Subfoveal Choroidal Thickness Measurement by Swept Source OCT in Retinitis Pegmentosa Patients

Thesis

Submitted for the Partial Fulfillment of the Master Degree in Ophthalmology

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Cairo, Egypt
2019

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH**, *the Most Kind and Most Merciful.*

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Tarek Ahmad El-Maamoun,** *Professor of Ophthalmology, Faculty of Medicine - Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Prof. Dr. Hala Mohammed El-Mofty,** *Professor of Ophthalmology, Faculty of Medicine, Cairo University, Head of Ophthalmology Department, MUST University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am deeply thankful to **Dr. Tamer Fahmy Eliwa,** *Assistant Professor of Ophthalmology, Faculty of Medicine - Ain Shams University, for her great help, active participation and guidance.*

I would like to express my hearty thanks to all **my family** *for their support till this work was completed.*

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Yasmeen El Kholy

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List of Abbreviations

Abb.	Full term
adRP	*Autosomal Dominant Retinitis Pigmentosa*
AUC	*Area Under the Curve*
BBS	*Bardet Biedl Syndrome*
BCVA	*Best Corrected Visual Acuity*
CME	*Cystoid Macular Edema*
CSF	*Cerebrospinal Fluid*
DI	*Digenic Inheritance*
ELM	*External Limiting Membrane*
EOG	*Electro-oculogram*
ERG	*Electroretinograms*
ET-1	*Endothelin*
HTS	*High-Throughput Sequencing*
ILM	*Internal Limiting Membrane*
INL	*Inner Nuclear Layer*
IS/OS junction	*Inner and Outer Segments Junction*
mfERG	*Multifocal ERG*
mtDNA	*Mitochondrial DNA*
mVEP	*Multifocal Visual Evoked Potential*
OCT	*Optical Coherence Tomography*
ONL	*Outer Nuclear Layer*
ORL	*Outer Retinal Layers*
RNFL	*Retinal Nerve Fiber Layer*
ROS	*Reactive Oxygen Species*
RP	*Retinitis Pigmentosa*
RPE	*Retinal Pigment Epithelium*
SD	*Standard Deviation*

List of Abbreviations (Cont...)

Abb.	Full term

SE .....*Standard Error*
SFCT .....*Subfoveal Choroidal Thickness*
SLS .....*Senior Loken Syndrome*
VEGF .....*Vascular Endothelial Growth Factor*

ABSTRACT

Background: Retinitis pigmentosa (RP) encompasses a group of hereditary retinal diseases that result in progressive loss of rod and cone photoreceptors. It occurs in approximately one in 4000 individuals, with a worldwide prevalence of 1.5 million affected individuals.

Aim of the Work: This study aimed measure the subfoveal choroidal thickness and outer retinal layer thickness in patients with Retinitis Pigmentosa and correlate them with visual acuity.

Methods: Fifty eyes of clinically and electrophysiologically confirmed retinitis pigmentosa patients compare to fifty eyes of normal healthy individuals of the same age group as controls.

Both groups were investigated for best corrected visual acuity (BCVA)(LogMAR) and Swept Source optical coherence tomography (SS-OCT) evaluating outer retinal layer thickness (ORL), central foveal thickness and subfoveal thickness (SFCT) and the integrity of inner segment-outer segment junction IS/OS as being (Intact (+) or disrupted (-)),

Results: Mean ages were 34.5 ± 11.3 years for controls versus 38.8 ±12.8 years for RP patients ($p>0.05$). Mean BCVA (logMAR) was 0.86 for RP group vesus 0.02 for control group. Mean subfoveal choroidal thickness (SFCT) measurements were significantly lower in RP group (288.4 µm) than control group (333.7µm) (P value = 0.008). Significant difference was found between choroidal thickness and BCVA (logMAR) (p-value <0.001). Presence of IS/OS was significantly correlated with BCVA (log MAR) (p value=0.0001). And finally, there was moderate negative correlation between central foveal thickness and BCVA (logMAR) (r = -0.414, p-value = 0.012).

Conclusion: Submacular choroidal thickness as measured by SS–OCT, is significantly reduced in patients with RP and significantly correlated to BCVA and IS/OS integrity.

Keywords: *Retinitis Pigmentosa, Inner Segment-Outer Segment Junction, Optical Coherence Tomography, Subfoveal Choroidal Thickness, Central Foveal Thickness*

INTRODUCTION

Retinitis pigmentosa (RP) refers to a heterogeneous group of inherited retinal diseases that cause degeneration of rod and cone photoreceptors in the human retina ***(Milam et al., 1998).***

RP results from defects in any of more than 60genes, it can be inherited in autosomal dominant, autosomal recessive, X-linked and non- mandlian pattern such as digenic and mitochondrial inheritance and it can occur either alone or with systemic disorders ***(Chang et al., 2011).***

In this disease, the photoreceptors undergo apoptosis which results in reduced outer nuclear thickness of the retina, the pigment deposits (bony spicules) result from both retinal pigment epithelium degeneration and migration into the neural retina in response to photoreceptors cell death ***(Shahsuvaryan, 2012).***

In most of the more common forms of RP, the rods are affected first between childhood and the age of 30. The patient usually notices first night blindness. Then he develops loss of some of his peripheral visual field. In a few cases cones are affected first causing loss of central vision ***(Hartong et al., 2006).***

All RP conditions are progressive, but the speed and pattern of deterioration of sight varies from one person to another. Most people with RP eventually have a very restricted visual field, leaving only a narrow tunnel of vision, most people

with RP retain useful central vision through their twenties, by the age of 50 most people's central vision is affected ***(Hartong et al., 2006).***

Fundus examination showed pigmentary deposits resembling bony spicules initially in the peripheral retina, attenuation of retinal vessels, waxy pallor of the optic disc and various degrees of retinal atrophy ***(Konieczka et al., 2012).***

OCT value in RP:

Structural assessment using optical coherence tomography (OCT) offers high reproducibility. In RP, macula thickness and retinal nerve fiber layer (RNFL) analyses show high reproducibility ***(Garcia-Marti et al., 2012).*** The introduction of OCT has improved image resolution and has enabled the analysis of various macular morphologies quantitatively.

Previous RP studies revealed that the photoreceptor inner segment/outer segment (IS/OS) length and foveal thickness, especially the outer retinal thickness, are related to retinal functions such as the visual field, visual acuity, and ERG ***(Aizawa et al., 2009).***

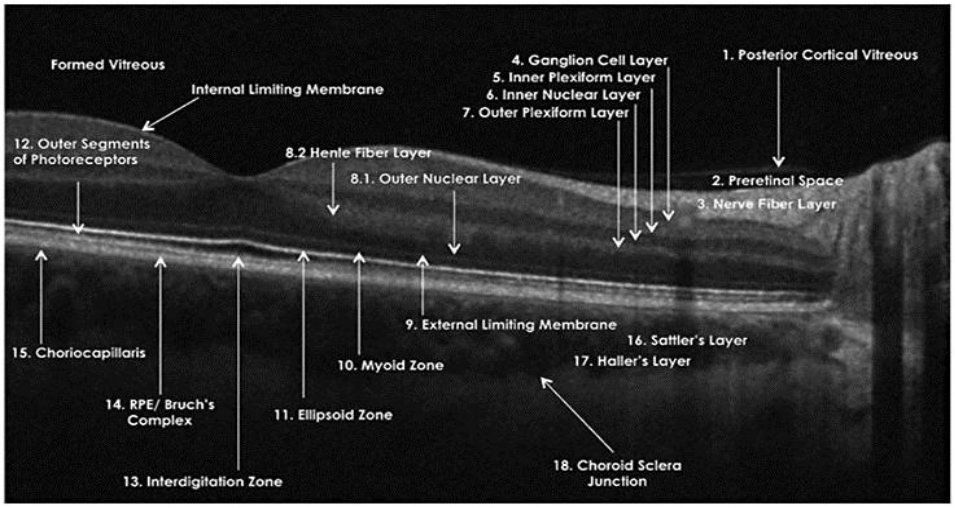

Fig. (1): Nomenclature for normal anatomic landmarks seen on SD-OCT images proposed and adopted by the International Nomenclature for Optical Coherence Tomography Panel. Healthy retina imaged using Zeiss Cirrus. The picture was taken from ***Staurenghi et al. (2014).***

In RP, the photoreceptor lines are shortened with the degeneration of photoreceptors. Rod photoreceptor death is followed by degeneration of the RPE cells and eventually leads to the loss of the cones ***(Milam et al., 1996)***.

In RP, thinning of the photoreceptor outer segments was found to be followed by a decrease in outer nuclear layer (ONL) thickness ***(Hood et al., 2011)***. Based on the SD-OCT line scans, the ONL thinning was found most in RP patients with more advanced disease and patients of older age (***Aleman et al., 2007).***

With the degeneration of the photoreceptors, retinal structural changes determined by OCT have been found to correlate with the visual functions in RP. Clinical studies

implied a correspondence between a loss of light sensitivity and a decrease in receptor layer thickness on OCT scans ***(Apushkin et al., 2007).*** The results showed that normal retinal thickness was observed with normal visual thresholds, and reduced retinal thickness was accompanied by elevated rod and cone thresholds.

Recently identified elliposoid zone which was previously believed to represent the junction between the inner and outer segments (IS/OS junction) of the photoreceptors ***(Spaide and Curcio, 2011)***. More recent evidence suggests that the second hyper-reflective band corresponds with the anatomical location of the ellipsoid portion of the photoreceptors inner segment ***(Lu et al., 2012).***

Studies showed that the length of the EZ line corresponded with a sharp drop in visual field sensitivity ***(Yokochi et al., 2012; Hood et al., 2011).*** The visual field extent was lost in RP patients without detectable photoreceptor outer segments ***(Rangaswamy et al., 2010).*** The studies implied that the absent border of the EZ provided a structural marker for the edge of the visual field. So the length of the photoreceptor segments provides a useful OCT parameter to assess the extent of the visual field.

What is more, the condition of the EZ line is an objective OCT index for assessing visual acuity in RP patients ***(Sugita et al., 2008).*** A number of clinical studies have reported