

**Correlation between Visual Functions  
and Optical Coherence Tomography,  
Fundus Auto Fluorescence and  
Fundus Fluorescein Angiography  
Findings in Treatment-Naive  
Diabetic Macular Edema**

*Thesis*

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## List of Abbreviations

Abb.	Full term
<b>11-cis RAL</b>	11-cis Retinal
<b>11-cis ROL</b>	11-cis Retinol
<b>A2 E</b>	Bioretinoids (N-retinylidene-N-retinylethanolamine)
<b>ABCR</b>	ATP binding cassette Transporter
<b>ACE inhibitors</b>	Angiotensin converting enzyme inhibitors
<b>At RDH</b>	All-trans Retinal Dehydrogenase
<b>BCVA</b>	Best Corrected Visual Acuity
<b>BRB</b>	Blood Retinal Barrier
<b>CPFT</b>	Central Point Foveal Thickness
<b>CME</b>	Cystoid Macular Edema
<b>CRT</b>	Central Retinal Thickness
<b>CSCR</b>	Central Serous Chorioretinopathy
<b>CSFT</b>	Central Subfield Foveal Thickness
<b>cSLO</b>	Confocal Scanning Laser Ophthalmoscope
<b>CSME</b>	Clinically Significant Macular Edema
<b>DCP</b>	Deep Capillary Plexus
<b>DRCR</b>	Diabetic Retinopathy Clinical Research
<b>DRIL</b>	Disorganization of Retinal Inner Layer

<b>Abb.</b>	<b>Full term</b>
<b>DM</b>	Diabetes Mellitus
<b>DME</b>	Diabetic Macular edema
<b>DMI</b>	Diabetic Macular Ischemia
<b>DNA</b>	Deoxyribonucleic acid
<b>DR</b>	Diabetic Retinopathy
<b>EDI</b>	Enhanced Depth Imaging
<b>ELM</b>	External Limiting Membrane
<b>ETDRS</b>	Early Treatment Diabetic Retinopathy Study
<b>EZ</b>	Ellipsoid Zone
<b>FAF</b>	Fundus Autofluorescence
<b>FAZ</b>	Foveal Avascular Zone
<b>FFA</b>	Fundus Fluorescein Angiography
<b>GAT</b>	Goldmann Applanation Tonometer
<b>GCC</b>	Ganglion Cell Complex
<b>HbA1c</b>	Hemoglobin A1C
<b>HRS/HRF</b>	Hyper Reflective Spots/Foci
<b>HTN</b>	Hypertension
<b>ICC</b>	Intraclass Correlation Coefficient
<b>IL-1<math>\beta</math></b>	Interleukin 1 beta
<b>INL</b>	Inner Nuclear Layer
<b>IPL</b>	Inner Plexiform Layer
<b>IRMA</b>	Intraretinal Microvascular Abnormalities
<b>LBs</b>	Lipid Bisretinoids

<b>Abb.</b>	<b>Full term</b>
<b>LF</b>	Lipofusin
<b>LMP</b>	Lysosomal Membrane Permeabilization
<b>Log MAR</b>	Logarithm of the Minimum Angle of Resolution
<b>LRAT</b>	Lecithin Retinol Acyl Transferase
<b>MAs</b>	Microaneurysms
<b>Mtorc 1</b>	Mammalian Target of Rapamycin
<b>nAMD</b>	Neovascular Age-related Macular Degeneration
<b>N- ret PE</b>	N-retinylidene phosphatidyl anolamine
<b>NALP3</b>	Cryopyrin
<b>NPDR</b>	Non Proliferative Diabetic Retinopathy
<b>NSD</b>	Neurosensory Detachment
<b>NVDs</b>	New Vessels at the Disc
<b>NVEs</b>	New Vessels Else where
<b>OCT</b>	Optical Coherence Tomography
<b>OCTA</b>	Optical Coherence Tomography Angiography
<b>ONL</b>	Outer Nuclear Layer
<b>OPL</b>	Outer Plexiform Layer
<b>OS-IS</b>	Outer Segment –Inner Segment
<b>PCV</b>	Polypoidal Choroidal Vasculopathy
<b>PDR</b>	Proliferative Diabetic Retinopathy
<b>PKc</b>	Protein Kinase C

<b>Abb.</b>	<b>Full term</b>
<b>POS</b>	Photoreceptor Outer Segment
<b>PVD</b>	Posterior Vitreous Detachment
<b>RNFL</b>	Retinal Nerve Fiber Layer
<b>RPE</b>	Retinal Pigment Epithelium
<b>SCP</b>	Superficial Capillary Plexus
<b>SD</b>	Standard Deviation
<b>SD-OCT</b>	Spectral-Domain Optical Coherence Tomography
<b>SS-OCT</b>	Swept- Source Optical Coherence Tomography
<b>SFCT</b>	SubFoveal Choroidal Thickness
<b>SRD</b>	Serous Retinal Detachment
<b>TFEB</b>	Transcription Factor EB
<b>VEGF</b>	Vascular endothelial growth factor
<b>VKH</b>	Vogt Koyanagi Harada
<b>VMT</b>	Vitreomacular Traction
<b>WESDR</b>	Wisconsin Epidemiologic Study of Diabetic Retinopathy

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## **Correlation between Visual Functions and Optical Coherence Tomography, Fundus Auto Fluorescence and Fundus Fluorescein Angiography Findings in Treatment-Naïve Diabetic Macular Edema**

### **Abstract**

**Background:** Diabetic macular edema (DME) is a sight-threatening consequence of diabetic retinopathy. Available treatment modalities for DME involve repeated and invasive intraocular injection of anti-VEGF and other substances, placing heavy burdens on the patient and the health care facilities. So, identifying reliable methods for DME prognosis is actually very helpful. Multimodal retinal imaging tools provide us with these predictive prognostic biomarkers

**Aim of the Work:** To correlate between visual functions (visual acuity and color vision) with macular features of OCT, FAF and FFA in patients with untreated (treatment-naïve) DME as a guide for visual prognosis of these patients.

**Patients and Methods:** Fifty eyes of 35 diabetic patients with untreated clinically significant macular edema (CSME) underwent best corrected visual acuity (BCVA) determination (logMAR), slit lamp biomicroscopy; fluorescein angiography (FFA; FAZ size, macular leakage pattern, areas of capillary dropout) optical coherence tomography (OCT; central point foveal thickness [CPFT], volume, outer and inner retinal layers integrity [ONL, INL], hyper-reflective foci [HRF], subfoveal choroidal thickness [SFCT]); fundus autofluorescence (Hyper FAF; absent or increased (FAF, single or multiple spots). Linear correlation and three-way analysis of covariance were used for statistics.

**Results:** In OCT, we found that CPFT & ORL integrity is significantly well correlated to visual function (BCVA, color vision). However, CSFT was only correlated to visual acuity but not color vision. Regarding FFA parameters, especially (FAZ size, areas of capillary drop out), we found that these parameters are correlated significantly to visual acuity but not color vision. On the other hand, we found that the presence of hyper FAF spots was not related significantly to visual acuity but related to a significant level to color vision. However, a number of spots were not correlated to visual acuity or color vision. There was significant correlation between retinal thickness in OCT and type of leakage in FFA. Also, large cystoid spaces and FAF spots in the fovea were significantly correlated together. However, there was no correlation between retinal thickness and subfoveal choroidal thickness in OCT.

### **Conclusions:**

- Multimodal retinal imaging is of great benefit not only in diagnosis but also in its prognosis.
- Integration between different retinal imaging tools helps in finding alternative and less invasive way in diagnosis.
- FAF is simple non-invasive imaging mode to assess RPE function with evolving application in DME.

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**Keywords:** Diabetic Macular Edema, Best Corrected Visual Acuity, Optical Coherence Tomography, Fundus Auto Fluorescence, Fundus Fluorescein Angiography.

## Introduction

Diabetes mellitus (DM) is a major health problem that affects 415 million people all over the world, and this number is estimated to reach 642 million by 2040 (*Cho et al., 2018*).

Due to this high prevalence of DM, it is not surprising that Diabetic Retinopathy (DR) is one of main causes of vision loss in adults aged 20–74 years. DR ranked as the fifth most common cause of preventable blindness. Over one-third of diabetics had signs of DR, and a third of these were afflicted with diabetic vision-threatening complications (*Lee et al., 2015*).

Diabetic Macular Edema (DME) involves accumulation of excess fluid and lipids in the macula due to breakdown in the Blood Retinal Barrier (BRB). When this fluid extends into the fovea, the patient becomes symptomatic with metamorphopsia and drop of vision. (*Antonetti et al., 1999*).

Most important risk factors for DME are the type of diabetes (type I or II), the treatment method (insulin, oral hypoglycemic drugs, or diet only), and the mean duration of diabetes. Other risk factors include high levels of

hemoglobin A1c (HbA1c), hypertension and hyperlipidemia, smoking, pregnancy, physical inactivity and renal disease, while use of angiotensin converting enzyme (ACE) inhibitors has a regressive effect on DR (*Muni et al., 2013*).

In the **Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)**, the 10-year rate of developing DME was 20.1% in patients with type I diabetes, 13.9% in patients with type II diabetes not using insulin, and 25.4% in type II diabetes patients using insulin (*Klein et al., 2009*).

DME can develop at any given stage of DR. However, its prevalence increases with the severity of DR; it affects 3% of eyes with mild non-proliferative diabetic retinopathy (NPDR), increases to 38% of eyes with moderate to severe NPDR, and reaches 71% of eyes with proliferative diabetic retinopathy (PDR) (Figure 1) (*Bandello et al., 2017*).