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Research Article

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Data Analyses with ImageJ Software in Diabetic Retinopathy, By Processing the Optical Coherence Tomography Images

D Moraru[1]*, S Istrate[2], C Eniceicu[3] and P Sterian[1,4]

[1]*Academic Centre for Optical Engineering and Photonics, Politehnica University, Bucharest, Romania*

[2]*Ophthalmology Department, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*

[3]*University Emergency Hospital Bucharest, Ophthalmology Department, Bucharest, Romania*

[4]*Academy of Romanian Scientists, Bucharest, Romania*

***Corresponding author**
D Moraru, Academic Centre for Optical Engineering and Photonics, Politehnica University, Bucharest, Romania, E-mail: moraru.danuta@gmail.com

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Abstract

The study is based on Optical Coherence Tomography images resulting from investigation of 24 patients (with a total of 33 eyes) with non-proliferative diabetic retinopathy and of 19 patients (with a total of 26 eyes) without diabetes mellitus as control group. Patients' age was between 43 and 92 years old, with a mean age of 66.4 years for first group, and a mean age of 67.6 years for the second one. From this large group, after the first data evaluation, we selected patients aged 40 to 65. We evaluated daily each patient, at 9 am, 12 pm, 3 pm and 6 pm, through glycemic level and Optical Coherence Tomography investigation using Macular Cube 512x128 images acquisition type. In the same time, we made specifically measurements of photoreceptor and retinal pigment epithelium layers thickness using ImageJ software. We analysed comparatively data given by Optical Coherence Tomography tool and those obtained through direct thickness measurements for three macular zones: one central (foveola) and two circulars (para-foveolar and peri-foveolar), having 1 mm, 3 mm, respectively 6 mm in diameter. We concluded that age and time of the day are significantly factors that influence the diabetic retinopathy. We also suggest this method as further investigation tool mostly for patients at the beginning of illness discovering, in order to diminishing and even stopping its evolution.

Keywords: Optical Coherence Tomography (OCT), Diabetes Mellitus (DM), Diabetic Retinopathy (DR), Retinal Thickness, Image J.

Introduction

Optical Coherence Tomography (OCT) has emerged during last decades as an important tool for the evaluation of retinal layers. This implies useful emerged data, in terms of images and figures, in order to identify and to monitoring more precisely different retinal diseases as diabetic retinopathy is the subject of this study.

Theoretical basics of OCT were established by two mathematicians (D. Huang and M.R. Lee) and this work was presented in [1]. In short time after the first OCT utilization, the number of researches in this field increased very much, therefore in 2009 were published in Web of Science, each day, 5 articles on the average [2]. Many authors have compiled and inventory of the field of using OCT, highlighting its advantages compared to other bio-imaging methods or the versatility of the system and its continued development [3].

In our study, we used images provided by OCT to measure some layers' thicknesses, meaning photoreceptors' layer and retinal pigment epithelium layer (RPE) [4]. Other authors, as Igor Kozac is, consider that Adaptive Optics (AO) is also a technology that could be used for determining different retinal parameters, as photoreceptors cells density, spacing and mosaic regularity, or for the visualization of the retinal pigment epithelium, retinal nerve fiber layer, and retinal vessel wall. OCT images were collected from 24 patients with diabetic retinopathy, and 19 patients without diabetes mellitus in the control group, for one or both eyes. From those two groups we selected only patients aged up to 65 years, because we supposed that, after 65 years old, retina structure would be more affected by age-related macular degeneration.

On the other hand, Diabetes Mellitus (DM) has become one of the most prevalent health worldwide problems during last years. If in 2013 the estimated number was 382 million people suffering from DM and 415 million in 2015, this number could rise to 592 million in 2035, or 642 million in 2040 [6]. "*International Diabetes Federation*" is making almost in real time estimation and prediction for figures regarding people with Diabetes Mellitus, type 1 or type 2, including demographic and geographic outline (https://diabetesatlas.org/en/sections/demographic-and-geographic-outline.html). It's known that DM is the cause of diabetic retinopathy (DR) which is

the major vision-threatening nowadays (around 30%). And from these around 2.6% are followed by blindness. That's why early detection and regular investigations of ocular complications of DM is important in order to decrease its negative impact on patients' view, to avoid eyesight losing or at least to obtain a slower DR evolution.

Materials and Methods

Our study is based on both OCT Macula Cube type images (taken with Cirrus TM HD-OCT model, produced by Carl Zeiss Meditec, Inc., class II, acc. 21 CFR 886.1570) and ImageJ measurement within images provided by OCT for probes from all 43 patients, with or without diabetes. Glycaemia level was measured with Beurer GL 42/ dl glucometer, and the systemic blood pressure with Beurer BM 44 electronic device. Patients have been tested also with Pelli Robson chart, and the results were already published [4, 7].

On one hand, OCT offers data of Early Treatment Diabetic Retinopathy-ETDR type (Fig. 1, right eye). In correlation with scanning plans made by OCT, there are 9 quadrants named after horizontal axis left ↔ right or nasal ↔ temporal and vertical axis superior ↔ inferior. The macular zone is divided in 3 circles: central zone (with 1mm diameter), para-foveolar zone (with 3 mm diameter) and peri-foveolar zone (with 6 mm diameter). OCT delivers data for all ten retinal layers thickness.

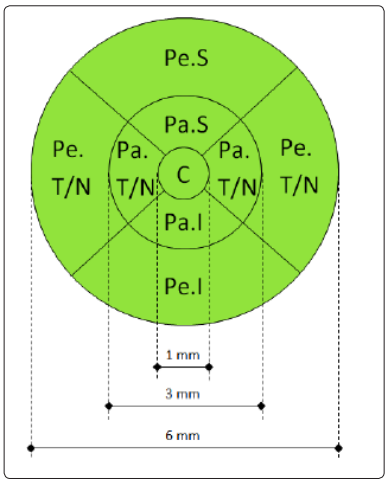

Figure 1: ETDR (Early Treatment Diabetic Retinopathy Study quadrants)

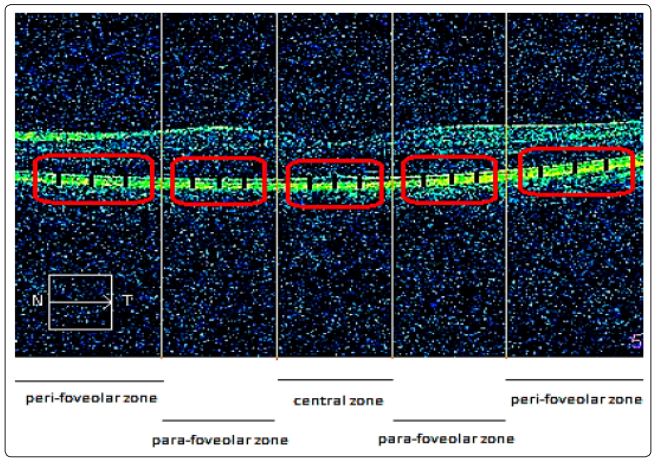

Figure 2: Measuring principle with Image J (for a left eye)

On the other hand, we used Image J software for measuring the thickness of some layers [8]. This software is a public domain Java image processing program, who can displays, edits, analyzes, processes, saves and prints images, who can calculates area of user-defined selection, who can measures distance and angles; it supports all standard image processing functions. We used it for retinal layers thickness and areas measurements, and for this work, we refer only on thickness measurements. In this respect, in each zone from vertical scan we made three different measurements (Fig. 2), indicated with black lines within red rectangular frames.

Some studies suggest that making separated measurements of RPE (retinal pigment epithelium) layer and photoreceptors layer could provide more detailed information [9].

Our study included measurement for 33 eyes affected by non-proliferative diabetic retinopathy and 26 non-diabetic eyes. There were 67% females in the first group and 58% females in the control group. Mean ages were almost similar: 66.4 years old, respectively 67.6 years old. From diabetic patients, 5 of them were insulin dependent. We didn't separate them from this research stage.

We investigated patients for four times on a day, regarding glycaemia level, systemic blood pressure, contrast sensitivity and macular cube image. For OCT, we excluded the scans with a score below 4/10, because of their poor quality.

For data examination, we used Origin 6.0 software for interactive scientific graphing and data analyses [10].

In this work, we present comparative data from two points of view. First: for entire groups and for patients aged up to 65 years old, which means 45% eyes from group affected by non-proliferative DR, respectively 31% eyes from control group. Secondly: for OCT data and for Image J data. We analyzed all data in three directions: daily thickness variations, thickness variation with age, respectively thickness variation with glycaemia level.

Results

Daily Thickness Variations

We put together all data and we analyzed them for all sectorial retinal zones: central, para-foveolar and peri-foveolar.

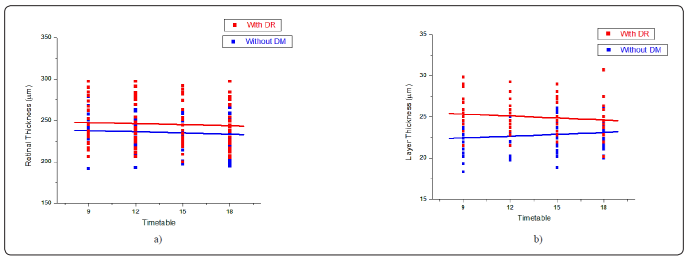

Figure 3: Daily central retinal thickness variation for all ages (a – OCT data; b – Image J data)

In (fig 3) could be observed a slow retinal thickness for both groups and all ages during the daytime and small differences between their values, for patients with DR values being grater. In the same time, Image J measurements for the same group characteristics shows a later thickness increasing for patients without DM. The same facts are valid for patients aged up to 65 from Image J point of view. But OCT data show a slow retinal thickness increasing and much

smaller differences between values for patients with DR and those without DM (Fig 4.)

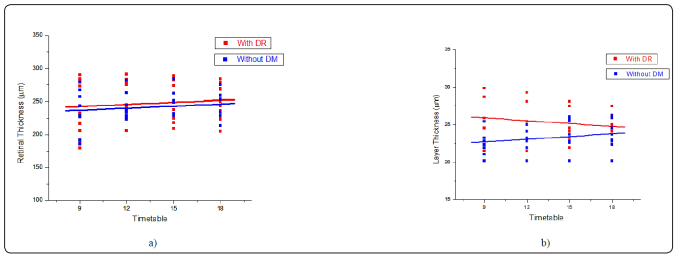

Figure 4: Daily central retinal thickness variation for patients aged up to 65 (a – OCT data; b – Image J data)

The same kind of analyze was made for para-foveolar (nasal and temporal) zones and peri-foveolar (nasal and temporal) zones.

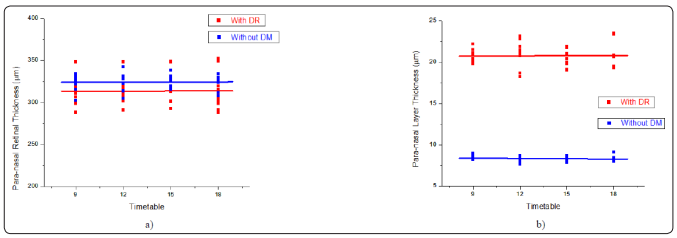

Figure 5: Daily para-nasal retinal thickness variation for all ages (a – OCT data; b – Image J data)

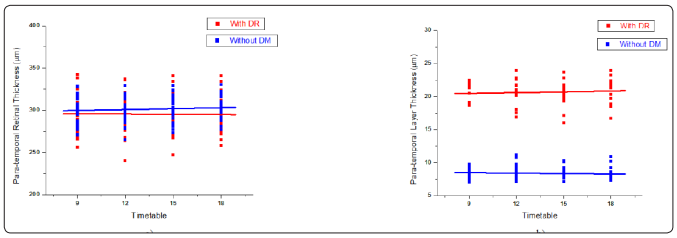

Figure 6: Daily para-temporal retinal thickness variation for all ages (a – OCT data; b – Image J data) 5

Fig. 5 and Fig. 6 show insignificant differences (from OCT point of view) between daily behaviors of para-foveolar retinal thickness for both groups. But Image J measurements indicate significant differences in values for same zones between patients with DR and from group control, having bigger values of retinal thickness for those from first group. In the same time, it could be observed slightly opposite variations of layer thickness for temporal zone, between the two groups.

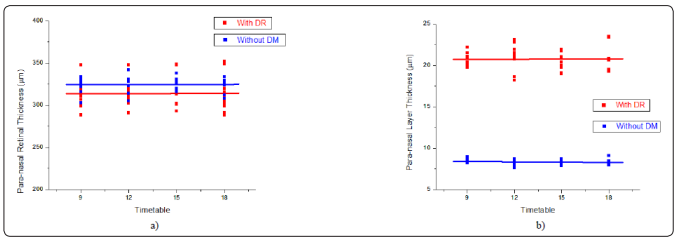

Figure 7: Daily para-nasal retinal thickness variation for patients aged up to 65 (a – OCT data; b – Image J data)

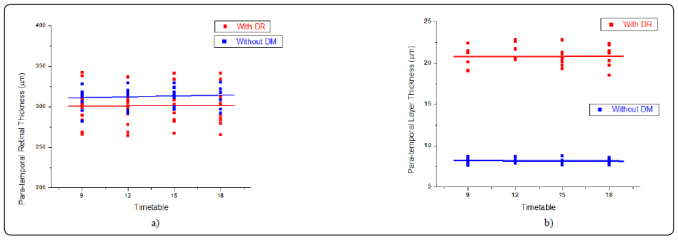

Figure 8: Daily para-temporal retinal thickness variation for patients aged up to 65 (a – OCT data; b – Image J data)

For groups of patients aged up to 65 are the same insignificant differences between groups and along the day, which allow us to make the hypothesis that retinal tissue is quite resistant to daily glycaemia variation. Also Image J measurements illustrate almost no variation for temporal zones comparing with nasal zones, which can lead to the hypothesis that vicinity of optical nerve head generates behavioral differences of retinal tissue.

Analyses results for peri-foveolar zone are shown below (Fig. 9, 10, 11 and 12). They indicate almost no differences between group, both for all ages and subjects aged up to 65, no differences between data delivered by OCT and by Image J measurements, between peri-nasal and peri-temporal quadrants. Our hypothesis in this case consists in: there are not changes in thickness because in peri-foveolar zone are not the same concentrations of photoreceptors that are in central and para-foveolar zones.

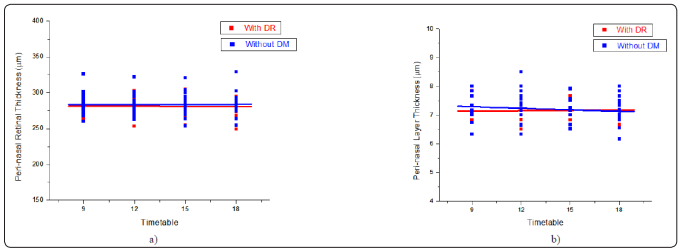

Figure 9: Daily peri-nasal retinal thickness variation for all ages (a – OCT data; b – Image J data)

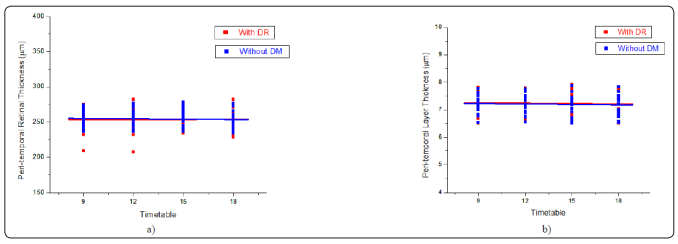

Figure 10: Daily peri-temporal retinal thickness variation for all ages (a – OCT data; b – Image J data)

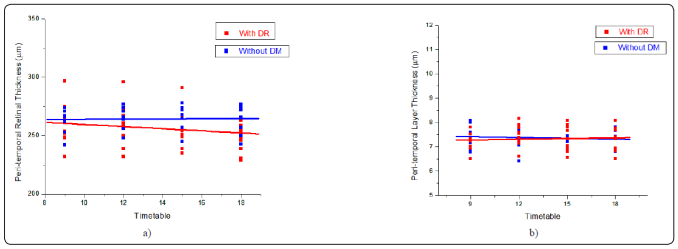

Figure 11: Daily peri-nasal retinal thickness variation for patients aged up to 65 (a – OCT data; b – Image J data)

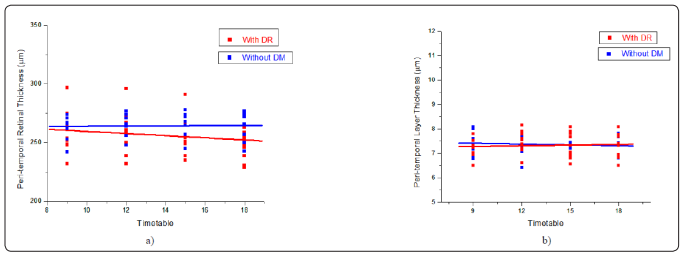

Figure 12: Daily peri-temporal retinal thickness variation for patients aged up to 65 (a – OCT data; b – Image J data)

Still there are small differences shown by OCT data between patients with DR for whom it is present a slowly thickness decreasing, meantime being almost constant for patients from control group, and having smaller values. But these differences are disappearing within Image J measurements data.

Thickness Variation with Age

The second direction on data analyzes is in finding correlations between retinal thickness and patients' age. We considered the same comparisons between entire groups and limited groups aged up to 65 years.

A global analyzes on OCT data shows some differences regarding variations and values. In Fig. 13 are visualized mean retinal thicknesses with age, for all sectors. There are greater values for para-foveolar zone and smallest for central zone. For patients without DM thicknesses are decreasing with age for all zones, more significant for para-foveolar quadrants. For patients with DR there is a thickness decreasing for para-foveolar zone, a slowly increasing for peri-foveolar quadrants, and almost no variation for central zone.

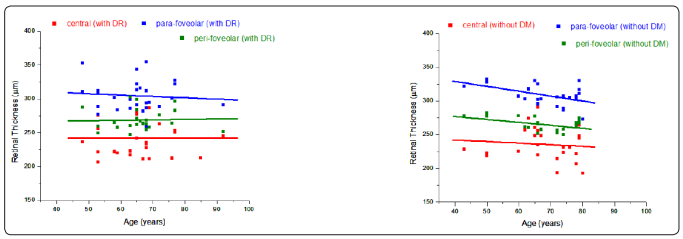

Figure 13: Mean retinal thickness variation with glycaemia for all patients (a – patients with DR; b – patients without DM) 8

More detailed analyzes provide other worthy facts. Comparing data from OCT and from Image J measurements for central thickness, we conclude that there are small variations with age, are no significant differences between those two variations, and for patients without DM the thickness values are smaller (Fig. 14.)

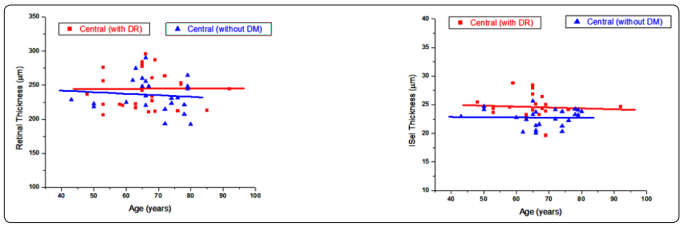

Figure 14: Mean central thickness variation with age for all patients (a – OCT data; b – Image J data)

But for para-foveolar zone (nasal – Fig. 15 and temporal – Fig.16) there are some differences. From OCT data, we have an increasing of retinal thickness with age within nasal quadrant for patients with DR and a decreasing for the other. Our hypothesis is that this difference appears because the vicinity of ONH (optical nerve head), because for temporal quadrant for both groups is the same decreasing with almost the same rate.

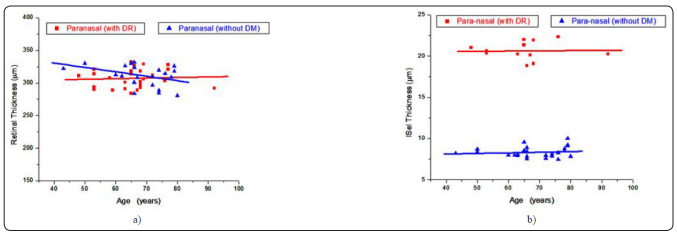

Figure 15: Mean para-foveolar nasal thickness variation with age for all patients (a – OCT data; b – Image J data)

From Image J data we obtained the same slowly increasing in thickness with age, but twice thicker for patients with DR, for both para-foveolar quadrants. These grater values could be a consequence of the increasing volume due to damages produced in time by fluid (hemoglobin, water, lipids) leakage.

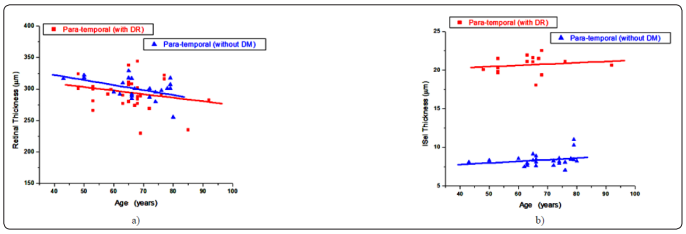

Figure 16: Mean para-foveolar temporal thickness variation with age for all patients (a – OCT data; b – Image J data)

For peri-foveolar, quadrants there are no differences between groups or between OCT and Image J data (Fig. 17).

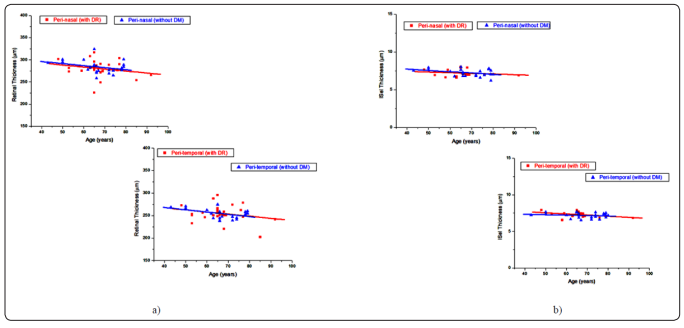

Figure 17: Mean peri-foveolar thickness variation with age for all patients (a – OCT data; b – ImageJ data)

From our point of view, two reasons could be right in this situation: lack of photoreceptors in this zone and too small values of thickness to be able to "see" its variation.

Thickness Variation with Glycaemia Level

The third direction we analyzed our data was the correlation between retinal and layers thicknesses and glycaemia. We did this analyze by comparing both entire groups (all ages) with data from patients aged up to 65 years old. Fig 18 and 19 show the variation of central thickness with glycaemia.

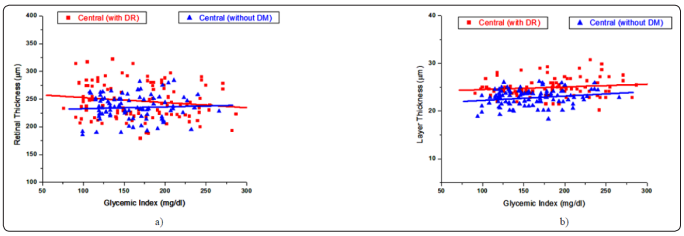

Figure 18: Mean central thickness variation with glycaemia for all ages (a – OCT data; b – Image J data)

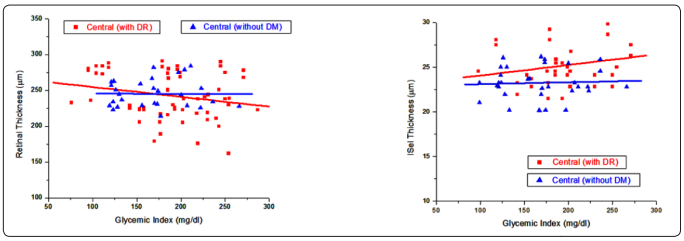

Figure 19: Mean central thickness variation with glycaemia for subjects up to 65 years old (a – OCT data; b – Image J data)

OCT shows a slowly decrease of central retinal thickness, while Image J measurements indicates a slowly increase of layer thickness for patients having Diabetic Retinopathy, and so we made the hypothesis that a higher glycemic level could determines significant volume increasing in central foveolar zone, which can't be determined through OCT data. There are no differences for patients without DM between data provided by OCT and Image J, both cases illustrating the same slowly increasing in thickness with glycemic level.

Following the same path, we analyze para-foveolar and peri-foveolar zones (Fig 20 to 26). For para-nasal quadrants, OCT shows no differences between groups and no thickness variations, but these are evident from Image J point of view. This identifies greater values of thickness for patients having DR and a consistent increasing of it with glycaemia; there is no variation in thickness for layers non-affected by DM.

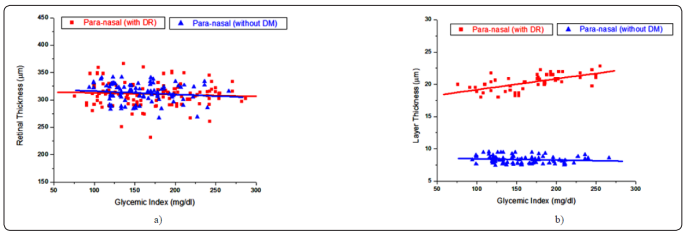

Figure 20: Mean para-nasal thickness variation with glycaemia for all ages (a – OCT data; b – Image J data)

For smaller groups appeared only one significant difference regarding the values of retinal thickness, this being slightly bigger for patients without DM. Maybe the more inclined slope for DR patients is a consequence of the optical nerve vicinity (for temporal quadrants not being available).

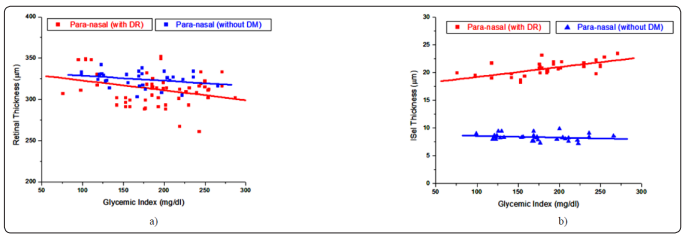

Figure 21: Mean para-nasal thickness variation with glycaemia for subjects up to 65 years old (a – OCT data; b – Image J data)

For para-temporal zone both lines fit for OCT, data are the same, and for Image J data, we have identical behavior as it is for para-nasal zone.

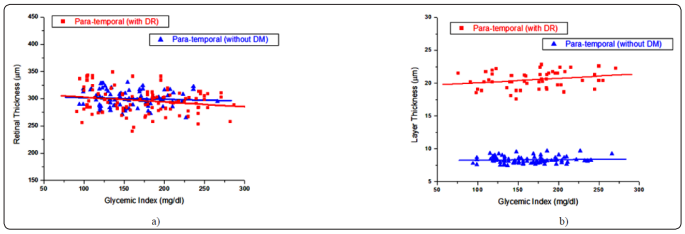

Figure 22: Mean para-temporal thickness variation with glycaemia for all ages (a – OCT data; b – Image J data)

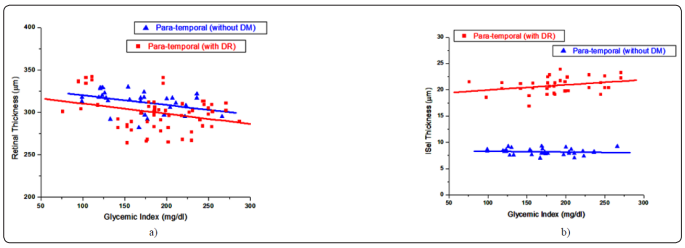

Figure 23: Mean para-temporal thickness variation with glycaemia for subjects up to 65 years old (a – OCT data; b – Image J data)

For peri-foveolar zones (both nasal and temporal), there are no differences, for entire groups, between OCT and Image J.

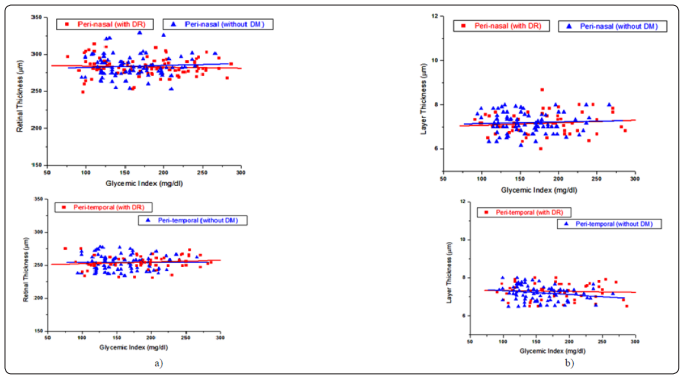

Figure 24: Mean peri-foveolar thickness variation with glycaemia for all ages (a – OCT data; b – Image J data)

But, for patients from smaller group, for peri-nasal quadrant appears a slightly difference on OCT data between patients with DR (slowly thickness decreasing) and those without DM (no thickness variation), and also an opposite variation shown by Image J data.

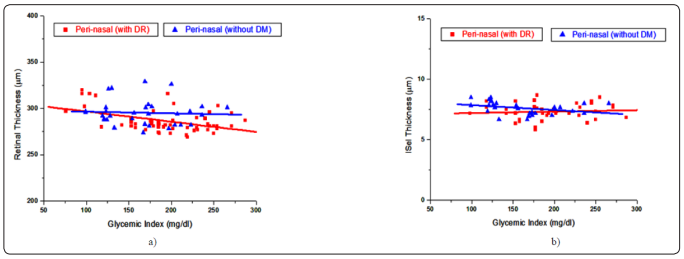

Figure 25: Mean peri-nasal thickness variation with glycaemia for subjects up to 65 years old (a – OCT data; b – Image J data)

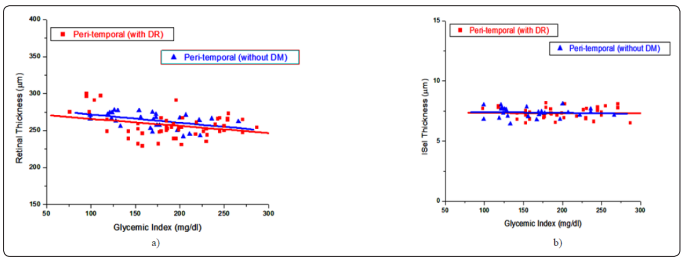

Figure 26: Mean peri-temporal thickness variation with glycaemia for subjects up to 65 years old (a – OCT data; b – Image J data)

As we have mentioned before, peri-foveolar zone has the smallest photoreceptors concentration and it is the thickest. Also, the vicinity to ONH creates different type of variation for nasal sectors.

Conclusions

In conclusion, this study revealed that glycaemia daily variation has influence on retinal thickness, but more important for patients having Diabetic Retinopathy, than for those who do not have diabetes. We can conclude that data obtained with Image J are almost the same with those resulted from OCT. the biggest difference appeared for para-foveolar sectors, for patients with Diabetic Retinopathy, in their case thickness values being bigger and thickness variation being inversed comparing with the group not affected by Diabetes Mellitus. There are also some interesting differences between nasal and temporal sectors, which need to be deeper, investigated. This will be done along new groups of patients aged between 40 and 65 years old, which retinal thickness variability seems to be partial or totally reversible; 65 years old is also the age when starts age-related macular degeneration who has maybe a seriously influence on retinal behavior especially for diabetic patients.

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