The FAZ area measurements in the SCP layer were significantly higher in females than in males.

**Conclusion:** Optical coherence tomography angiography is a useful tool to study different pathologies in the posterior segment and can take over invasive imaging techniques.

**Keywords:** Deep capillary plexus, Foveal avascular area, Optical coherence tomography angiography, The superficial capillary plexus layer

## 1. Introduction

According to an international photographic categorization system, high myopia is defined as myopic refraction greater than  $-6.0$  diopter or axial length greater than 26 mm, while pathological myopia is defined as high myopia in addition to myopic maculopathy.<sup>1</sup> High myopia is a condition that is spreading quickly around the globe. In 2000, there were 163 million highly myopic individuals, or 2.7% of total of the world's population. By the year 2050, that figure is expected to rise to around 1 billion, or about 10% of the worldwide population.<sup>2</sup>

The definitive standard for identifying vascular changes related to chorioretinal dysfunction is still FFA. However, due to the risk of anaphylactic reactions, time commitment, and associated costs, repeated use is restricted, which sparked the need for a rapid, non-invasive test to take its place.<sup>3</sup>

Optical coherence tomography - angiography (OCT-A) is a device to be volition for fluorescein angiography (FA). It is fast in detecting blood stream, which enables the creation of an image of the vascular architecture of the retina in addition to being dye-free and thus lacks pitfalls of the fluorescein injections as acuity responses. It also, provides for the *in-situ*, high-resolution imaging of the

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middle capillary plexus as well as the superficial, deep, and choroidal vascular layers. Contrary to FA, which only shows the surface-level capillary network.<sup>4</sup> OCT-A was found to be suitable for describing the most severe choroidal neovascularizations in myopic individuals with high-quality pictures, eliminating the need for traditional fundus FA.<sup>5</sup>

We evaluated how high myopia and pathological myopia affected the inner and outer microvasculature of the retina. The thickness of the outer retinal sublayers and visual acuity were related to the alterations in the deep retinal microvasculature density of the pathologically myopic eyes. Changes in the choroid's thickness, DRCP density, and the thickness of the outer retinal sub-layer may all be significant contributors to the pathophysiology of pathological myopia-related visual impairment. As a result, their relation has been researched. In pathological macular degeneration, the modification of the outer retinal layer and the reduction in the deep retinal capillary plexus were all associated.<sup>6</sup>

## 2. Patients and methods

### 2.1. Design of the study

It was prospective, cross-sectional, descriptive Study.

### 2.2. Site of study

Ophthalmology department, Sayed Galal university hospital, Al-Azhar University.

### 2.3. Inclusion criteria

Both sex were included. Age range: 18–40 years. High myopia with refraction greater than or equal to 6D or axial length greater than or equal to 26 mm.

### 2.4. Exclusions criteria

Patient with significant corneal opacities. Astigmatism more than 2.00 Diopters. Retinopathy. Optic neuropathy. Myopic maculopathies as: macular hole, epiretinal membrane, Fuch's spot, myopic CNV, posterior staphyloma and foveoschisis. History trauma or intraocular surgery. Systemic disorders which affect the ocular circulation such as diabetes mellitus and hypertension. Intraocular pressure (IOP) greater than 21 mmHg.

### 2.5. Methods

The study was done between March 2021 and September 2021 on 40 eyes of patients at the Ophthalmology clinic, Sayed Galal University Hospital, Al Azhar University. All participant names were hidden and replaced by code numbers maintaining privacy of the patients, all patients had detailed medical History and complete ocular examination including refraction, uncorrected visual acuity (UCVA) and Best corrected visual acuity (BCVA) using Snellen chart, using LogMAR conversion table to document visual acuity in decimal form notation for statistical analysis.

Anterior segment examination, IOP by applanation tonometer, and posterior segment examination by indirect ophthalmoscopy were also done. Axial length was measured optically using Topcon Aladdin, biometer.

OCT-A was done by Topcon DRI-OCT, a machine with Swept Source OCT technology, operated by SMART Track system. The fovea served as the central focus of the OCTA scan, which had a field of view of 3 mm<sup>2</sup> by 3 mm<sup>2</sup>, or 10°.

### 2.6. The following protocol was applied

An OCTA was performed on the superficial and deep plexuses, segmenting the SCP from the ILM to the IPL and the DCP from the INL to the OPL. Using the software's 'Draw region' tool, the FAZ area (inner edge of the most observable central capillary walls) was manually measured in both layers, and the software automatically calculate the outlined area. Measurements were corrected for magnification errors according to Littmann's method and Bennet's formula Based on measured axial length.<sup>7</sup> The main outcomes of the study were the area of the FAZ of the SCP and the DCP.

We collected an informed consents from all cases considering the ethical standards of Al-Azhar Medical Research Ethical Committee.

## 3. Results

The study included fourteen eyes of 23 patients with high myopia, 14 males and 9 females. 17 patients had high myopia in both eyes while 6 patients had high myopia in one eye only. (4 right eye, 2 left eye).

Axial length measurements ranged from 24 to 28 mm (mean 25.86 ± 0.98). Mean OCTA measurements showed wider FAZ area in the superficial vascular plexus layer than in the deep vascular

plexus layer ( $0.37 \pm 0.06$  and  $0.31 \pm 0.07$  mm<sup>2</sup>, respectively), (Table 1).

Axial length showed no correlation to the area of the FAZ in both SCP and DCP layers, while it had a negative correlation to BCVA and a positive correlation to the patients' age and IOP measurements. Data are presented in (Table 2).

Patients' age, BCVA, IOP, or axial length did not correlate with the area of the FAZ in the superficial capillary plexus layer, but it did correlate negatively with UCVA and positively with the FAZ area in the deep capillary plexus layer. Data presented in (Table 3).

Patients' age, BCVA, UCVA, IOP, or axial length did not correlate with the area of the FAZ in the deep capillary plexus layer, but they did correlate positively with the area of the FAZ in the superficial capillary plexus layer. Data presented in (Table 4).

#### 4. Discussion

High myopia, a refraction error with a spherical equivalent more than minus 6 D and an axial lengths (AL) greater than 26 mm, affects predominantly younger people globally and the major causes of irreversible vision impairment. Excessive axial elongation is considered the main pathophysiological mechanism of high myopia causing chorioretinal stretching and reduction of the retinal nerve fiber layer (RNFL) thickness, macular hole formation, atrophy of the macula and a macula with a dome shape. Thinning of the chorioretinal tissue is linked to poor blood flow, which induces neovascularization Kumar and colleagues, Kamal Salah and colleagues.<sup>8,9</sup>

The amazing techniques of OCT and OCT-A are used for patient monitoring and the symmetry of macular diseases. Without the use of contrast agents, OCT-A is a cutting-edge ocular imaging technology for evaluation of the vascular

Table 1. Axial length and FAZ area in retinal vascular plexuses of the studied cases.

	Total number = 40
Axial length (mm)	
Mean $\pm$ SD	25.86 $\pm$ 0.98
Range	24–28
FAZ area in SCP (mm <sup>2</sup> )	
Mean $\pm$ SD	0.37 $\pm$ 0.06
Range	0.29–0.51
FAZ area in DCP (mm <sup>2</sup> )	
Mean $\pm$ SD	0.31 $\pm$ 0.07
Range	0.21–0.44

DCP, deep capillary plexus; FAZ, foveal avascular zone; SCP, superficial capillary plexus.

Table 2. Relation between axial length and other factors.

	Axial length		
	R	P value	Significance
Age	0.416	0.008	HS
FAZ area in SCP (mm <sup>2</sup> )	0.239	0.138	NS
FAZ area in DCP (mm <sup>2</sup> )	−0.071	0.662	NS
UCVA	0.107	0.512	NS
BCVA	−0.562	0.000	HS
IOP	0.589	0.000	HS

BCVA, best corrected visual acuity; DCP, deep capillary plexus; FAZ, foveal avascular zone; HS, Highly significant; IOP, intraocular pressure; NS, Nonsignificant; r, Spearman correlation coefficient; SCP, superficial capillary plexus; UCVA, uncorrected visual acuity.

architecture in different levels of the retina De Carlo and colleagues.<sup>10</sup>

The main purpose of study was to evaluate the changes in the retinal vascular plexuses in high myopia in adults using enhanced depth imaging OCT-A.

This is a cross sectional, descriptive study which was conducted at Ophthalmology department, Sayed Galal University Hospital, Al Azhar University. The study included 40 eyes of 23 patients with high myopia. Spherical equivalent ranged from −6.5 D to −11D, while astigmatism was less than 2D in all cases. Axial length measurements ranged from 24 to 28 mm (mean  $25.86 \pm 0.98$ ).

To avoid bias that may result from degenerative myopic changes, the International Photographic Classification and Grading System for Myopic Maculopathy has been taken into consideration while identifying fundus alterations Ohno-Matsui and colleagues.<sup>11</sup>

The study only included patients who had category 1 (tessellated fundus) and category 0 characterized by no myopic retinal degenerative lesion, while Category 2 characterized by Diffuse chorioretinal atrophy, 3 characterized by Patchy chorioretinal atrophy, 4 characterized by Macular atrophy,

Table 3. Relation between FAZ area in SCP and other factors.

	FAZ area in SCP		
	r	P value	Significance
Age	0.061	0.713	NS
Axial length	0.239	0.138	NS
FAZ area in DCP	0.780**	0.000	HS
UCVA	0.394*	0.012	S
BCVA	−0.189	0.242	NS
IOP	0.265	0.099	NS

BCVA, best corrected visual acuity; DCP, deep capillary plexus; FAZ, foveal avascular zone; HS, Highly significant; IOP, intraocular pressure; NS, Nonsignificant; r, Spearman correlation coefficient; S, significant; SCP, superficial capillary plexus; UCVA, uncorrected visual acuity.

Table 4. Relation between FAZ area in DCP and other factors.

	FAZ area in DCP		Significance
	R	P value	
Age	-0.109	0.508	NS
Axial length	-0.071	0.662	NS
FAZ area in SCP	0.780	0.000	HS
UCVA	0.189	0.242	NS
BCVA	0.074	0.651	NS
IOP	-0.021	0.899	NS

BCVA, best corrected visual acuity; DCP, deep capillary plexus; FAZ, foveal avascular zone; HS, Highly significant; IOP, intraocular pressure; NS, Non significant; r, Spearman correlation coefficient; SCP, superficial capillary plexus; UCVA, uncorrected visual acuity.

as well as those with plus lesions (posterior staphyloma, Lacquer cracks, CNV and Fuch's spot) were excluded.

Participants in the studies investigating dynamic retinal vessel were advised to stop any substances affecting the dynamic vessel properties as alcohol, caffeinated beverages, and vasoactive medication in the 12 h to the study La Spina and colleagues.<sup>12</sup> As such substances were not proposed to affect our measurements, these precautions were not considered in our work.

The FAZ, which is a grid-like area in the macula and has the largest concentration of cones photoreceptors, is one of the crucial dimension parameters in OCTA. The superficial plexus in the ganglion cell layer is made up of branches of the central retinal artery that branch at the level of retinal nerve fiber layer, making up the capillary network that connects the FAZ Zivkovic and colleagues.<sup>13</sup> The deep plexus is made up of deeper branches that extend into the inner nuclear layer. Therefore, Alternations in the microvasculature of central retina and reduction in central visual function show changes on FAZ area Piao and colleagues.<sup>14</sup>

We have used the OCTA, where the SCP was split automatically from the ILM to the IPL, and the DCP was split automatically from the INL to the OPL. Same segments boundaries definitions were used by Li and colleagues, for Angioplex OCTA device (Carl Zeiss Meditec, Dublin, CA),<sup>15</sup> and Ucak and colleagues, for OCT-A (Nidek RS3000 Advance).<sup>5</sup> Other machines have different definitions for segments boundaries, Min and colleagues, and Piao and colleagues, used OCTA (Optovue, Fremont, CA, USA), An inner border of 3 m below the ILM and an outside limit of 15 m under the IPL were used to segment the SCP enface OCTA image. The inner limit of the DCP image segmentation was 15 m under the IPL, and the outside limit was 70 m below the IPL.<sup>14,16</sup> So, the instrument used, the operating

system and segmentation method should be considered on comparing results.

We outlined the FAZ area using the technology 'Draw region' (the most noticeable inner boundary of the central capillary walls) in both layers manually, and the Software Automatically calculated the outlined area. A similar technique was used by Li and colleagues, to manually outline the FAZ of the superficial vascular plexus in retinal images using ImageJ (Ver. 1.48, National Institutes of Health, Bethesda, MD).<sup>15</sup> Other studies used different software programs for automated FAZ outlining and measurements: Ucak and colleagues, used an image analysis program AngioScan software to autodetect the FAZ metrics,<sup>5</sup> and Milani and colleagues, used the 'nonflow' measure function in AngioVue software to calculate the FAZ area automatically in mm<sup>2</sup>.<sup>17</sup> The FAZ measurements can only be calculated using these software programs at the level of the superficial capillary plexus. We failed to get a study to compare accuracy of manual and automated FAZ measurements.

Measurements obtained from fundus photos subject to magnification errors, especially with ametropic eyes. For analyzing the retina's dimensional information, an appropriate magnification adjustment is necessary, and this can be determined using the Littmann formula:  $t = 1.37qs$  Bennett and colleagues.<sup>7</sup>

According to this, a retinal feature's actual size (t) and the size (s) of its picture on the fundus camera film are related. The supplied eye's optical characteristics have an impact on the factor (q), which is a variable and can be calculated from keratometry measurements or axial length. Bennet and colleagues, Garway-Heath and colleagues concluded that the adjusted axial length is possibly the most effective and practical approach.<sup>7,18</sup> As the machine we used in this work did not have the proper software for magnification correction, we used the equation recommended by Bennet and colleagues<sup>7</sup> for (q) factor calculation:  $q = 0.01306(x - 1.82)$  where (x) relates to the measured axial length.

Magnification corrected mean area of FAZ in the SCP in our study was  $0.37 \pm 0.06$  mm<sup>2</sup>. In high myopia group, Li and colleagues., reported a mean area of  $0.28 \pm 0.12$  mm<sup>2</sup>,<sup>15</sup> Ucak and colleagues, reported a mean area of  $0.31 \pm 0.06$  mm<sup>2</sup> Ye and colleagues,<sup>6</sup> and Min and colleagues, reported a mean area of  $0.39 \pm 1.3$  mm<sup>2</sup> Wang and colleagues.<sup>19</sup> In the later three studies, authors compared FAZ areas in the SCP in normal controls and high myopic differences between normal controls and myopic eyes were insignificant. Piao and colleagues,<sup>14</sup> reported a mean FAZ area of  $0.43 \pm 0.22$  mm<sup>2</sup> in the SCP, they

reported that the FAZ regions of eyes without high myopia were significantly smaller than those of eyes with high myopia.

We reported a smaller FAZ in the DCP with a mean area of  $0.31 \pm 0.07 \text{ mm}^2$ . In contrary to our results, Ucak and colleagues findings in the high myopia group showed wider FAZ in the DCP (mean  $0.47 \pm 0.08 \text{ mm}^2$ ).<sup>5</sup> Similarly, Piao and colleagues, reported a wider mean FAZ area of  $0.66 \pm 0.25 \text{ mm}^2$  in the DCP, They also noted that the deep FAZ layers showed more differences between normal and myopic eyes, indicating that the deep capillary plexus is more vulnerable to myopia-related alterations. They supposed this divergence to result from the difference in arterial blood supply between the SCP and DCP, as the central retinal artery supplies nutrition and oxygen to the superficial retina, but the choroidal vascular system supplies the deep retina. Although several theories have been put forth, the nature of FAZ elongation in myopic eyes is still unknown. One theory is that, axial elongation with macular thinning case of retinal oxygenation second, progresses causing retinal vascular trunk dragging and a decrease in retinal blood flow and furthermore variations in the FAZ size., resulting in increase in FAZ area and decrease in the retinal blood flow Piao and colleagues.<sup>14</sup>

In contrary to these findings and explanations, Wang and colleagues, demonstrated association between larger FAZ area and hypermetropia and short axial length.<sup>19</sup>

Our correlation analyses agreed to Ucak and colleagues, regarding age and AL that had no correlation to FAZ area in SCP and DCP Ye and colleagues.<sup>6</sup> While, Min and colleagues<sup>16</sup> associates reported a positive correlation of the axial length with the FAZ area in the SCP ( $r = 0.239$ ,  $P = 0.025$ ), in their study they did not report the FAZ area in the DCP.

The present study showed that area of the FAZ in the superficial capillary plexus layer showed no correlation to the patients' age, BCVA, IOP, or axial length, while it demonstrate a positive relation with FAZ area in the deep capillary plexus layer and a negative relation with UCVA. Area of the FAZ in the deep capillary plexus layer showed no correlation to the patients' age, BCVA, UCVA, IOP, or axial length, while it showed a positive correlation to FAZ area in the superficial capillary plexus layer. Measurements of axial length, FAZ area in the SCP layer, and FAZ area in the DCP layer showed no correlation to eye laterality. Both measurements of axial length and FAZ area in the DCP layer showed no correlation to patients' sex, while FAZ area measurements in the SCP layer were significantly higher in females than

in males. None of the reviewed articles have correlated FAZ measurements to participants' age, sex, visual acuity or IOP.

Differences in reported results may be due to different instruments used, layer segmentation and FAZ outlining methods or participants differences (number, demographics, or ethnicity and racial factors). Li and colleagues<sup>15</sup> concluded that there are lack of data about the FAZ area in myopic patients and that individual variances in age and other factors are likely to be the cause of the differences in the results.

#### 4.1. Conclusion

The axial length had a negative link to BCVA and a positive correlation to the patients' age and IOP readings, but it did not correlate with the area of the FAZ in the SCP or DCP layers. The area of the FAZ in the superficial capillary plexus layer showed no correlation to the patients' age, BCVA, IOP, or axial length, while it showed a positive correlation to FAZ area in the deep capillary plexus layer and a negative correlation to UCVA. Area of the FAZ in the deep capillary plexus layer showed no correlation to the patients' age, BCVA, UCVA, IOP, or axial length, while it showed a positive correlation to FAZ area in the superficial capillary plexus layer.

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#### Conflicts of interest

The authors declared that there were No conflicts of Interest.

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