

***OCT-measurement of Pericentral Retinal Thickness in Patients with  
Diabetes Mellitus Type 2 with No or Minimal Diabetic Retinopathy***

**THESIS**

**SUBMITTED FOR PARTIAL FULFILLMENT OF THE MD DEGREE IN OPHTHALMOLOGY**

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# *OCT-measurement of Pericentral Retinal Thickness in Patients with Diabetes Mellitus Type 2 with No or Minimal Diabetic Retinopathy*

## **INTRODUCTION**

Diabetic retinopathy (DR) is one of the leading causes of blindness especially in patients between 20 and 60 years of age. Early detection of DR is important to prevent loss of vision in patients with diabetes mellitus (DM). DR classically presents with micro-aneurysms and small haemorrhages in an early stage of the disease, and is detected with slit-lamp biomicroscopy and fundus photography.

Although DR is generally regarded as a vascular disease, several studies have indicated that neural loss may also occur in a very early stage of DR, even before any sign of vasculopathy can be observed.<sup>1-8</sup> Human<sup>1-4</sup> and experimental<sup>1-8</sup> animal studies have shown apoptosis of neural and glial cells in the retina in a very early stage of retinopathy. Functional deficits in patients with DM have been described, such as a disordered multifocal electroretinogram,<sup>9-14</sup> colour vision disturbances<sup>15-20</sup> and abnormal microperimetry.<sup>10 21-23</sup> These abnormalities were present in the earliest stages of DR, even before development of micro-aneurysms or haemorrhages. However, gross neuroglial cell loss, as observed in rodents with experimental DM, has not been confirmed in humans as yet.

A loss of neuroglial tissue should decrease retinal thickness (RT) in the macular area. This effect of neuroglial loss would be most pronounced in the pericentral ring around the fovea, where the neuroglial cell layer is thickest. Optical coherence tomography (OCT) is the most sensitive, clinically available, non-invasive method to measure RT, able to detect even very small changes.<sup>24</sup>

To investigate whether neuroglial loss is a very early manifestation of DR. OCT will be used to compare pericentral RT in patients with type **2** DM, with no or minimal DR, to a healthy control group.

Minimal DR is defined as the presence of two or more micro-aneurysms and/or minor haemorrhages in the central retina and a healthy peripheral retina, as seen on slit-lamp biomicroscopy or stereo fundus photography.

## **AIM OF THE STUDY**

It is an observational cross-sectional study in which a comparison of retinal thickness (RT) measurements with optical coherence tomography (OCT) in patients with type **2** diabetes mellitus (DM) with no or minimal diabetic retinopathy (DR) versus healthy controls.

## **MATERIALS AND METHODS**

**Patients will be recruited** from the outpatient clinic of the department of Internal Medicine at Ain Shams University Hospitals and will be asked to participate in an observational cross-sectional study.

**Number of all study population: 90**

- Patients with DM type **2** with no DR: **30**
- Patients with DM type **2** with minimal DR: **30**
- Healthy control group: **30**

Ethics Committee approval will be obtained and all participants will be asked to give written informed consent.

**Eligibility criteria** included

- 1- Age :between **40-60** years.
- 2- Gender : more or less equal male to female ratio.
- 3- Diagnosis of DM type **2**.
- 4- No or minimal DR, as detected by slit-lamp biomicroscopy and stereoscopic fundus photographs.
- 5- Duration of diabetes is between **5-10** years.

**Patients will be excluded** if they have

- 1- Refractive errors of more than Sphere **+2** or Sphere **-4** dioptries,
- 2- Significant media opacities,
- 3- Glaucoma,
- 4- Uveitis or any other clinically relevant ocular disease.
- 5- Systemic hypertension, collagen and autoimmune diseases.

. A healthy control group (n = **30**) will be matched for gender and age. These individuals don't have a history of ocular disease, no family history of glaucoma nor any relevant systemic disease.

## PATIENT EXAMINATION

### **1- General Examination**

All patients will undergo a physical examination, with review of medical history and current medication.

Age, gender and onset of DM type **2** will be recorded.

### **2- Laboratory Investigations**

- a. Glycosylated haemoglobin (HbA<sub>1c</sub>),
- b. Total cholesterol and triglycerides,
- c. Serum creatinine.

### **3- Ophthalmic Examination**

- a- **Visual acuity** will be measured using **Snellen** chart.
- b- Refraction and best **corrected** visual acuity will be recorded .
- c- Pupil dilation with **2.5%** phenylephrine hydrochloride and **1%** tropicamide.
- d- Patients will be examined with **slit-lamp biomicroscopy**, and
- e- Stereo **fundus photographs** of the **50°** central posterior segment will be taken.
- f- Fluorescein angiography.

## OCT MEASUREMENTS

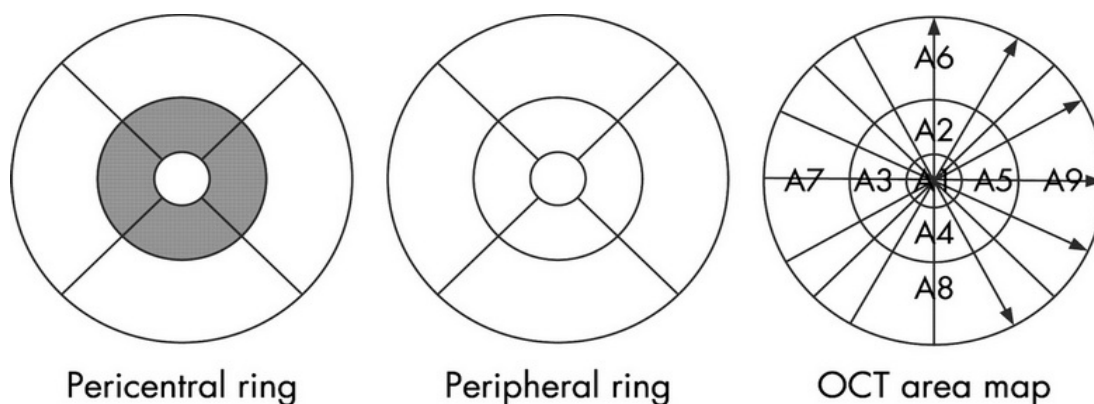
Subsequently, all subjects are examined with the OCT.

Both the fast macular thickness and regular macular thickness OCT scan protocols will be performed on both eyes. Both scan protocols obtain six cross-sectional scan lines, 6 mm in length, at equally spaced angular orientations ( $30^\circ$ ) in a radial spoke pattern centred on the fovea.

**Retinal thickness** (RT) is defined by the software algorithm as the distance between the surface of the retina and the first highly reflective layer visible at the level of the outer retina and retinal pigment epithelium. An interpolated RT map is constructed from the six scan lines by the software.

For analysis of the RT, the mean RT Will be calculated in four areas:

- 1-The central fovea (the cross-section of the six radial scans),
- 2-The fovea (central circle, with a diameter of 1 mm, area **A1**),
- 3-The pericentral area (donut shaped ring with an inner diameter of 1 mm and an outer diameter of 3 mm, area **A2-5**) and
- 4-The peripheral area (inner diameter of 3 mm and outer diameter of 6 mm, area **A6-9**)



**Figure 1** Definition of the optical coherence tomography (OCT) scanning areas around the fovea in patients with diabetes mellitus type 2 and healthy controls. The crossing of the six radial scan lines is the central fovea, area A1 is the fovea (right). The pericentral ring consists of the areas A2 to A5 (left) and the peripheral ring consists of the areas A6 to A9 (middle).

The mean RT in all four areas will be compared between patients with minimal DR, patients with no DR and healthy control subjects.

## **STATISTICAL ANALYSIS**

-Statistical analysis will be performed using :

**Analysis of variance** (ANOVA) to compare the differences in demographics between the patients with diabetes with minimal DR, the patients with no DR and the healthy control group.

Mean RT measurements will be compared using the **unpaired Student t test**.

A  $p < 0.05$  is considered statistically significant.

***Abbreviations:*** DM, diabetes mellitus; DR, diabetic retinopathy; OCT, optical coherence tomography; RT, retinal thickness.

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