

# Foveal Avascular Zone Evaluation in Patients with Diabetic Retinopathy without Diabetic Macular Edema Using Optical Coherence Tomography Angiography

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## Research Article

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# Abstract

**Purpose:** To evaluate dimensions of Foveal Avascular Zone (FAZ) at level of superficial and deep capillary plexuses (SCP/DCP), in patients with different grades of non proliferative diabetic retinopathy without Diabetic Macular Edema (DME) using Optical Coherence Tomography Angiography (OCTA).

**Patients and Methods:** 80 type II diabetes mellitus patients and 20 healthy control subjects were included in this cross sectional study, aged from 40-60 years with DM type 2 of more than five years, excluding proliferative diabetic retinopathy and DME. Patients were subdivided into four groups according to ETDRS Classification (without retinopathy, mild, moderate and severe retinopathy). All subjects underwent: measurement of glycosylated hemoglobin level, standard Structural Optical coherence tomography for the macula and optic nerve head with OCTA for evaluation of FAZ in both SCP and DCP networks of all eyes using (Heidelberg engineering, OCT spectralis, Germany) (SD-OCT).

**Results:** Mean total macular thickness in control group ( $322.89 \pm 16.31 \mu\text{m}$ ) vs ( $316.57 \pm 20.21 \mu\text{m}$ ) in patients group.  $\text{Avera} \geq \text{RNFLthick} \neq \text{ss}(158.61 \pm 12.99 \mu\text{m}) \in \text{controlgroupvs}(156.07 \pm 22.58) \mu\text{m} \in \text{patients}$  group. Mean FAZ in SCP in control group ( $0.32 \pm 0.12$ ) mm<sup>2</sup> versus ( $0.44 \pm 0.17$ ) mm<sup>2</sup> in patients' group, while FAZ IN DCP ( $0.23 \pm 0.12$ ) mm<sup>2</sup> in controls versus ( $0.34 \pm 0.16$ ) mm<sup>2</sup> in patients. There was a statistically significant wider FAZ in DR patients (P-value 0.003).

**Conclusion:** Enlargement of FAZ in SCP and DCP in patients with moderate to severe NPDR without DME was detected using OCTA, proceeded by neurodegenerative changes with reduction in thickness of ORL and GCC layer. This can be used to monitor the progression of the disease and to evaluate the response to treatment.

## Introduction

Diabetic retinopathy (DR) is the most frequent complication of diabetes and the major preventable blindness cause, between working-age individuals in most of the developed countries [1]. Increased inflammation, hypoxia, and oxidative stress, all of which are caused by chronic hyperglycemia and lead to microvascular retinal changes [2]. Adequate evaluation of these changes during the different stages of DR, is a clue for perfusion status of the retina and the probability of developing more severe retinopathy. Fluorescein angiography (FA) was the gold standard imaging modality for the diabetic macular ischemia (DMI) qualitative evaluation, specifically the size and contour of the FAZ [2,3]. Nevertheless, quantitative FAZ FA based evaluation is inconvenient and unreliable in clinical settings, Optical coherence tomography angiography (OCTA) offers a convenient and safe alternative to FA, and is more reproducible to automated quantification, specifically for vascular lesions near the fovea, especially the FAZ [4,5]

OCTA is a rapid, safe, and noninvasive technique for retinal and choroidal microvessels visualization with a resolution outstands fundus FA [6]. OCTA can allow detailed quantification the SCP and DCP, capillary perfusion impairment, and neovascularization with high resolution [7]. OCTA also provides information on the dimensions and shape of the FAZ, with macular ischemia related changes, especially in DR [8]

It is proven in several studies that FA photographs correlated only with large superficial retinal vessels anatomical arrangement, within the nerve fiber layer and the ganglion cell layer, and visibility of deeper retinal vasculature perfusion was not possible [9]. This was attributed to Light scattering within the retina [10].

It has been stated that (OCTA) can detect microvascular changes (e.g. capillary dropout, neovascularization, FAZ enlargement, microaneurysms) in diabetic eyes FAZ enlargement is correlated with visual acuity reduction [11]

Detailed detection of FAZ enlargement and distortion, retinal capillary dropout, and pruning of arteriolar branches have been guaranteed with the introduction of OCTA. Especially areas of capillary loss obscured by fluorescein leakage on FA.

Focal leakage areas on FA that were believed to be microaneurysms, were proven to be neovascularization small tufts extended above the inner limiting membrane [12].

For DR, multiple retinal vasculature and FAZ fundusoscopic abnormalities have been described [13]. Studies have found that the FAZ circumference, maximum and mean diameter are significantly wider in diabetic eyes compared to healthy controls. microinfarction within the surrounding vascular arcades explains the pathophysiology of FAZ enlargement in DR [14].

**The aim of our study to** evaluate dimensions of foveal avascular zone FAZ at level of superficial and deep capillary plexuses (SCP, DCP) in patients with different grades of non proliferative diabetic retinopathy DR without diabetic macular edema DME, using optical coherence tomography angiography OCTA ; and to correlate these changes with the best corrected visual acuity, glycemic control of the patients and retinal neuro degenerative changes.

## Patients And Methods

This cross sectional study was carried out from February 2018 to August 2018 on 100 eyes of patients attending outpatient clinic of Ophthalmology Department of Research Institute of Ophthalmology in Giza. The ethical standards stated by the ethical committee of Ain Shams University hospitals, were followed. This study was followed the tenets of the Declaration of Helsinki on Ethical Principles for Medical Research Involving Humans

### Inclusion Criteria

1. Age: 40-60 years.
2. History of diabetes mellitus type II for more than 5 years.

### Exclusion Criteria

1. Proliferative diabetic retinopathy.
2. OCT evidence of diabetic macular edema of different types.
3. Refractive error of more than 6 diopters.
4. Opaque media.
5. Previous intra ocular surgeries except cataract extraction of more than one year
6. Previous treatment of diabetic retinopathy or DME.
7. Congenital or acquired retinal and optic nerve disorder with effect on the results.
8. Uncooperative patients and patient with poor fixation.

### Study Tools

- Control group: 20 eyes of 20 normal healthy individuals of the same age and sex matched group. Right eye was examined in each individual as recommended for correct statistical analysis.
- Study group: 80 eyes of diabetic patients were subdivided into four groups according to ETDRS Classification of Non Proliferative Diabetic Retinopathy (13)
  - ✓ Study group (a): 20 eyes with diabetic patients without DR.
  - ✓ Study group (b): 20 eyes with mild NPDR.
  - ✓ Study group (c): 20 eyes with moderate NPDR.
  - ✓ Study group (d): 20 eyes with severe NPDR.

**All subjects were evaluated by:** history,full ophthalmological examination, measurement of glycosylated hemoglobin level (HbA1c),standard Structural Optical coherence tomography the macula and optic nerve head using (Heidelberg engineering, OCT spectralis, Germany) (SD-OCT) with imaging protocol of Macula scan and Optic disc scan ,also Optical coherence tomography angiography for evaluation of foveal avascular zone FAZ of all eyes using the same machine.FAZ area was measured in both superficial and deep capillary networks (SCP and DCP layers) using software "Draw region" tool to outline FAZ area (inner border of the most visible central blood capillaries) manually, and software automatically calculate the outlined area.

This manual measurement was done by two independent investigators who were masked to all other results including BCVA and retinal thickness. The average of their measurements were calculated and used to optimize the study results.

This study was followed the tenets of the Declaration of Helsinki on Ethical Principles for Medical Research Involving Humans. Study protocol was approved by the local research ethics committee.

### Statistical analysis

We used Statistical Package for Social Science (IBM SPSS) version 23. Chi-square test and/or Fisher exact test ,*Independent t-test , Mann-Whitney test,One Way ANOVA , Kruskal-Wallis test,Spearman's correlation coefficients* were used

## Results

This study included 100 eyes of 66 patients, 30 (45.5%) males and 36 (54.5%) females with age ranging from 40 to 60 years, 20 eyes of normal healthy individuals (control group) and 80 eyes of diabetic patients were included. Diabetic divided according to severity to mild, moderate and sever. There was no history of hypertension or other medical conditions in all candidates.

**Table (1):** Summary of demographic data:

- There was no statistically significant difference found between control group and patients' group regarding mean age (P-value 0.103), also regarding Sex distribution (P-value 0.118).
- Comparison between patients 'sub groups was done regarding mean duration and revealed highly statistically significant difference (*P-value*000).
- The mean HbA1c ( $\pm$  SD) in control was ( $4.25\% \pm 0.83$ ), ranged was from 2.3 – 5.4 % and in diabetic patients was ( $8.93 \pm 2.33$ ), ranged from 5.5 – 14 %, with highly statistically significant difference found between control group and patients group regarding, HbA1c level (*P-value*00), same for between control group and patients 'sub group (*P-value* 0.00).

**Graph (1):** Column graph shows comparison between control group and patients sub groups regarding HbA1c.

### ■ Ophthalmological examinations

- **Mean BCVA (log. MAR):**The mean BCVA ( $\pm$  SD) recorded using Log. MAR in control was ( $0.0 \pm 0.0$ ) and in diabetic patient was ( $0.11 \pm 0.11$ ). There was highly statistically significant difference found between: control group and patients group regarding BCVA (*P-value*000) and between control group and patients 'sub group(*P-value* 0.000).
- **Cup disc ratio:** The mean ratio ( $\pm$  SD) in control was ( $0.44 \pm 0.07$ ), ranged from 0.35-0.57 and in diabetic patients was ( $0.40 \pm 0.10$ ), ranged from 0.1 – 0.64. With no statistically significant difference found between control group and patients' group (*P-value*098).
- **Structural OCT data:**Comparison was done between control group and patients' group as regards:

- **Mean total macular thickness ( $\mu\text{m}$ ):** there was no statistically significant difference (*P-values* were  $>0.05$ ) in average, central, superior, inferior, nasal and temporal quadrants. Average thickness in control group ( $89 \pm 16.31 \mu\text{m}$ ) versus ( $316.57 \pm 20.21 \mu\text{m}$ ) in patients' group.
- **Mean peripapillary retinal nerve fiber layer thickness ( $\mu\text{m}$ ):** there was no statistically significant difference (*P-values* were  $>0.05$ ) in all quadrants. Average RNFL thickness was ( $158.61 \pm 12.99 \mu\text{m}$ ) in control group vs. ( $156.07 \pm 22.58 \mu\text{m}$ ) in patients' group.
- **Mean GCC layer thickness ( $\mu\text{m}$ ):** There was no statistically significant difference in all quadrants (*P-values* were  $>0.05$ ) except the nasal (*P-value* 0.12) and average (*P-value* 0.039) where there was statistically significant difference.

Comparison between control group and patients 'sub group was done regarding mean GCC layer thickness, revealed a highly statistically significant difference between the control group and;

- The moderate NPDR group regarding only mean superior (*P-value* 0.10).
- The severe NPDR group regarding average and in all quadrants of the mean GCC layer thickness (*P-values* were  $\leq 0.05$ ) except the central ones shown in **(Table 2)**.
- **Mean outer retinal layer thickness ORL( $\mu\text{m}$ ):** there was a statistically significant difference in mean average, central and in all quadrant (*P-value* were  $\leq 0.05$ ) except the temporal one (*P-value* was 0.13).
- Comparison between control group and diabetic retinopathy 'sub group was done; revealed:
  - A statistically significant difference between control group and no retinopathy group regarding mean average and inferior ORL .
  - A statistically significant difference between control group and the moderate NPDR regarding mean average and central ORL .
  - A statistically significant difference between control group and the severe NPDR regarding mean average and central and inferior ORL **(Table 3)**

#### OCTA data:

- **Mean FAZ area in SCP ( $\text{mm}^2$ ):**
- There was a statistically significant wider area in DR patients (*P-value* was 0.003) **(Graph 2)**. Mean FAZ in SCP in control group ( $0.32 \pm 0.12 \text{mm}^2$ ) versus ( $0.44 \pm 0.17 \text{mm}^2$ ) in patients' group.
- Comparison between control group and patients 'sub group was done, revealed highly statistically significant difference between control group and moderate NPDR group and severe NPDR group regarding mean FAZ area ( $\text{mm}^2$ ). **(Table 4)**.
- **Mean FAZ area in DCP ( $\text{mm}^2$ ):**
- FAZ IN DCP ( $0.23 \pm 0.12 \text{mm}^2$ ) in controls versus ( $0.34 \pm 0.16 \text{mm}^2$ ) in patients.
- There was a statistically significant wider area in DR patients (*P-value* was 0.006) **(Graph 2)**
- Comparison between control group and patients 'sub group was done regarding mean FAZ area in DCP ( $\text{mm}^2$ ) and revealed highly statistically significant difference between control group and severe NPDR group regarding mean FAZ area ( $\text{mm}^2$ ) in DCP as shown in **(Table 4) (Fig. 1)**.
- There was no statistically significant difference found between the increases in SCP in patients than control when compared to the increase in DCP in patients than control (*P-value* was 0.320).
- **Spearman's correlation coefficient:**

Correlation was done between various study variables and mean FAZ area ( $\text{mm}^2$ ).

- In SCP and in DCP and there was a statistically significant positive correlation between mean FAZ area (mm<sup>2</sup>) in SCP and mean FAZ area (mm<sup>2</sup>) in DCP and BCVA (Log. MAR)
- A statistically significant negative correlation between mean FAZ area (mm<sup>2</sup>) in SCP with mean superior, inferior, nasal, temporal and central ganglion cell complex layer thickness, mean central ORL thickness
- No statistically significant correlation was found between the other studied parameters (**Table 5**).
- There was no statistically significant relation between gender distribution and mean FAZ area (mm<sup>2</sup>) in SCP (*P-value* was 0.552) and DCP (*P-value* was 0.576).
- Correlation was done between BCVA (Log. MAR) and mean central GCC layer thickness and mean ORL thickness and there was no any statistically significant correlation found between them (*P-values* were > 0.05).

## Discussion

OCTA is a novel technique doesn't need dye for visualization of the retinal microvasculature. Therefore, the FAZ area can be optimally evaluated without the obscure of dye leakage [15] which occurs in the FFA, where capillary details are best evaluated during the transit phase, for that bilateral reliable evaluation of the FAZ is not possible. The choroidal and retinal circulation cause diffuse fluorescein leakage. Moreover microaneurysms and neovascularization obscure capillary details in FFA but not in OCTA [16].

OCT images enable comparing the thickness and reflectance measurements of the various cellular layers of the retina in diabetic patients with DR against normal healthy subjects and diabetic patients who have no retinopathy. Thus allows better understanding of early histological changes of the macula in diabetes [17].

In this study, the FAZ areas of SCP and DCP were detected by OCTA in diabetic eyes without DME and correlated with BCVA, HbA1c and neurodegenerative changes. This study revealed a statistically significant enlargement of FAZ in patients with moderate NPDR group in SCP and severe NPDR group in both SCP and DCP.

These results came in agreement with Freiberg., 2016 [18] who noticed enlargement of the FAZ in SCP in eyes with diabetic retinopathy with significant difference against the control group.

Moreover, Samara et al., 2017 [19] stated that a significantly greater FAZ area and significantly lower vascular density were noticed, in all diabetic eyes when compared with control eyes.

Tang et al., 2017 [20] reported that DR severity had the most influence and caused FAZ area increase and FAZ circularity decrease, concluding that the OCT-A can quantify the extent of microvascular breakdown (e.g. macular ischemia).

This study found that there was a statistically significant positive correlation between FAZ in SCP and in DCP and BCVA (Log MAR). These results came in agreement with Samara et al., 2017 [19] who stated that, a positive correlation was noticed between logMAR FAZ area and visual acuity in both the SCP/DCP networks.

There was no statistically significant difference found between control group and patients' group regarding full macular thickness as we exclude DME.

There was no statistically significant difference was found between control group and patients' group regarding peripapillary retinal nerve fiber layer thickness RNFL and cup to disc ratio. This was in agreement with Vujosevic and Miden, 2013 [21] although RNFL thickness was reduced in diabetics versus controls, it did not reach statistical and clinical significance, probably due to the fact that in this area, small changes are more difficult to be clinically detected because of the high density of retinal nerve fibers.

Pekel et al., 2018 [22] stated that, there were no statistically significant differences between the diabetic patients and healthy controls regarding RNFL, rim area, disc area, vertical cup-to-disc ratio, cup volume.

In the present study, there was a statistically significant decrease in mean superior, inferior, nasal, temporal, ganglion cell complex layer GCL thickness in severe NPDR group and in mean superior GCL thickness in moderate NPDR group versus controls. There was, a statistically significant negative correlation between FAZ in SCP with superior, inferior, nasal, temporal and central GCL thickness.

This was in agreement with DeBuc and Somfai, 2010[23] who noticed a reduction of thickness of ganglion cell/inner plexiform layer (GCL+IPL) complex in the pericentral macular area in the mild diabetic retinopathy group.

Fernández et al., 2008 [24] reported that the GCL+IPL complex thickness is significantly reduced in the pericentral macular area in the mild diabetic retinopathy group when compared to controls.

The current study shows that there was a statistically significant decrease in mean central and inferior (ORL) thickness in severe NPDR group and in mean central (ORL) thickness in moderate NPDR group and in mean inferior (ORL) thickness in no retinopathy group versus controls and there was a statistically significant negative correlation between FAZ in SCP and central (ORL) thickness.

This was concordant with Wang et al., 2018[25] who found that a significant reduction in the mean (ORL) thickness in DME and non DME groups compared to the control group.

Sohn et al., 2016 [26] reported that retinal diabetic neuropathy may precede signs of micro vasculopathy or DR in people with DM, this came in agreement with the present study that there was neurodegenerative change even in no retinopathy patients.

## Conclusion

Enlargement of FAZ in SCP and DCP in patients with moderate to severe NPDR without DME was detected using OCTA with accurate delineation of the edges of these zones. These finding was preceded by neurodegenerative changes in the form of reduction in thickness of ORL and GCC layer. These vascular and neurological changes were moderately correlated to each other and to BCVA and severity of the diseases. These may determine the prognosis prior to any further treatment.

## Declarations

**Funding:** No funding was received to assist with the preparation of this manuscript.

**Conflicts of interest:**

**Financial interests/Non-financial interests:** The authors have no conflicts of interest to declare that are relevant to the content of this article.

**Ethics approval:** Approval was obtained from the ethics committee of the Faculty of Medicine, Ain Shams University. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

**Availability of data and material (data transparency):** Available

**Code availability (software application or custom code):** not applied

**Consent to participate:** Informed consent was obtained from all individual participants included in the study.

**Consent to publish:** Patients signed informed consent regarding publishing their data and photographs

**Author Contribution Statement:**

**Mohamed Mahmoud Mostafa** was responsible for designing the study protocol, writing the protocol and report, conducting the search, screening potentially eligible studies, extracting and analyzing data, interpreting results, updating reference lists and creating 'Summary of findings' tables. **Abdel Rahman ,Azza and Tarek** were responsible for designing the study protocol and revising the results and discussion. **Marwa** contributed by writing the paper, extracting and analyzing data, interpreting results and creating tables. Azza conducted the statistical analyses.

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## Tables

**Table (1)original: Summary of demographic data**

		Control group	Patients group	Test value	P-value	Sig.
Age (years)	Mean $\pm$ SD	48.9 $\pm$ 6.72	51.54 $\pm$ 6.32	-1.648•	0.103	NS
	Range	40 – 60	40 – 60			
Sex	Male	12 (60.0%)	18 (39.1%)	2.449*	0.118	NS
	Female	8 (40.0%)	28 (60.9%)			
Eye	Right	20 (100%)	38 (47.5%)	–	–	–
	Left	0 (0.0%)	42 (52.5%)			
	Unilateral DR	20 (100.0%)	12 (26.1%)	–	–	–
	Bilateral DR	0 (0.0%)	34 (73.9%)			
Duration (years)	Mean $\pm$ SD	–	12.69 $\pm$ 4.65	–	–	–
	Range	–	6 – 20			
HbA1c (%)	Mean $\pm$ SD	4.25 $\pm$ 0.83	8.93 $\pm$ 2.33	-8.808•	0.000	HS
	Range	2.3 – 5.4	5.5 – 14			

\*: Chi-square test; •: Independent t-test

**Table (2)original: Comparison between control group and patient's subgroup regarding mean ganglion cell complex layer thickness.**

Ganglion Cell Complex layer thickness (µm)		No retinopathy	Mild	Moderate	Severe	Control group	Test value*	P-value	Sig.
		No. = 20	No. = 20	No. = 20	No. = 20	No. = 20			
Average	Mean ± SD	43.31 ± 3.2	40.51 ± 6.37	39.92 ± 2.91	37.15 ± 7.82	43.17 ± 4.77	4.554	0.002	HS
	Range	38.2 – 47.6	25 – 49.8	33.2 – 43.8	19 – 47.2	30.6 – 49			
Central	Mean ± SD	14 ± 3.52	13.9 ± 3.57	14.05 ± 3.95	12.5 ± 3.79	14.85 ± 4.18	0.993	0.415	NS
	Range	8 – 21	8 – 22	7 – 23	7 – 20	8 – 22			
Superior	Mean ± SD	52.6 ± 3.25	49.95 ± 7.01	46 ± 7.09	44.35 ± 10.76	51.9 ± 5.33	5.201	0.001	HS
	Range	47 – 58	31 – 60	23 – 55	24 – 60	35 – 58			
Inferior	Mean ± SD	53 ± 3.48	49.1 ± 6.43	49.1 ± 3.6	46.95 ± 10.85	51.7 ± 5.16	2.707	0.035	S
	Range	47 – 58	35 – 58	41 – 57	23 – 69	40 – 59			
Nasal	Mean ± SD	50.25 ± 5.62	47.5 ± 7.33	47.3 ± 2.74	42.8 ± 8.54	51.25 ± 5.75	5.437	0.001	HS
	Range	35 – 58	27 – 58	42 – 53	22 – 57	38 – 58			
Temporal	Mean ± SD	46.7 ± 4.32	42.1 ± 11.96	43.15 ± 3.76	39.15 ± 9.83	46.15 ± 6.82	2.998	0.022	S
	Range	40 – 53	9 – 55	36 – 49	19 – 53	29 – 54			
Post hoc analysis									
	No vs control group	Mild vs control group		Moderate vs control group		Severe vs control group			
Superior	0.757	0.389		0.010		0.001			
Inferior	0.528	0.208		0.208		0.023			
Nasal	0.617	0.063		0.051		0.000			
Temporal	0.828	0.112		0.238		0.007			
Average	0.934	0.119		0.058		0.001			

Table (3 )original: Comparison between control group and patient's subgroup regarding mean (ORL) thickness

Mean (ORL) thickness		No retinopathy	Mild	Moderate	Severe	Control group	Test value	P-value	Sig.
		No. = 20	No. = 20	No. = 20	No. = 20	No. = 20			
Average	Mean ± SD	80.13 ± 2.05	81.89 ± 4.29	80.27 ± 3.5	79.3 ± 3.79	82.56 ± 2.46	3.284	0.014	S
	Range	75.8 – 85	75 – 93.8	75.4 – 89.2	75 – 87.8	79.2 – 88.2			
Central	Mean ± SD	86.2 ± 3.04	88.6 ± 7.39	84.25 ± 4.35	82.95 ± 4.3	88.45 ± 2.86	5.739	0.000	HS
	Range	81 – 91	76 – 107	76 – 92	76 – 92	83 – 93			
Superior	Mean ± SD	78.4 ± 2.28	80.3 ± 2.66	79.6 ± 4.52	78.65 ± 3.5	81.15 ± 2.87	2.459	0.051	NS
	Range	74 – 83	75 – 87	72 – 92	74 – 84	76 – 86			
Inferior	Mean ± SD	77.35 ± 2.54	78.9 ± 2.73	78.05 ± 3.1	77 ± 3.48	79.75 ± 3.01	2.840	0.028	S
	Range	73 – 82	74 – 86	73 – 84	72 – 84	77 – 88			
Nasal	Mean ± SD	79.8 ± 2.31	80.35 ± 2.52	80.05 ± 4.3	79.9 ± 7.12	82.2 ± 2.55	1.132	0.346	NS
	Range	77 – 85	74 – 86	74 – 91	73 – 105	78 – 87			
Temporal	Mean ± SD	78.9 ± 2.29	81.3 ± 8.42	79.4 ± 4.41	78 ± 3.76	81.25 ± 2.77	1.824	0.131	NS
	Range	74 – 84	76 – 110	73 – 93	72 – 86	77 – 88			
Post hoc analysis									
	No vs control group	Mild vs control group		Moderate vs control group		Severe vs control group			
Inferior	0.013	0.371		0.075		0.005			
Central	0.132	0.919		0.006		0.000			
Average	0.023	0.525		0.032		0.003			

Table (4)original: Comparison between control group and patient's subgroup regarding mean FAZ (mm<sup>2</sup>) area in SCP and DCP

		No retinopathy	Mild	Moderate	Severe	Control group	Test value•	P- value	Sig.
		No. = 20	No. = 20	No. = 20	No. = 20	No. = 20			
FAZ IN SVP	Mean ± SD	0.36 ± 0.1	0.35 ± 0.11	0.43 ± 0.16	0.6 ± 0.16	0.32 ± 0.12	14.783	0.000	HS
	Range	0.2 – 0.55	0.16 – 0.57	0.2 – 0.68	0.36 – 0.88	0.18 – 0.62			
FAZ IN DVP	Mean ± SD	0.28 ± 0.09	0.26 ± 0.09	0.31 ± 0.12	0.5 ± 0.18	0.23 ± 0.12	13.937	0.000	HS
	Range	0.16 – 0.46	0.1 – 0.44	0.13 – 0.54	0.17 – 0.83	0.08 – 0.49			
Post hoc analysis									
	No vs control group	Mild vs control group		Moderate vs control group		Severe vs control group			
FAZ IN SVP	0.294	0.358		0.009		0.000			
FAZ IN DVP	0.231	0.409		0.059		0.000			

Table (5)original: Correlation of FAZ in SCP and DCP with the other studied parameters

	FAZ IN SCP		FAZ IN DCP	
	r	P-value	r	P-value
Age	0.015	0.892	0.043	0.708
Duration	0.150	0.183	0.146	0.197
HbA1c	0.158	0.160	0.135	0.231
BCVA	<b>0.251*</b>	<b>0.025</b>	0.216	0.054
C/D Ratio	-0.056	0.622	-0.105	0.353
FAZ IN SVP			<b>0.896**</b>	<b>0.000</b>
FAZ IN DVP	<b>0.896**</b>	<b>0.000</b>		
<b>Ganglion Cell Complex</b>				
Superior	<b>-0.440**</b>	<b>0.000</b>	<b>-0.481**</b>	<b>0.000</b>
Inferior	<b>-0.228*</b>	<b>0.041</b>	<b>-0.277*</b>	<b>0.013</b>
Nasal	<b>-0.444**</b>	<b>0.000</b>	<b>-0.468**</b>	<b>0.000</b>
Temporal	<b>-0.408**</b>	<b>0.000</b>	<b>-0.495**</b>	<b>0.000</b>
Central	<b>-0.592**</b>	<b>0.000</b>	<b>-0.614**</b>	<b>0.000</b>
Average	<b>-0.489**</b>	<b>0.000</b>	<b>-0.557**</b>	<b>0.000</b>
<b>(ORL) thickness</b>				
Superior	-0.013	0.910	-0.082	0.467
Inferior	-0.008	0.943	-0.108	0.339
Nasal	-0.111	0.326	-0.184	0.103
Temporal	-0.092	0.416	-0.115	0.310
Central	<b>-0.337**</b>	<b>0.002</b>	<b>-0.277*</b>	<b>0.013</b>
Average	-0.115	0.309	-0.172	0.128