AIM OF THE WORK

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The aim of the work was to compare between choroidal thickness in patients with diabetic retinopathy and normal persons using enhanced-depth imaging spectral-domain optical coherence tomography.

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SUBJECTS AND METHODS

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SUBJECTS AND METHODS

The study included 40 eyes of adult subjects half of them diabetics who recruited from the ophthalmology department at Alexandria main university hospital.

Eyes were equally divided into two groups:

Group (1): Included 20 eyes of diabetic patients having either non-proliferative diabetic retinopathy or proliferative diabetic retinopathy.

Group (2): Included 20 eyes of normal subjects used as control.

Exclusion criteria

1. Central retinal vein occlusion.
2. Branch retinal vein occlusion.
3. Secondary optic atrophy.
4. Choroidal neovascularization.
5. Media opacity.
6. Pan retinal photocoagulation.
7. Macular laser treatment.
8. Previous intravitreal injection.

The diabetic patients and the healthy adults were subjected to the following:

- Full history taking including, age, sex, past ocular and systemic history.
- In the diabetic group, further inquiry was done on diabetes mellitus type, duration and previous treatments applied to the eye.
- Full ophthalmic examination including visual acuity assessment, IOP measurement, anterior segment and posterior segment examination.

Investigations included

- Fluoresein angiography to determine the stage of diabetic retinopathy. (in the diabetic group only).
- Optical coherence tomography of the macular area and of the choroid using enhanced depth imaging of the Heidlberg spectralis OCT. (in both groups).
  - OCT study was done for the choroid in the macular area in cases & controls using single line in vertical & horizontal directions by enhanced depth imaging mode.
  - Manual measurement was done in the horizontal and the vertical scans at the foveal center and at distance of 500 μm & 1500 μm in both directions from the fovea.
  - Measurement was taken from the outer limit of RPE line to the end of choroidal image on the OCT.

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RESULTS

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RESULTS

The study included 40 adult eyes divided into two groups: group (I) 20 normal eyes and group (II) 20 eyes of diabetic patients diagnosed with non-proliferative diabetic retinopathy or proliferative diabetic retinopathy who were recruited from the outpatient clinic of Alexandria main university hospital.

Table (2): Comparison between the studied groups according to demographic data.

	Control (n=20)		Cases (n=20)		Test of Sig.	p
	No.	%	No.	%		
Sex						
Male	11	55.0	6	30.0	χ^2=2.558	0.110
Female	9	45.0	14	70.0		
Age						
Min. – Max.	22.0 - 64.0		26.0 – 69.0			
Mean ± SD.	50.15 ± 9.36		48.50 ± 10.84		t= 0.962	0.342
Median	50.0		49.50			

χ^2: Chi square test
t: Student t-test
Comparing age and sex in diabetics and control.
Showed no significant difference between the two groups.

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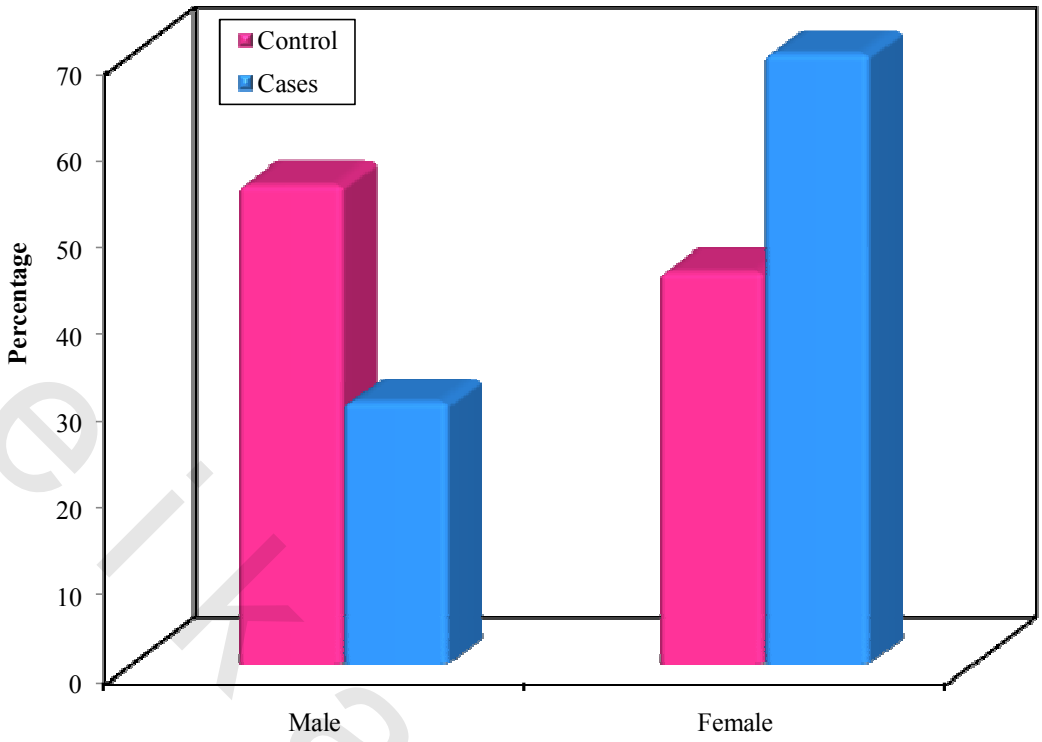

Figure (10): Comparison between the studied groups according to sex.

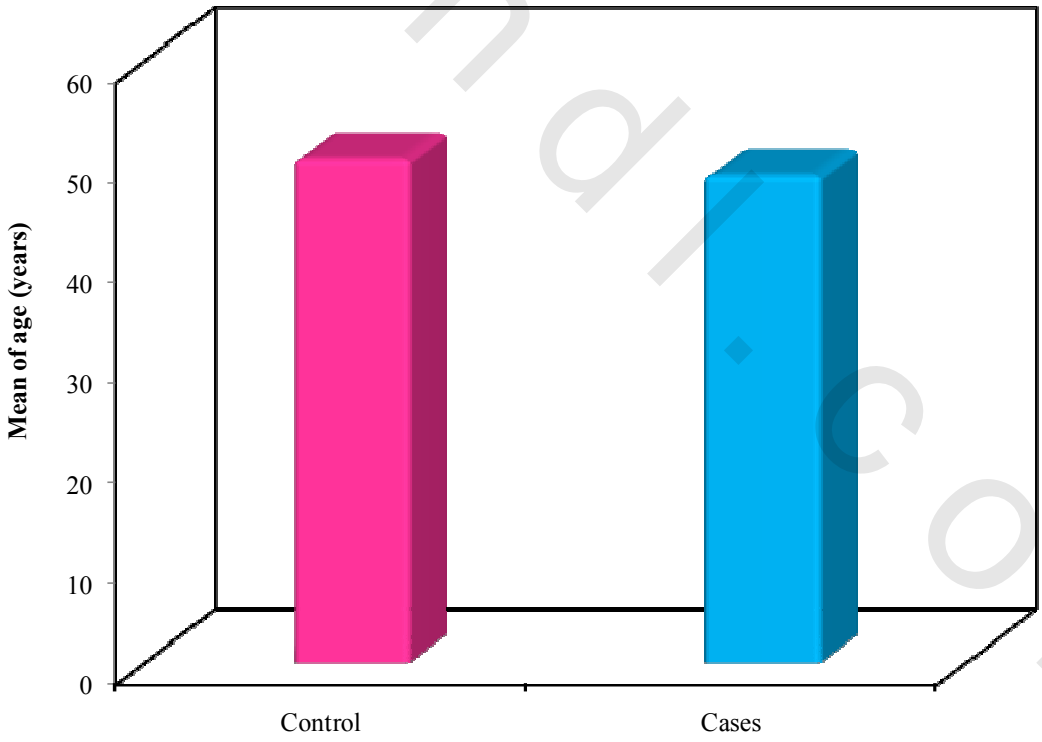

Figure (11): Comparison between the studied groups according to age.

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Table (3): Comparison between the studied groups according to side

	Control (n=20)		Cases (n=20)		χ^2	p
	No.	%	No.	%		
Side						
OS	8	40.0	5	25.0	1.026	0.311
OD	12	60.0	15	75.0		

χ^2: Chi square test
Comparing the side between diabetics and controls.
Showed no significant difference between the study group according to side.

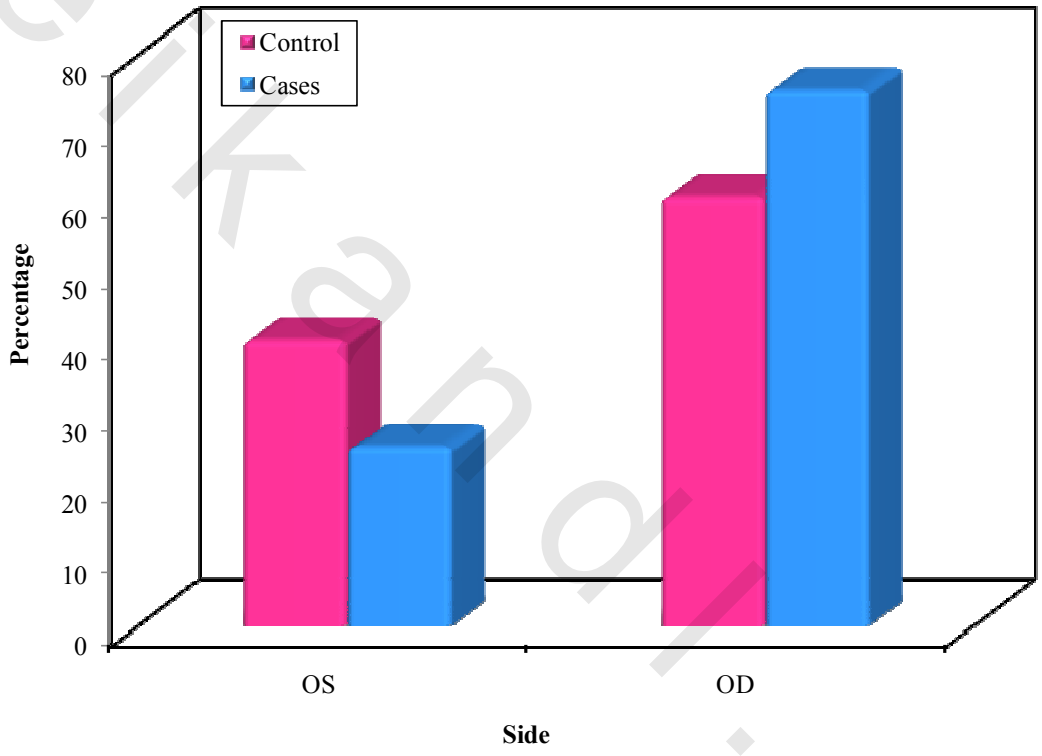

Figure (12): Comparison between the studied groups according to side

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The diabetic group

- Included 20 eyes of 20 diabetic patients.
- The mean duration of diabetics was 9 years ± 1.3 years.
- 6 patients had type I DM and 14 patients had type II DM.
- The mean visual acuity in the diabetic eyes was 0.8 log Mar ± 0.12.

Table (4): Distribution of studied sample according to type of macular edema and Type of diabetic retinopathy in cases group (n=20)

	No.	%
Macular edema by OCT		
No macular edema	12	60.0
Macular edema	**8**	**40.0**
Type of macular edema by OCT		
Cystoid macular edema	5	62.5
Spongyform macular edema	3	37.5
Type of diabetic retinopathy		
Mild NPDR	11	55.0
Severe NPDR	4	20.0
PDR	5	25.0

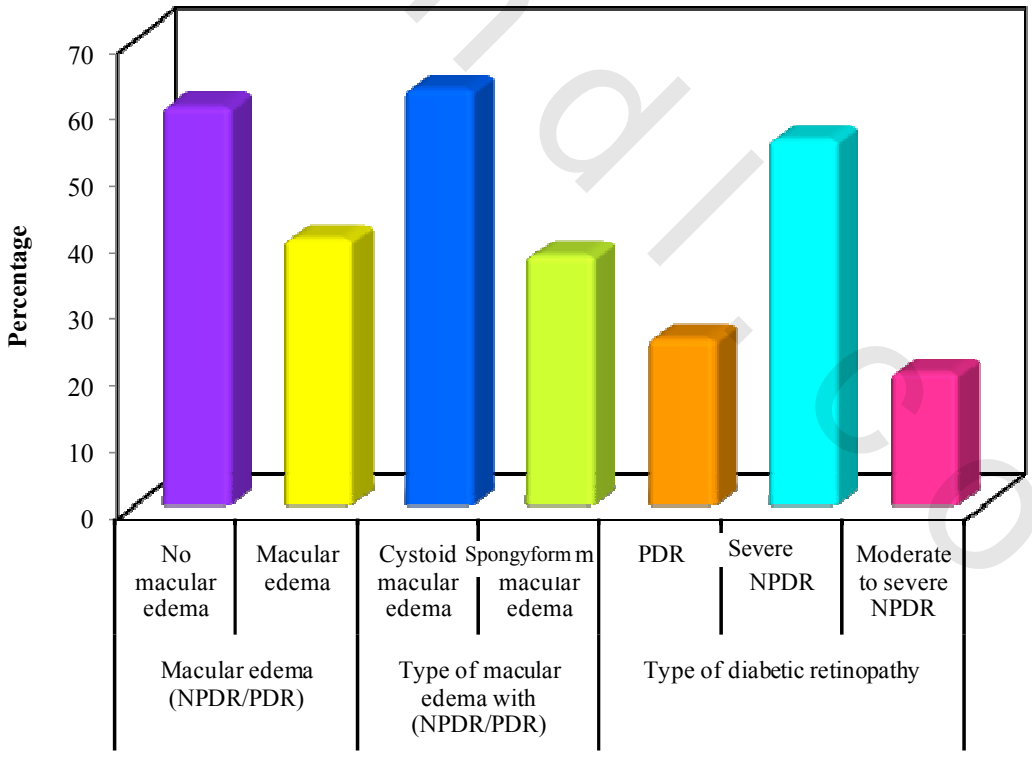

Figure (13): Distribution of studied sample according to type in cases group

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- OCT study was done for the choroid in the macular area in cases & controls using single line in vertical & horizontal directions by enhanced depth imaging mode:
- Manual measurement was done in horizontal and vertical scan at the foveal center & at distance of 500 μm & 1500 μm in both direction from the fovea.
- Measurement was done from outer limit of RPE line to the end of choroidal image on the OCT.
- We compared the choroidal thickness at the studied points between cases & controls in the horizontal line scan. The choroidal thickness was lower in the diabetics than controls.

Table (5): Comparison between the studied groups according to HT and HF and HN and average H

	Control (n=20)	Cases (n=20)	t	p
HT1500				
Min. – Max.	73.0 – 590.0	124.0 – 422.0		
Mean ± SD.	339.90 ± 126.95	246.40 ± 85.22	2.735*	0.009*
Median	333.50	235.0		
HT500				
Min. – Max.	114.0 – 593.0	79.0 – 395.0		
Mean ± SD.	360.0 ± 122.24	265.75 ± 80.86	2.876*	0.007*
Median	348.50	269.0		
HF				
Min. – Max.	84.0 – 572.0	147.0 – 432.0		
Mean ± SD.	372.95 ± 119.19	284.95 ± 75.70	2.787*	0.008*
Median	366.0	283.0		
HN500				
Min. – Max.	114.0 – 628.0	113.0 – 418.0		
Mean ± SD.	367.75 ± 124.55	283.35 ± 76.98	2.578*	0.015*
Median	335.50	274.0		
HN1500				
Min. – Max.	165.0 - 600.0	143.0 - 370.0		
Mean ± SD.	351.85 ± 119.60	262.20 ± 61.38	2.982*	0.006*
Median	307.0	250.0		
Average H				
Min. – Max.	110.0 – 596.60	106.4 - 335.8		
Mean ± SD.	358.49 ± 118.24	224.0 ± 65.1	3.842*	<0.001*
Median	343.60	222.6		

t: Student t-test
*: Statistically significant at $p \leq 0.05$

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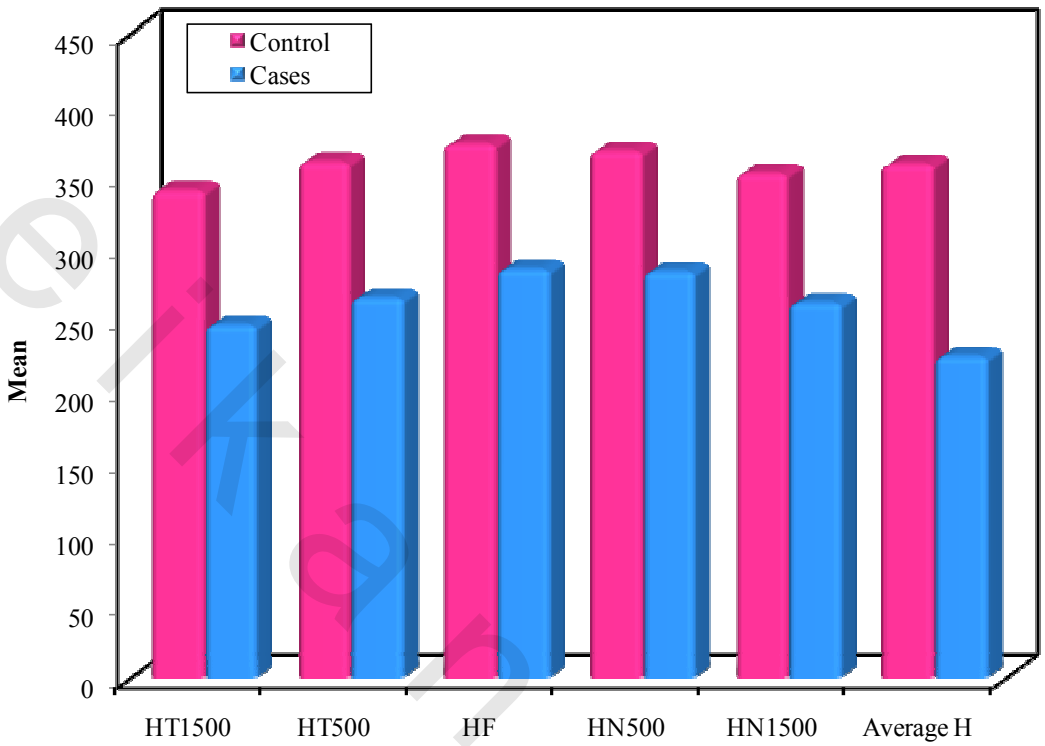

Figure (14): Comparison between the studied groups according to Horizontal temporal (HT)$^{(\mu m)}$and Horizontal foveal (HF)$^{(\mu m)}$ and Horizontal Nasal (HN)$^{(\mu m)}$ and average Horizontal (H)$^{(\mu m)}$.

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- We compared the choroidal thickness at the studied points between eyes of diabetic patients and controls in the vertical line scan. The choroidal thickness was lower in the eyes of diabetic patients than controls.

Table (6): Comparison between the studied groups according to vertical temporal (VT)$^{(\mu m)}$ and vertical foveal (VF)$^{(\mu m)}$ and vertical nasal (VN) $^{(\mu m)}$ and average vertical (V)$^{(\mu m)}$.

	Control (n=20)	Cases (n=20)	t	p
VT1500				
Min. – Max.	140.0 – 564.0	111.0 – 401.0		
Mean ± SD.	360.60 ± 97.90	267.05 ± 79.36	3.320*	0.002*
Median	362.50	274.0		
VT500				
Min. – Max.	93.0 – 568.0	108.0 – 368.0		
Mean ± SD.	346.55 ± 118.25	272.55 ± 68.17	2.425*	0.021*
Median	339.50	282.0		
VF				
Min. – Max.	115.0 – 527.0	104.0 – 400.0		
Mean ± SD.	357.55 ± 118.30	270.45 ± 70.24	2.831*	0.008*
Median	337.50	276.50		
VN500				
Min. – Max.	125.0 – 580.0	165.0 – 375.0		
Mean ± SD.	352.70 ± 124.19	269.60 ± 65.51	2.647*	0.013*
Median	311.50	281.50		
VN1500				
Min. – Max.	77.0 – 570.0	180.0 – 400.0		
Mean ± SD.	345.65 ± 125.27	281.25 ± 69.93	2.007	0.052
Median	332.0	284.0		
Average V				
Min. – Max.	110.0 – 530.20	87.8 - 316.8		
Mean ± SD.	352.61 ± 110.07	206.6 ± 70.3	5.002*	<0.001*
Median	338.70	232.2		

t: Student t-test

*: Statistically significant at $p \leq 0.05$

The choroidal thickness was lower in the eyes of diabetic patients than controls.

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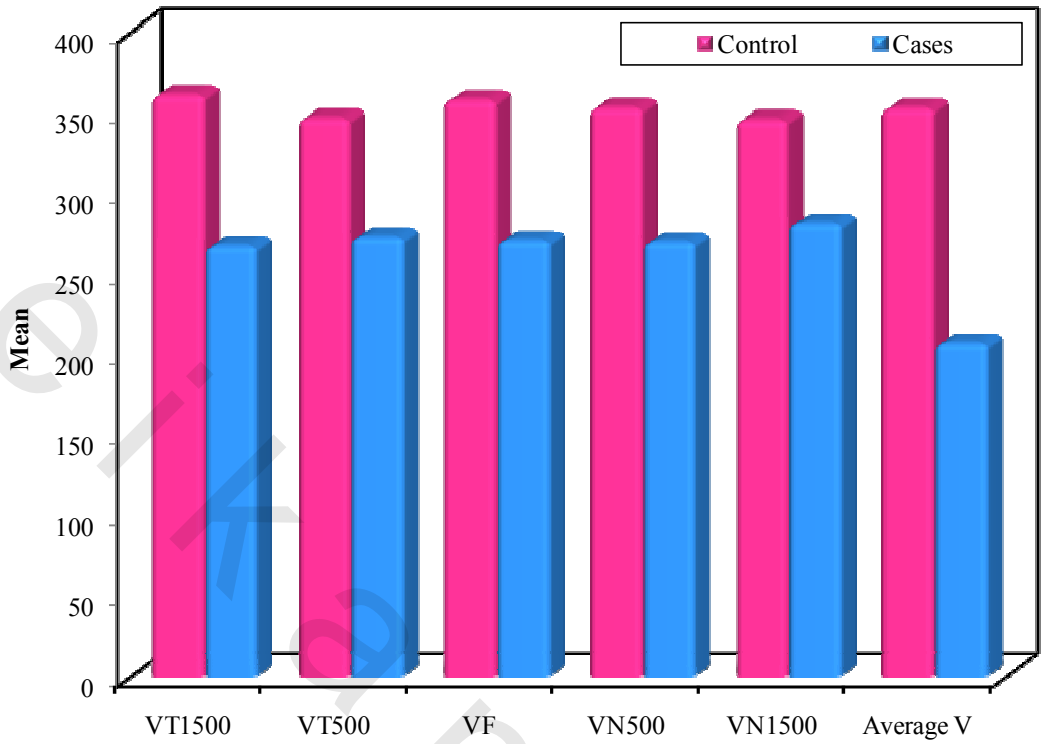

Figure (15): Comparison between the studied groups according to vertical temporal (VT)$^{(\mu m)}$ and vertical foveal (VF)$^{(\mu m)}$ and vertical nasal (VN) $^{(\mu m)}$ and average vertical (V)$^{(\mu m)}$

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Table (7): Comparison between Type of diabetic retinopathy according to Average Horizontal (H)$^{(\mu m)}$ and Average vertical (V)$^{(\mu m)}$ choroidal thickness.

	Type of diabetic retinopathy				F	p
	Control (n =20)	Mild NPDR (n = 11)	Severe NPDR (n = 4)	PDR (n = 5)		
Average H						
Min. – Max.	110.0 – 596.60	195.60 - 335.80	145.40 - 212.0	106.40 - 281.0		
Mean ± SD.	358.49 ± 118.24	260.35 ± 44.98	185.20 ± 31.55	175.12 ± 78.63	8.164*	<0.001*
Median	343.60	269.0	191.70	148.60		
Sig. bet. types	$p_1 = 0.039^*$, $p_2 = 0.009^*$ $p_3 = 0.002^*$					
Average V						
Min. – Max.	110.0 – 530.20	143.20 - 291.40	106.20 - 316.80	87.80 - 242.00		
Mean ± SD.	352.61 ± 110.07	232.29 ± 53.24	198.05 ± 87.38	156.76 ± 75.11	9.208*	<0.001*
Median	338.70	251.60	184.60	136.20		
Sig. bet. types	$p_1 = 0.007^*$, $p_2 = 0.020^*$ $p_3 = 0.001^*$					

F: F test (ANOVA)
p_1 : p value for Post Hoc test (Tukey) for comparing between control and Mild NPDR
p_2 : p value for Post Hoc test (Tukey) for comparing between control and Moderate to severe NPDR
p_3 : p value for Post Hoc test (Tukey) for comparing between control and PDR
*: Statistically significant at $p \leq 0.05$
Chroridal thickness is decreased in diabetes and related to severity of retinopathy.

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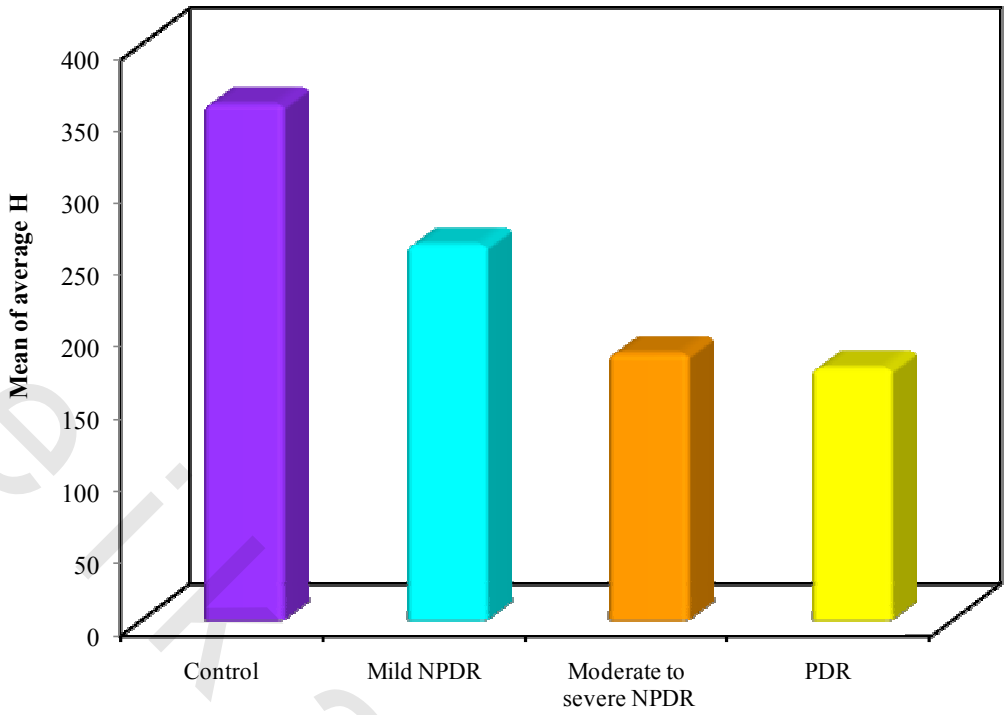

Figure (16): Comparison between Type of diabetic retinopathy according to Average Horizontal (H)$^{(\mu m)}$ choroidal thickness.

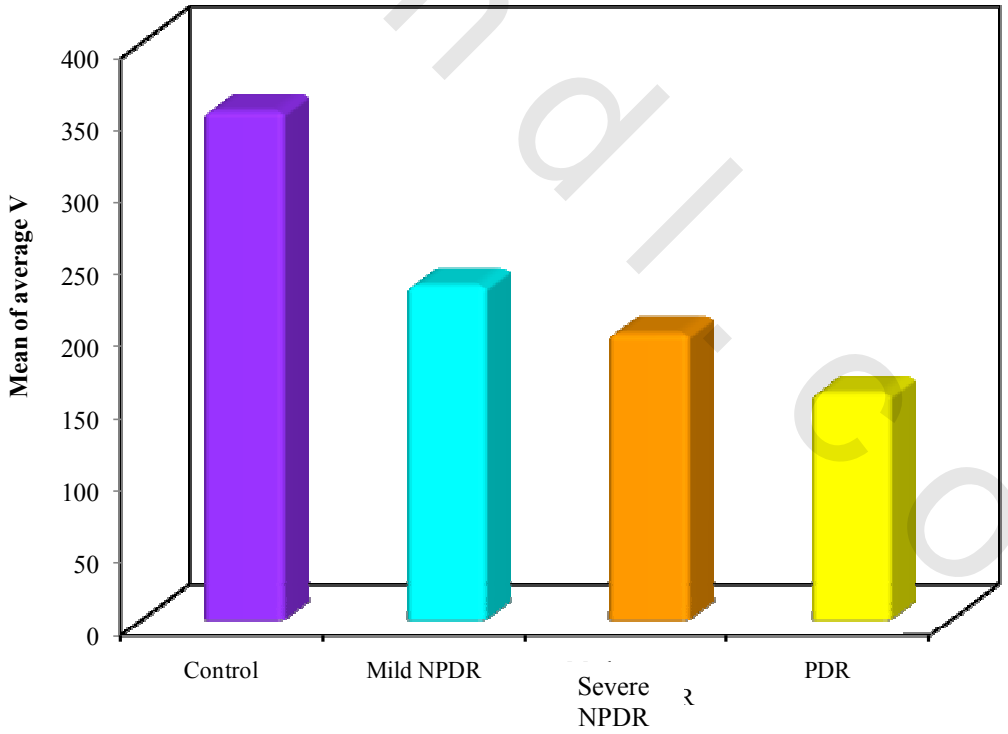

Figure (17): Comparison between Type of diabetic retinopathy according to Average vertical (V)$^{(\mu m)}$ choroidal thickness.

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Table (9): Comparison between cases with and without Macular edema (NPDR/PDR) according to Average horizontal and Average vertical choroidal thickness.

	Macular edema (NPDR/PDR)				F	p
	Control (n =20)	**No macular edema (n = 12)**	**Cystoid macular edema (n = 5)**	**Spongyform macular edema (n = 3)**		
Average H						
Min. – Max.	110.0 – 596.60	148.60 - 335.80	106.40 - 281.0	195.60 - 270.80		
Mean ± SD.	358.49 ± 118.24	244.72 ± 56.22	174.48 ± 78.91	223.73 ± 41.02	6.853*	0.004*
Median	343.60	254.80	145.40	204.80		
Sig. bet. types	p_1= 0.006*, p_2 = 0.006*, p_3 = 0.131					
Average V						
Min. – Max.	110.0 – 530.20	136.20 -316.80	87.80 - 242.0	143.20 - 251.60		
Mean ± SD.	352.61 ± 110.07	233.93 ± 58.54	150.76 ± 78.29	190.07 ± 55.67	9.723*	0.001*
Median	338.70	252.50	106.20	175.40		
Sig. bet. types	p_1= 0.003*, p_2 =0.002*, p_3 = 0.042*					

F: F test (ANOVA)
p_1 : p value for Post Hoc test (Tukey) for comparing between control and no Macular edema.
p_2 : p value for Post Hoc test (Tukey) for comparing between control and Cystoid macular edema.
p_3 : p value for Post Hoc test (Tukey) for comparing between control and Spongyform macular edema
*: Statistically significant at $p \leq 0.05$

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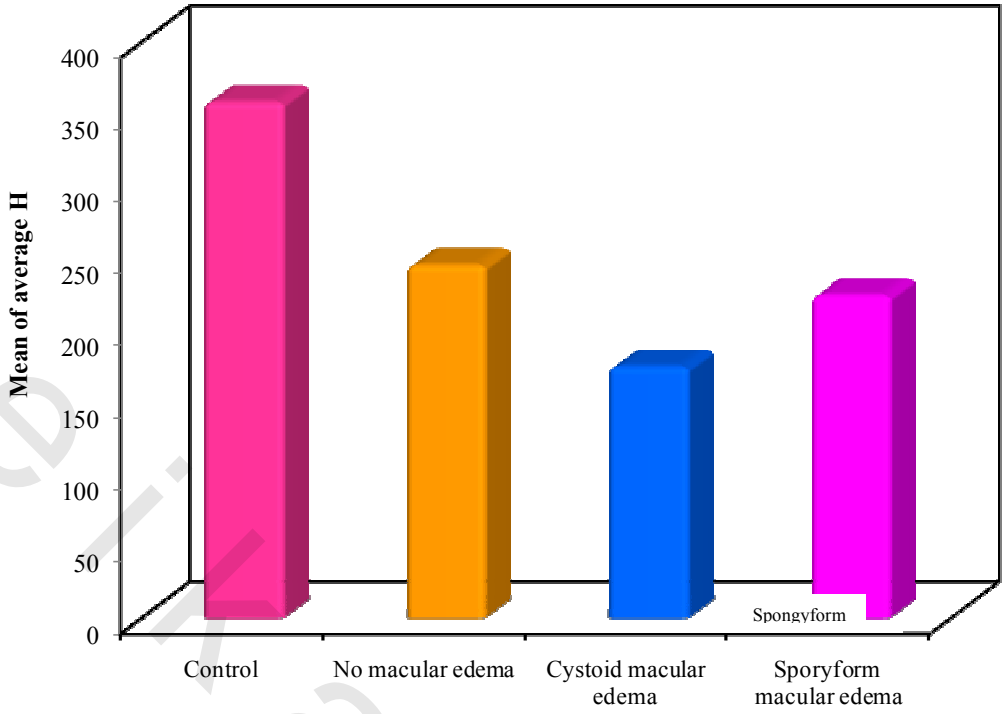

Figure (18): Comparison between Macular edema groups according to Average horizontal choroidal thickness.

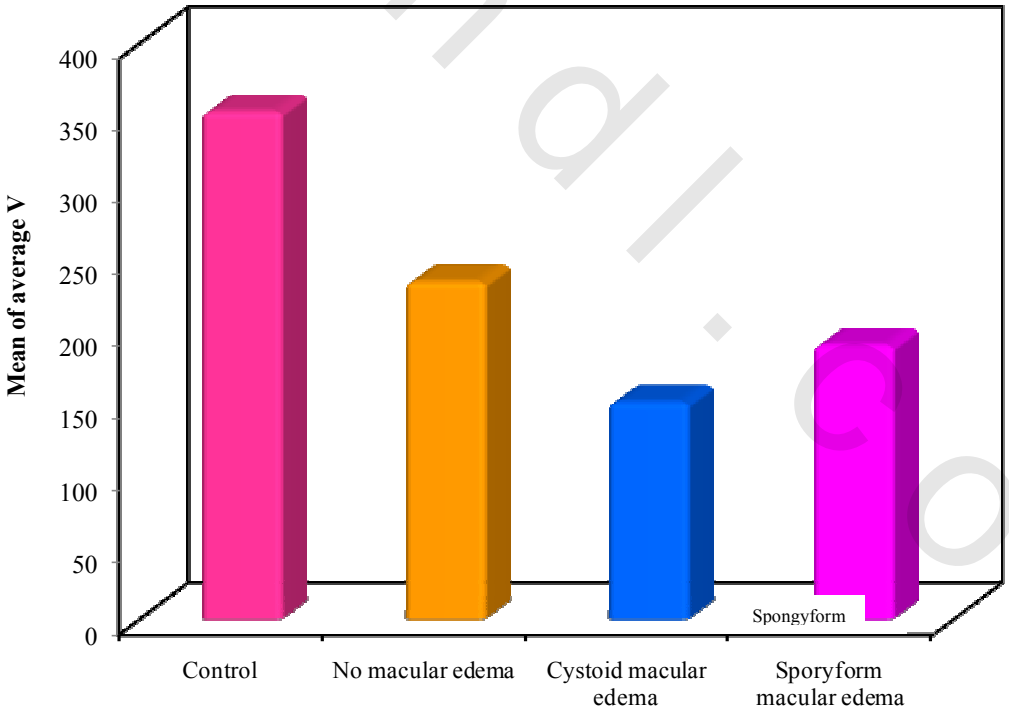

Figure (19): Comparison between Macular edema groups according to Average vertical choroidal thickness.

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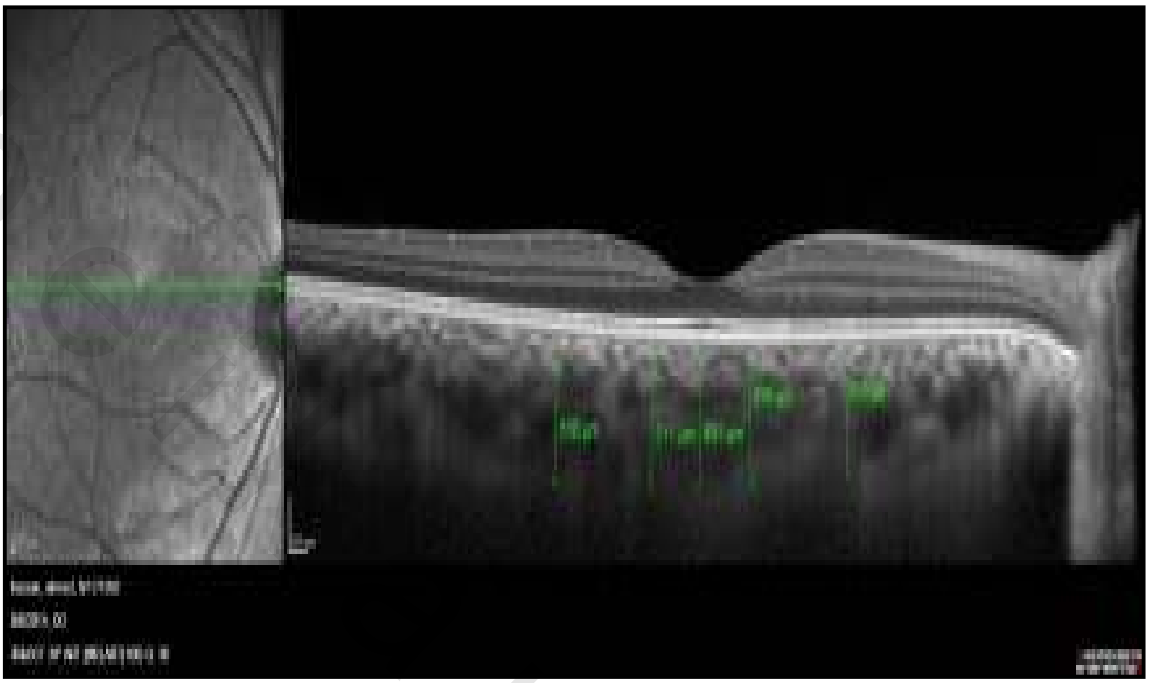
Examples for OCT study for the choroidal thickness the macular area in diabetics and controls using single line in vertical & horizontal directions by enhanced depth imaging mode OCT.

(A)



(B)

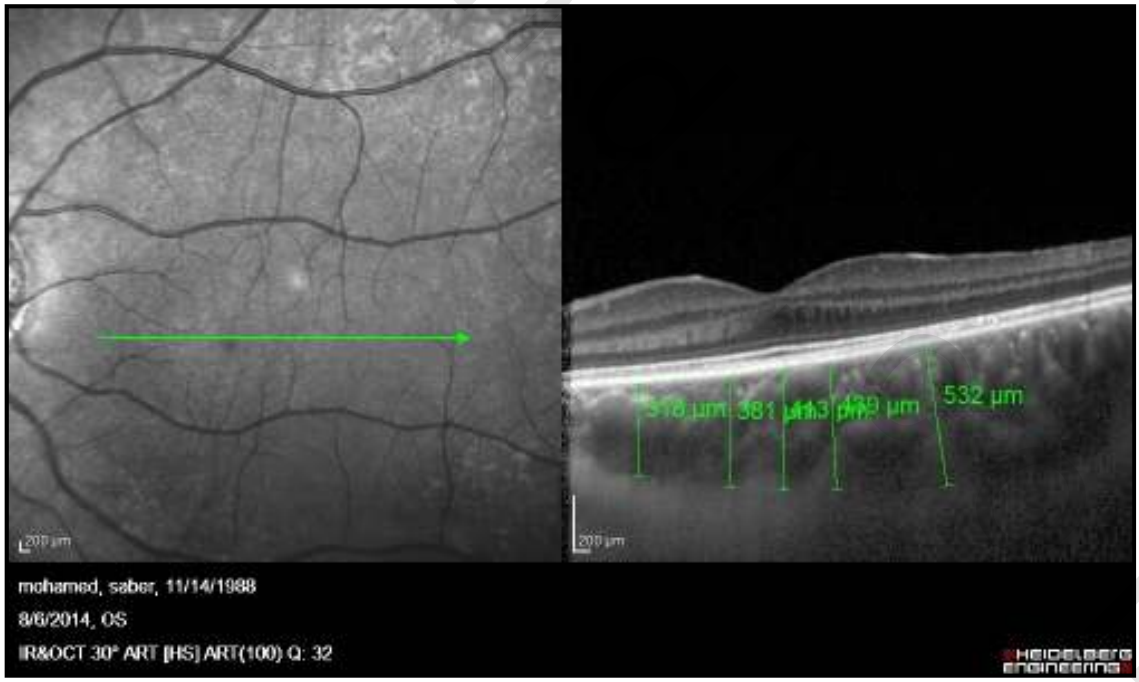
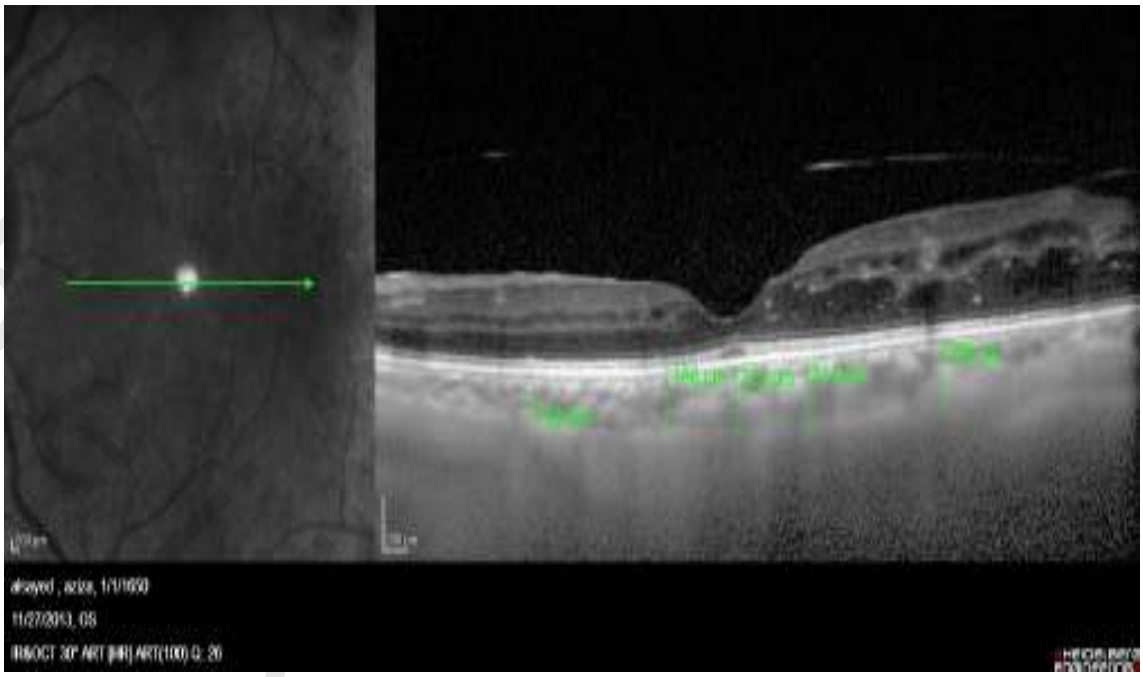


Figure (20): Optical coherence tomography image of the normal choroid taken on Spectralis with EDI and over sampling. The central subfoveal choroidal thickness was 491µ in case A and 413 µ in cases B.

(A)



(B)

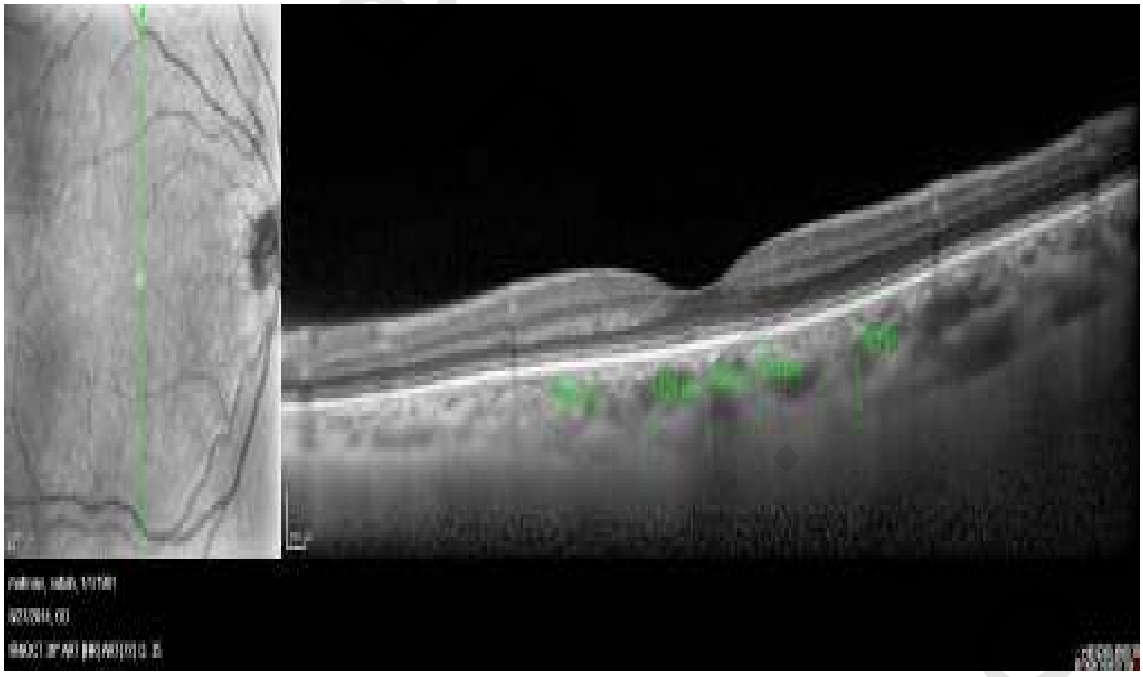


Figure (21): Optical coherence tomography image of the choroid of eyes with non proliferative diabetic retinopathy taken on Spectralis with EDI and over sampling. The central subfovea choroidal thickness was 222 µ in case A and 325 µ in case B.

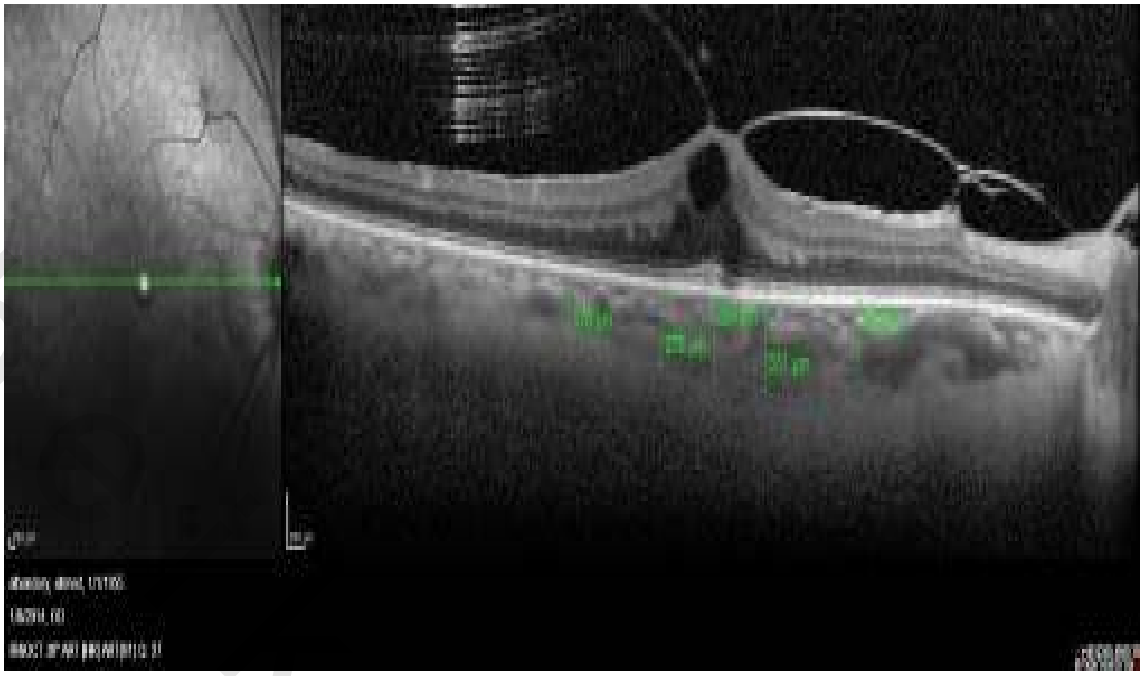


Figure (22): Optical coherence tomography image of the choroid of an eye with non proliferative diabetic retinopathy with cystoid macular edema and vitromacular traction taken on Spectralis with EDI and over sampling. The central subfovea choroidal thickness was 287 µ.

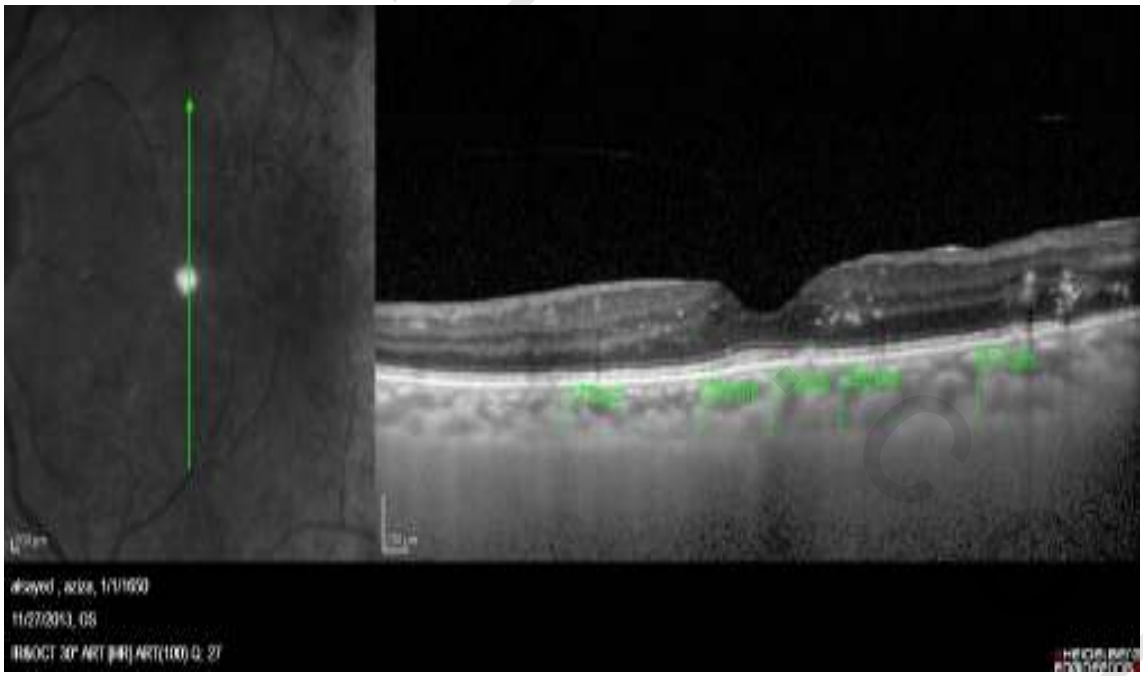


Figure (23): Optical coherence tomography image of the choroid of an eye with severe proliferative diabetic retinopathy taken on Spectralis with EDI and over sampling. The central subfovea choroidal thickness was 212 µ.

DISCUSSION

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DISCUSSION

In this study, we aimed at comparing the choroidal thickness in diabetic patients with healthy controls. We found that CT decreased as the disease progressed from mild to severe NPDR to PDR. The choroidal thickness was significantly thinner in diabetics than control. Average horizontal choroidal thickness was 224 μ in diabetic patients and 358.4 μ in controls.

Regatieri et al compared NPDR, PDR, and DME patients with healthy controls using a Cirrus™ HD-OCT (Carl Zeiss Meditec, Dublin, CA, USA) and reported significant difference between the NPDR, PDR, DME and control groups, the CT was decreased in the NPDR, PDR and DME groups.[29]

In the study by Kim et al, CT was found to be significantly decreased as the disease progressed in severity from moderate–severe NPDR to untreated PDR.[28]

In our study, the CT of patients with diabetic macular edema was significantly thinner than that of non-DME patients.

In our study, as in other studies, CT was thickest in the sub-foveal area and get thinner towards the nasal or temporal area.[27,28]

Spaide has reported that CT decreases with age. We included patients of similar age, so the age factor was eliminated.[27]

In this study, CT in the NPDR, PDR and DME groups was significantly thinner than in the control group. Decreased CT can indicate that NPDR, PDR and DME patients may have decreased choroidal blood flow. Earlier studies with laser Doppler flowmetry in NPDR patients have shown a reduction in choroidal blood flow and selective filling of the choriocapillaris during indocyanine green angiography.[5,13] So, decreased CT can be related to hypoxia of the choroidal tissue.

Nagaoka et al showed that NPDR patients with DME have a reduction in choroidal circulation compared with NPDR patients without DME. They presumed this decreased circulation could be secondary to choroidal hypoxia because of the inadequate blood flow, and that this could cause the macular edema.[9]

In our study, CT was found to decrease along with the progression of the retinopathy.

Recently Esmaeelpour et al.[42] mapped the choroidal thickness in patients with diabetes using high speed three-dimensional (3D) OCT imaging at 1060 nm. Overall, they found a central and inferior thinning in diabetic eyes compared with healthy eyes. In our series, we used a standard 870 nm SD-OCT device (Heidelberg Engineering). By positioning the device closer to the eye than ordinary, such that a stable inverted image is produced, and the sensitivity of the imaging in deeper layers of tissue is increased (EDI OCT), we found choroidal thickness values overall similar to those reported by Esmaeelpour et al. obtained using 3D 1060-nm OCT imaging. In the series of Esmaeelpour et al.,[42] the generation of choroidal thickness maps based on manual segmentation revealed a reduced subfoveal thickness in all diabetic groups. Similarly, in the current series, the manual measurements of choroidal thickness (future use of the method would benefit from an automated algorithm for making the measurements), which was performed on the horizontal and vertical axis (in the subfoveal area, and at 500-μm intervals from the fovea to 1500 μm nasal, 1500 μm temporal, revealed a reduced subfoveal thickness in all diabetic groups.

A structurally and functionally normal choroidal vasculature is essential for the function of the retina: abnormal choroidal blood volume and/or compromised flow can result in photoreceptor dysfunction.[29]

The possible role of choroidal vessels in the pathophysiology of diabetic changes in the retina has been evaluated by histologic examination. The pathologic findings included increased tortuosity of the blood vessels, focal vascular dilatation and narrowing, hypercellularity, vascular loops and microaneurysm formation and areas of nonperfusion.[29]

Further, previous investigations reported selective filling of the choriocapillaris during indocyanine green angiography and choroidal blood flow decrease during laser Doppler flowmetry in association with non-proliferative diabetic retinopathy. Such findings indicate that there may be diabetic choroidopathy before the onset of diabetic retinopathy in a subset of patients. Further development of OCT technology would likely prove valuable in the investigation of diabetic choroidopathy.[29]

We can speculate that the thinner choroid may indicate an overall reduction of choroidal blood flow in patients with DME and more prominent in patients with PDR, as was previously demonstrated with laser Doppler flowmetry and indocyanine green angiography.[5,11,12] Therefore, it is likely that the decreased CT may be related to retinal tissue hypoxia, as the choroid is the major source of nutrition for the RPE and outer retinal layers.

There are also some limitations to the present methodology. First, the 20 participants in the diabetic group was a relatively small number. Second, because we measured the subfoveal choroidal thickness manually, the results might contain slight errors, though this is the best clinical method currently available with the current OCT equipment. Lastly, we did not consider the diurnal change of choroidal thickness. Unlike retinal thickness, it has been reported that the choroid shows a diurnal variation of about 30 μm[26,27]. Additional clinical studies on larger populations are needed for a more detailed evaluation of choroidal thickness changes.

The choroid thickness was significantly decreased in diabetic retinopathy patients compared with controls. The proliferative change or presence of macular edema lead to additional choroidal thinning. Further investigation will be required before the precise role of choroidal thickness changes in the development of diabetic retinopathy can be determined.

Spectral-domain OCT is a noninvasive technology to assess the choroid and may be a useful tool in the evaluation of chorioretinal vascular changes in diabetic retinopathy.

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SUMMARY

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SUMMARY

Diabetic retinopathy is a leading cause of vision loss worldwide. The development of macular edema and proliferative retinopathy are major causes of visual impairment.[1,2]

Choroidal vasculopathy in diabetes may play a role in the pathogenesis of diabetic retinopathy.[3–5]

The aim of the work was to compare between choroidal thickness in patients with diabetic retinopathy and normal persons using enhanced-depth imaging spectral-domain optical coherence tomography.

The study included 40 adult eyes of adults recruited from the ophthalmology department at Alexandria main university hospital.

Group (1) included 20 eyes of diabetic patients having either non-proliferative diabetic retinopathy or proliferative diabetic retinopathy.

Group (2) included 20 eyes of normal subjects as control.

OCT study was done for the choroid in the macular area in cases & controls using single line in vertical & horizontal directions by enhanced depth imaging mode. The choroidal thickness was measured manually perpendicularly from the outer edge of the hyperreflective RPE to the inner sclera (choroid–sclera junction) using the OCT software.

Choroidal thickness was altered in diabetes and may be related to the severity of retinopathy. Presence of diabetic macular edema is associated with a significant decrease in the choroidal thickness.

A structurally and functionally normal choroidal vasculature is essential for retinal function, abnormal choroidal blood volume and/or compromised flow can result in photoreceptor dysfunction.

This retrospective study has some limitations. Patients with diabetes and no diabetic retinopathy were not included because these patients do not require OCT examination. Additionally, patients with treated PDR were not included.

In conclusion, the choroid thickness of was significantly decreased in diabetic retinopathy patients compared with controls. The proliferative change or presence of macular edema lead to additional choroidal thinning. Further investigation will be required before the precise role of choroidal thickness changes in the development of diabetic retinopathy can be determined.

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