

**EVALUATION OF RETINAL NERVE FIBER LAYER
THICKNESS AND OPTIC NERVE HEAD CHANGES IN
EARLY TO MODERATE GLAUCOMA PATIENTS AND
COMPARE THEM WITH AGE MATCHED
INDIVIDUALS USING SPECTRAL DOMAIN OPTICAL
COHERENCE TOMOGRAPHY**

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CERTIFICATE

Certified that this dissertation entitled “EVALUATION OF RETINAL NERVE FIBER LAYER THICKNESS AND OPTIC NERVE HEAD CHANGES IN EARLY TO MODERATE GLAUCOMA PATIENTS AND COMPARE THEM WITH AGE MATCHED INDIVIDUALS USING SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY” submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai December 2012 is the Bonafide work done by DR.SUVITHA.P.K.S. under our supervision and guidance in the Department of Glaucoma Services, Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai during her residency programme from May 2010 to April 2013.

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PART I

CONTENTS	PAGE NO
1. Introduction	1
2. Review of literature	3
3. Glaucoma	7
4. Glaucomatous morphology of the optic nerve	7
5. Glaucomatous visual field progression	10
6. Natural history of open angle glaucoma	11
7. History of OCT	16
8. OCT Techniques	20
9. OCT in glaucoma	25
10. Optic nerve head imaging	27
11. RNFL thickness measurement in glaucoma	29
12. The need for improved imaging in glaucoma	30
13. Why compare with age matched individuals	32

PART II

CONTENTS	PAGE NO
14.Aims and objectives	33
15.Materials and methodology	34
16.Grading of glaucomatous damage	36
17. SDOCT	39
18.Statistical methods	40
19.Results	41
20.Discussion	51
21.Limitation	59
22.Conclusion	60
Annexure	
• Bibliography	
• Proforma	
• Master chart	
• Abbreviations	
• Anti plagiarism certificate	

INTRODUCTION

Glaucoma has always been one of the leading cause of blindness in the developed countries. Changing trends have now been noted in developing countries like India . where glaucoma is the second leading cause of blindness . It was estimated that the prevalence of Glaucoma in India would be 11.9 million by the year 2010 and 20% of the world glaucoma population would be in India by the year 2020¹⁻³ . Clinical diagnosis of glaucoma is possible only after about 40% of the retinal ganglion cells are lost irreversibly. Though there is retinal ganglion cell loss as age advances in normal individuals, this progressive loss is hastened in patients with glaucoma. Since glaucoma causes an irreversible changes in the Optic Nerve head and the Retinal nerve fiber layer, prompt diagnosis is warranted⁴. If these RNFL and ONH changes were detected objectively earlier before the visual field loss has set in with a relatively new imaging technology like SD-OCT, this progressive disease can either be halted or slowed down by providing apt treatment and preventing the vision loss as the current modalities that are used are subjective and diagnose only later .According to the population based surveys, prompt diagnosis and treatment was given to less than 50% of patients with a documented visual field loss, which urges us for the use of a better diagnostic instrument.⁵⁻⁷

In recent years Optical Coherence Tomography (OCT) has emanated as a cutting edge technology in imaging the eye providing high resolution ocular images in 3 dimension. Optical Coherence Tomography (OCT) works under the principle of low-coherence interferometry to determine the echo time delay of the light reflected from various layers of retina is compared with the light reflected from the reference mirror used. This real time tomogram uses a very high axial resolution (3 to 15 μm) for imaging the retina and optic nerve head⁹⁻¹³.

This dissertation aims to evaluate the retinal nerve fiber layer thickness and the optic nerve head changes in early to moderate glaucoma patients using spectral domain optical coherence tomography and compared them with age matched individuals.

REVIEW OF LITERATURE

Spectral Domain Optical Coherence Tomography in Glaucoma: Qualitative and Quantitative Analysis of the Optic Nerve Head and Retinal Nerve Fiber Layer (An AOS Thesis)

This study was done to analyze the ONH and RNFL changes qualitatively and quantitatively using SD-OCT. SD-OCT was done on patients with four stages of glaucoma, and they were compared with age matched individuals. They used two SD-OCT systems with one using titanium:sapphire as the light source and the other using Super-luminiscent diode. They concluded that SD-OCT can detect the classic glaucomatous optic neuropathy and RNFL structural changes. The reference plane was kept at 139 μ above the Retinal pigment Epithelial layer that correlated well with the subjective assessment. The minimum distance band best correlated with the subjective assessment.

Comparison of Retinal Nerve Fiber Layer Thickness Measurements in Healthy Subjects Using Fourier and Time Domain Optical Coherence Tomograph

The study was conducted to analyze the RNFL parameters using two machines and to detect the reproducibility of Fourier domain measurement in normal individuals. They analyzed the average RNFL

thickness, quadrant wise and clockhour wise in the peripapillary area. They analyzed the repeatability the intraclass correlation co-efficient and co-efficient of variation in the RNFL parameters. They inferred that the Fourier domain OCT had better reproducibility than stratus OCT.

Comparison of Different Spectral Domain Optical Coherence Tomography Scanning Areas for Glaucoma Diagnosis

This is a case-control study done to evaluate the RNFL, ONH and macular thickness in glaucoma patients using SD-OCT. They found that ROC for the inferior quadrant was the best among the RNFL as compared to the ONH parameters. But no significant difference was found between the ROC curve areas of macular thickness and RNFL parameters. They concluded that both RNFL and macular thickness parameters are good at detecting glaucoma than the ONH parameters.

Detection of Early Glaucoma with Optical Coherence Tomography (StratusOCT)

The study was done to differentiate early glaucoma from the normal subjects using stratus OCT. The study included patients with early field defects, glaucoma suspects and age matched normal eyes. The study concluded that good sensitivity and specificity was found in patients with

early field defects. Among the glaucoma suspects, analyzed using stratus OCT, 50% were consistent with the subjective assessment.

Retinal Nerve Fiber Layer Imaging with Spectral-Domain Optical Coherence Tomography Analysis of the Retinal Nerve Fiber Layer Map for Glaucoma Detection

This was a prospective, cross-sectional study done to find if there is a difference in the RNFL thickness measurement done using conventional peripapillary RNFL measurement and the deviation map in SD-OCT. They concluded that the RNFL thickness deviation map is superior in identifying the nerve fiber layer damage as compared to the standard peripapillary RNFL measurement.

Retinal Nerve Fiber Layer Measures in High- and Normal-Tension Glaucoma

This study was done to evaluate the RNFL defects in primary open angle glaucoma patients with high intraocular pressure and in patients with normal tension glaucoma using OCT. Regression analysis was done to correlate the parameters . They found that there was no significant difference in the RNFL defects among the high tension and normal tension glaucoma patients.

Structure–Function Relationships in Normal and Glaucomatous Eyes Determined by Time- and Spectral-Domain Optical Coherence Tomography

This was a comparative study done to evaluate the relationship between retinal mean sensitivity found using visual field perimetry and RNFL thickness measurement done using Time domain and Spectral domain OCT. They studied on glaucomatous eyes, glaucoma suspects and in normal subjects. The parameters were analyzed using linear and logarithmic regression analyses. They concluded that SDOCT is superior in detecting the structure function relationship as compared to Time domain OCT.

GLAUCOMA:

Glaucoma is the most common cause of irreversible blindness worldwide. Population based studies have estimated, that the prevalence of glaucoma was 60.5 million worldwide by the year 2010³. The prevalence of Primary Open Angle Glaucoma (POAG) is estimated to be around 0.41–3.51%^{14-17,19-21}. Prevalence surveys in Mongolia, Singapore, China and India have observed prevalence of both the primary angle closure and of open angle glaucoma to be same. A greater proportion of people in Asia are bilaterally blind due to angle closure glaucoma, 25 % of those with PACG are blind as compared to 10% of those with POAG³.

POAG is defined as a chronic progressive optic neuropathy with characteristic changes in the optic nerve head and visual field. Heredity, high myopia, older age, race, family history (first-degree relative), thinner central corneal thickness and elevated intraocular ocular pressure (IOP) are the proposed risk factors for glaucoma²¹

GLAUCOMATOUS MORPHOLOGY OF THE OPTIC NERVE:

The loss of retinal ganglion cells (RGCs) is found to be the basic pathology in the development of glaucoma, which results in characteristic optic nerve and visual field abnormalities. The nerve fiber layer is

composed primarily of retinal ganglion cell axons, neuroglia, and astrocytes²². The visual field changes can be detected with Standard Automated Perimetry only after about 40% of the retinal nerve fibers are lost irreversibly. So, structural changes are seen clinically after functional loss has occurred. Focal Retinal NFL defects may be an early sign of glaucoma, preceding optic disc and visual field changes²³. The Retinal nerve fiber layer defects follow the normal anatomical pattern of the Nerve fiber layer in the retina. Normally, Fibres from nasal half of the retina come directly to the optic disc as superior and inferior radiating fibers and is thickest in the superior and inferior poles, compared with the nasal and the temporal poles. There are many changes in the RNFL that are observed in glaucoma which includes a focal wedge-shaped defects, seen best with the red-free filter clinically or as a loss of the striated pattern in RNFL²³. These focal changes are best observed in the superior or the inferior areas of the nerve fibers as glaucoma tends to affect these fibers more often.

Glaucoma can present with many progressive and asymmetric disc changes. The neuroretinal rim begins to thin as the axons are degenerated. The focal degeneration of these retinal ganglion cells are observed as a focal thinning of the neuroretinal rim which is known as polar notching is the earliest sign of glaucoma. There is a selective loss of the inferior fibers earlier than the other quadrants, so this focal notching is observed

more often in the inferotemporal region of the ONH, followed by the focal notching in the superior region less frequently. So there is a vertical enlargement of the cup, which makes it clinically more significant than the horizontal enlargement. This is followed by the loss of fibers in the temporal quadrant and the nasal fibers are spared till the disease is in its advanced stages. Not more often, concentric enlargement of the cup is also observed as one of the early signs of glaucoma. In few cases, the pores of the lamina cribrosa are exposed till the margin of the disc as the cup deepens, which is known as Lamina Dot sign, is seen in glaucomatous optic atrophy. There can also be a shallow cupping of the optic disc with retention of the central cup known as saucerization extending upto the disc margin. Sloping is another early sign of glaucoma. Eventually all the neural rim tissues are lost leading to a total cupping and the vessels bending at the margins of the disc known as bean-pot cupping.

Vascular signs of glaucomatous optic atrophy include splinter hemorrhages, usually seen near the disc margin. Splinter haemorrhages are seen more often in patients with normal-tension glaucoma than in patients with Open angle glaucoma and glaucoma suspects with the incidence being 35.3% in normal-tension glaucoma, 10.3% in open angle glaucoma and 10.4% in glaucoma suspects²⁴. These splinter

haemorrhages were localized near the nerve fiber layer defect. The most common location for these hemorrhages is the inferior quadrant, but they may also be seen at any other point around the disc. They are rarely seen in advanced stages of glaucoma, but are more often seen in early to moderate stages of glaucoma^{25,26}. The deepening of the cup can lead to overpassing vessels. The circumlinear vessels are bared along the margin of the cup known as baring of circumlinear vessels. Bayonetting of the vessel is the vessel that bends along the rim edge and there occurs nasalization of vessels.

GLAUCOMATOUS VISUAL FIELD PROGRESSION:

Visual field changes seen in early glaucoma can be generalized depression and/or localized visual field defects. The early change in the visual fields can be observed only in the periphery. Most of the times these early clues can be missed, as only 24 to 30 degree of central visual fields are checked as time saving method. The visual field pattern fluctuates in these patients. As the inferior pole of ONH is involved in early glaucoma, Isolated visual field defects are observed in the superior half of the field. Very rarely the central fields may be affected early in glaucoma. In 41% of the patients²⁷ the initial glaucomatous change that might be seen in the visual field is isolated paracentral scotoma.

The visual field damage does not follow typical pattern always, it may manifest differently in different patients. As the disease progresses,retinal threshold increases gradually and uniformly along the field. Isolated defects can fuse and further above and below the horizontal midline forming a Ronnes nasal steps. Paracentral scotomas can coalesce to form arcuate scotomas.Arcuate scotomas above and below the midline forms the double arcuate scotoma . New defects can also appear with further progression. The central and temporal islands are spared till the end stage glaucoma leading to tubular vision . With further damage ,these fields are lost , central being lost earlier than the temporal field. In the end stage disease,all the nerve fibres ar lost leaving the patient blind.

NATURAL HISTORY OF OPEN ANGLE GLAUCOMA :

The word glaucoma is derived from the Greek word glaucosis, which means clouded or blue-green hue. This probably was used to describe the decompensated edematous cornea or the cataract which develops as a sequelae to the raised intraocular pressure . POAG is the most dreadful blinding disease, as being symptomless in the initial stages with just peripheral field loss, patient does not seek any health care , delaying the diagnosis . By the time the patient becomes symptomatic and approaches the clinician irreparable damage has already occurred to

the visual fields. The disease progression differs in each patient, and each patient respond differently to the treatment, though aimed at preserving the remnant field, may not be fruitful despite aggressive therapy^{28,29}.

A Study conducted in white population by Hattenhauer et.al. has estimated that approximately 9% patients may go blind in both eyes after 20 years³⁰. Population based studies have found that the mean deviation in visual field testing varies for various ethnic groups, though they were not statistically significant.³¹

The Landmark study, The Ocular Hypertension Treatment Study was done basically to identify the percentage of conversion to Open angle glaucoma from ocular hypertension. The study also tried to find if the incidence of developing open angle glaucoma can be reduced by reducing the intraocular pressure. The cases were followed for 60 months, and the inference was that 9.5% of the untreated group developed glaucoma whereas it was reduced to 4.4% in the treated group. So, the reduction of intraocular pressure had a beneficial effect in 54% of the study group. But no glaucomatous changes were observed in the optic nerve head or the visual field in 90% of the control population. So if the patient does not have any known risk factors like high myopia, thin corneas, increased vertical cup to disc ratio, high intraocular pressure, old age and increased

pattern standard deviation on the visual field then they can just be observed and kept on a regular followup.^{32,33}

The visual loss due to glaucoma can be predicted from the pathogenesis of Open Angle glaucoma that has been elucidated from the data available in the no treatment group of Randomized Early Manifest Glaucoma Trial (EMGT). At 4 years, nearly 50% of the individuals who didn't receive treatment have shown progression compared with 30% of the individuals who received treatment with the average Intra-Ocular Pressure (IOP) lowering seen at 25% in the later^{34, 35}. More than 60% of the untreated individuals at 6 years follow up have showed distinct progression in the visual loss with the overall median time being 42.8 months. This study has also shown that each individual had varied progression of the disease. Some had a rapid progression, with MD Index more than 10dB per year while others had a minimal or no progress at all even when they were followed up for a long time. The progression is seen in more than two-third of individuals with Intra Ocular Pressure ≥ 21 mm Hg i.e. High Tension Glaucoma group with a median time at 44.8 months while only just over 50% in NTG showed progression with a median time at 61.1 months. The percentage of progression in Pseudoexfoliation patients (PXEG) is more than 93% with median time at 19.5 months.

Though some individuals showed rapid progression majority of these patients progressed slowly³⁶.

This variation in the disease progression is also similar to the findings of Collaborative Normal Tension Glaucoma Study (CNTGS). EMGT and CNTGS have similar documentation of the disease progression of untreated NTG³⁷. The main focus of this study is on visual field loss and the optic neuropathy in glaucoma with normal range of Intra Ocular Pressure.

After a follow up of 5-7 years, 60 % progressive visual field defect is seen in untreated individuals with glaucomatous optic neuropathy and IOP less than 21 mm Hg. Intervention targeting individuals with IOP lowering of > 30% has lowered the rate of progression by 20%³⁷.

The manifestation of the disease varies to extremes. Slow progression is seen in some taking several years to manifest itself while some manifested the deterioration within 1 year.

The untreated subjects had their mean slope of MD index deterioration at - 0.41dB/year with index ranging from -0.2dB/year to - 2dB or more/year. This only represents the wide range in the rates of deterioration.

This high variation warrants in identifying factors that can aid in clinical diagnosis, monitoring of progression and intervention at appropriate time.

In the EMGT, when comparing the clinical course of the disease of younger individuals with individuals older than 68 years of age, the later manifested the disease faster. Prediction of this early manifestation and progression can be done with the help of factors like frequent disc hemorrhages, both eyes with glaucoma and larger field defects at initial diagnosis as measured by perimetric MD. In individuals with PXEG glaucoma is more aggressive disease than NTG and HTG wherein the mean for attaining full field blindness is within 10 years.

Intra Ocular Pressure also yields in faster progression of the disease. Individuals with IOP > 21 are more likely to progress faster than those with IOP < 21³⁸.

While the risk of rapid development of blindness is very low in NTG, this risk is high in patients with HTG and PXEG, thus the aggressiveness of the therapy varies according the groups. But keeping in mind the high variation within the groups the treatment is tailored to each individual based on their clinical presentation and interpretation.

It is evident from the two prospective studies EMGT and CNTG that involves the individuals with glaucoma who are not treated that clinical course of the disease and its progression varies widely and every individual should be monitored carefully with tailored line of treatment.

HISTORY OF OPTICAL COHERENCE TOMOGRAPHY

The first retinal imaging was performed in 1989 by David Huang. The first prototype ophthalmic OCT was placed at the New England Eye Center in 1994. In 2002 ,OCT 3 (Stratus OCT), became commercially available which was then considered the “gold standard” for retinal imaging till the advent of Fourier domain OCT or SD-OCT, or hsHR-OCT came into picture in 2006²²

In 1991, Huang and his coworkers³⁹ first demonstrated using a prototype OCT with 15- μm axial resolution in Science ,its role in imaging a human retina. They were able to compare OCT images with histology of the retina. In 1993, Fercher and associates⁴⁰ were successful in presenting the first in vivo OCT images, and in 1995 it was Huang and his coworkers again who produced the first images of retinal disease^{41,42}. Retinal images were presented using an OCT with improved axial resolution of 10 μm . The prototype instrument was a

modification of slit-lamp biomicroscope and would enable simultaneous OCT imaging. Using this system, they demonstrated imaging of both the foveal contour and optic nerve head in vivo²².

The spatial location of reflected light was determined by the light wavelengths instead of echo time delay which was the milestone in the evolution of OCT. Using Fourier transformation, the OCT has evolved from TD-OCT to SD-OCT. The TD-OCT used the position of a moving reference mirror which was used to encode the location of each reflection in the time information,^{39,40} whereas SD-OCT, which has a stationary reference mirror, gives the required information using a spectrometer. By this way, we get more information, increase in the number of scans within a short duration, making SD-OCT, a very useful tool clinically for both the anterior and the posterior segment^{11,42,43,44}

In 2001, Wojtkowski and colleagues presented the first in vivo SD-OCT scans and gave the technical details of the method. The data capture was rapid, however as the processing of images took 30 minutes to obtain, the clinical use of this technology was impractical at that period of time. The SD-OCT ophthalmic scans were⁴⁵ had a dramatic improvement with this technology in which each 500×500-pixel image could be processed in only 20 seconds. US Food and Drug Administration (FDA) has approved to use SD-OCT devices for clinical purposes, for its much

faster acquisition speed, 3D data that can be acquired and a good resolution of the structures. Faster machines are used for the Research purposes with better axial resolution are now available though not used clinically¹⁴.

Besides observing the structural anatomy of retina and other tissues, role of OCT has now been extended to monitor the physiological and pathological function of tissue characteristics. Doppler OCT methods similar to Doppler ultrasound are being used in Retinal blood flow studies which are in their initial stages, to look at flow both quantitatively and qualitatively⁴⁵⁻⁴⁸. Assessment of blood oxygenation in retinal arteries and vein was done by Kagemann and colleagues using the spectral data of SD-OCT⁴⁹. The role of OCT to study the retinal functions was emphasized by three published studies demonstrating “optophysiology,” in which following exposure of light to retina, OCT analyzed the layers of the retina in vivo⁵⁰⁻⁵².

Optical coherence tomography technology has evolved substantially over a relatively short span of time, from Time Domain to the Spectral Domain OCT, which takes much less time that allow researchers to identify properties of the retinal tissue beyond structure. This shows the rapid evolution of the OCT which is becoming an inevitable tool in the field of Ophthalmology²².

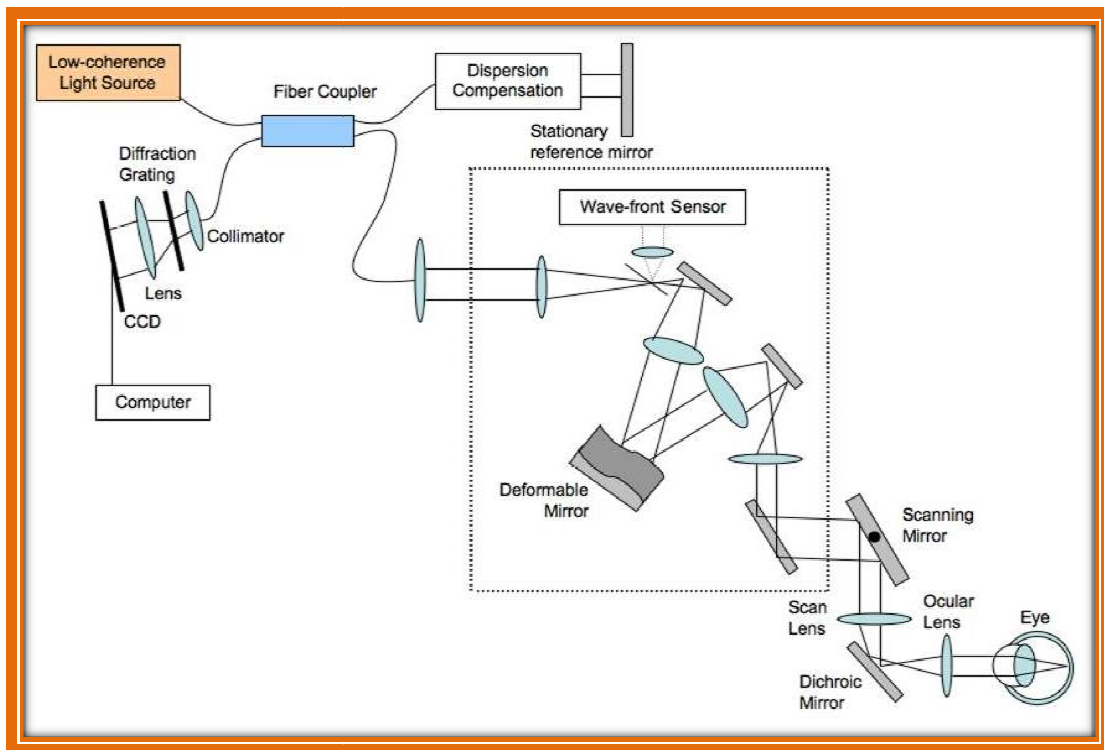


Figure: Schematics of spectral domain optical coherence tomography

OCT TECHNIQUES:

Spectral Domain OCT uses similar hardware as Time Domain OCT with a few modifications. The basic principles of OCT and ultrasound are similar with exception of OCT using light as its medium while ultrasound uses sound. The SD OCT uses spectrometer to analyze the reflected light. The above methods results in a creation of three dimensional images based on measuring the echo time delay and intensity of reflection and back scattered light or sound. The A scan is the image of the variations in the optical reflectance through the depth of the tissue depicted along a point by the OCT whereas B-scan is the cross sectional image of these single axial scans through the tissue which are gathered linearly across the tissue. 3D data set is then constructed based on the collection of parallel B-scans. Summing all the pixels in each given scan A and presenting to 3D data cube produces an OCT fundus image⁵⁷⁻⁵⁹.

Advantage of using OCT fundus image is that it has actual OCT topographic data but the SLO or fundus photograph has an upper edge in faster acquisition and minimal movement artifact. The difference in the medium makes OCT have much higher axial resolution compared to ultrasound. Time domain OCT uses an axial resolution of 10 μm [9,13,53] whereas for an spectral domain OCT it is 5 to 7 μm . Ultrasound uses an

axial resolution of $150\ \mu\text{m}$ at a frequency of 10 MHz. With higher frequencies of ultrasound, higher axial resolutions can be achieved. Anterior segment OCT uses an ultrasound frequency of approximately 60 MHz and axial resolution of approximately 40 to $20\ \mu\text{m}$ and poor depth of penetration 4 to 3 mm. Light being the medium in OCT has the advantage of non-contact while ultrasound requires a medium like water to pass the sound waves between transmitter and tissue. Hence, ultrasound is more useful in detecting the axial length and the anterior segment, whereas OCT is more useful technique to detect in detail the structures in the retina and anterior segment. Though OCT and ultrasound creates images using principles of reflection, the methods for detecting these reflections is however different for both. The speed of light being much faster than sound, the time delay in reflections from different layers being in the order of femtoseconds cannot be measured directly. Hence the principle of low-coherence interferometry is used in OCT to measure the delay in time corresponding to distances between structures. A laser with broad bandwidth or a source of super luminescent diode source is used and the beam travels to a beam splitter. This beam is split into two, one goes to a mirror at a known position on a reference arm while the other to sample arm and gets scattered and reflected from the tissue structure. The light beams from reference and sample arms travels back to the beam splitter and recombines forming a constructive interference

pattern. This pattern is then sensed by a photodetector. The resolution of the interferometer is defined by the width of the signal envelope and is based on the coherence length of the light used. The coherence length is in turn dependent on the bandwidth, the broader the bandwidth, the lower the coherence length. Finer resolution can be obtained when the light of shorter coherence wavelength is used²².

In TDOCT, the reference mirror is placed at a known distance and the position is altered for each axial scan to allow imaging of the depths of the tissue. Each pixel in the A-scan presents the reflection intensity at that position. This reflection intensity is converted to a log scale because it varies widely up to 45-dB approximately. Initially, the OCT system was based on the principle of Michelson interferometer²². TD-OCT uses a fiber-optics system. SD-OCT and TD-OCT has similar principle; however, the signal acquisition is better in SD-OCT as compared to TD-OCT. The TD-OCT has a moving reference mirror, whereas it is kept stationary in SD-OCT. The interference pattern in SD-OCT is split by a grating into its frequency components, simultaneously these components are then detected by the charged-couple device(CCD). This device has group of arranged photodetectors, each photodetectors individually responds only to a specific frequency range^{12,42-44}. These frequencies specifically correspond to certain depth within the tissue after Fourier

transform of received signal allowing simultaneous gathering of all points along each A scan and thus increasing the scan speed. Like TD-OCT, B scan be obtained by using A scan along the transverse plane. SD-OCT is also called as Fourier domain OCT because of encoding of distances in the Fourier transform of the frequencies of light reflected. The advantage of SD OCT over TD OCT is that it takes 40,000 axial scans per second as against TD OCT which takes only 400 axial scan per Second. The speed restriction of TD OCT is because it uses a moving reference mirror calculate the time taken by the light to be reflected⁴². The beam waist size defines the Transverse resolution⁵⁴ fundamentally by projecting the beam as well as any aberrations in the eye. Scan density which is dependent on A-scan sampling rate is sometimes incorrectly interpreted as transverse resolution^{6,34,35,55}. The resolution of TD OCT depends on the number of A scan that were taken. Arbitrarily the scan time increases with increase in the number of A scan taken. The transverse resolution is higher with better scan density in a long duration scan but is highly susceptible to artifacts created due to movement of eyes. The chances of motion artifacts is reduced with shorter-duration scans. As said earlier SD-OCT devices are approximately 100 times faster than the conventional TD-OCT.^{39,40,53,55} 3D data can be constructed based on these set of Bscans acquired on a faster rate. With the faster speed of the scan, images can be improved with lesser artifacts. 3 D images can be

further worked upon and processed for better visualization and to acquire further quantitative and qualitative data. Graphically these images can be displayed as either grayscale or false color images. With Grayscale there is better interpretation and smaller details can be picked up easily. As it is easier for the human eye to differentiate multiple colors rather than various shades of gray, use of false color imaging in OCT makes it easier to identify the tissue structures. But this carries the disadvantages of inducing artifacts. False color imaging shows highly reflective structures in bright colors like red and white with the intensity as high as $\sim -50\text{dB}$ while darker colors like blue and black represent low reflectivity structures with intensity as low as $\sim -95\text{dB}$ and green represents intermediate reflectivity.

OCT data can often be compared to histological sections. To find out the pathology and identify the inter visit variabilities observed to detect any progression, automated segmentation techniques are important. Segmentation is possible using SD-OCT through which we can analyze and determine the inner retinal complex which includes RNFL, retinal ganglion cell layer (RGCL), and inner plexiform layer. Three steps are involved in segmentation which includes smoothing, edge detection, and error correction. OCT has a normative database in its printouts so makes it easier for the clinicians to interpret the data of the patients and to

correlate whether the data is normal or outside normal limits. So segmentation is vital in glaucoma. Segmentation helps in the quantitative analysis of the RNFL thickness, in this the highly reflective layers appear in hot colors like red. Since RNFL thinning is noticed in the pre-clinical stage of glaucoma, before any field defect would appear, measuring the RNFL thickness is very important^{41,60}. So, analyzing the RNFL quadrant wise and clock hour wise may give a more valuable information than just measuring the average thickness. Schuman and colleagues⁶¹ defined the 3.4-mm circumpapillary RNFL thickness scan as the standard for TD-OCT glaucoma assessment in the earlier periods.

OCT IN GLAUCOMA :

Since the diagnosis of glaucoma in its early stages may be very critical and is more subjective, we need an objective method to diagnose glaucoma. Optical Coherence Tomography is a robust technology in glaucoma providing objective, high resolution images . The clinical signs of glaucoma include polar notching, more often seen in the inferior and superior poles of the optic nerve head, disc haemorrhages, asymmetric cupping of more than 0.2 between the two eyes, asymmetric appearance of the neuroretinal rim.^{62,63} The diagnosis of Glaucoma is made when there is a loss of neural rim with its corresponding visual field defects⁶⁴. The visual field defects observed in glaucoma are generalized depression,

paracentral scotoma, arcuate scotoma, nasal step of Ronne, a double arcuate scotoma, as the disease progresses can result in a temporal or a central island of vision⁶⁵. The proposed risk factors of glaucoma include high intraocular pressure (IOP), thin corneas, heredity, old age, high myopia, diabetes, hypertension and cardiovascular disease⁶⁶⁻⁶⁸. Loss of retinal ganglion cells is the finding in glaucoma⁶⁹⁻⁷⁰ leading to exposure of the lamina cribrosa and is often associated with transsynaptic degeneration in the lateral geniculate nucleus and beyond as well⁷¹⁻⁷⁵. TD-OCT used a 3.4mm circumpapillary scans to image the RNFL⁷⁶⁻⁸⁰.

The retinal segmentation helps us to analyse the course of the disease and its progression by comparing the Retinal nerve fiber layer thickness in glaucomatous eyes with the normative data base.^[80] Inter-test reproducibility was less for average RNFL thickness and can be improved in a well dilated pupil.^[78,81] Better imaging with finer details of the retinal layers and the nerve fiber layer thickness can be obtained with Fourier domain OCT (~2 to 3 μm) due to its high resolution than the conventional TD-OCT that increases the reliability of the test. The scan quality should be good to get a reliable Segmentation algorithms^{82,83}. The newer softwares in SD OCT has helped better detection and progression analysis in glaucoma. Commercially available OCT's like the Cirrus HD-OCT has improved software packages like Ganglion Cell Analysis and Optic

Nerve Head Progression Analysis for glaucoma . It also includes the Guided Progression Analysis which detects the RNFL changes over time, it creates a report, where the average RNFL thickness based on 4 visits is analysed in a linear regression pattern against the follow up duration and this change is expressed in $\mu\text{m}/\text{year}$. The Spectralis OCT has softwares to reduce motion artifacts and improve repeatability results like the TruTrak and Noise Reduction OCT signal and newer software like Posterior Pole Asymmetry Analysis which plots asymmetry in the RNFL thickness along the posterior pole across the horizontal hemisphere and between the two eyes .3D data sets can be created with newer OCT's like 3D OCT-1000 (Topcon) and Cirrus HD OCT . Since the OCT scans a larger area and in depth we get better information about the retinal ganglion cell defects. Functional data in glaucoma can obtained using SD-OCT to measure physiological parameters like the retinal blood flow in glaucoma and the oxygenation which is still in its research stage⁴⁵⁻⁴⁹.The pathology of glaucoma can be assessed by Optophysiology for functional assessment of glaucoma.^{51,52,84}

OPTIC NERVE HEAD IMAGING:

Spectral domain optical coherence tomography, a relatively new a imaging modality which can be said as a boon to the posterior segment ophthalmic surgeons as it gives a three dimensional structure of the

ONH^{85,86}, through which we can now acquire a 3D-isotropic image of the structures to be studied. Isotropic means that the size of each imaged element, or voxel, is the same in all three dimensions¹²¹. With the advent of this isotropic imaging technology, we can get almost an accurate measurement of the optic nerve head. So this is a very useful technology which takes us one step higher in the treatment and follow up of the patients with glaucoma. However, as a routine glaucoma management was based on the clinical findings like IOP measurement, ONH imaging and the visual field parameters. Due to the narrow band width in SD-OCT, the clinical findings like the properties of the disc like the colour changes are missed in SD-OCT¹²¹.

Though SD-OCT provides a detailed information about the ONH parameters, we are not able to assess which of these parameters are more useful in detecting the progression of glaucoma. Since glaucoma is a disease of chronic optic neuropathy, the disease undergoes changes over many years¹²¹. However, the data provided by SD-OCT may be useful in the evaluation and interpretation. Hence, as elucidated by Burgoyne et al, SD-OCT may be used to evaluate the progression of glaucoma⁸⁸⁻⁹⁰.

Cirrus system software could detect the changes in the optic nerve head margins.. Kim et al used two methods to detect optic nerve head margins which are centred each time method and centred once method ,

and found no difference in the data. Gabriele et al analyzed no significant difference with the RNFL measurements than the ONH measurements⁹¹. The present result of 58 µm ONH centre location deviation is well within this stability margin.

RNFL THICKNESS MEASUREMENT IN GLAUCOMA :

Clinically RNFL defect can be detected using a red-free photograph qualitatively, the quantitative assessment can be done using the two imaging technology– OCT and scanning laser polarimetry. RNFL is highly reflective on an OCT. The various RNFL thickness measurement analysis protocol includes RNFL thickness circle scan, fast circle scan, concentric three ring protocol, RNFL map and proportional circles. Circular scan of 1.34 mm radius centered on the ONH exhibit maximum reproducibility for RNFL measurement .

The measurement of RNFL thickness is determined by the difference in distance between the vitreoretinal interface and a posterior boundary, based on a predefined reflectivity signal level. In SLP the RNFL thickness is measured based on its birefringence property .

With the advent of SD-OCT, the RNFL thickness measurement reproducibility has considerably improved as quoted by many studies. It

gives a statistically significant data as compared to the conventional TD-OCT. This could be because SD-OCT provides the data in 3 dimension and reduces the motion artifact due to the faster imaging technology. Moreover SD-OCT with its high axial resolution can define RNFL boundaries more accurately, which makes it a more powerful tool as compared to the TD-OCT.¹²²

THE NEED FOR IMPROVED IMAGING IN GLAUCOMA :

Better objective screening methods is needed to diagnose glaucoma early in a population hugely affected by this disease . As the damage caused is irreparable, early diagnosis and prompt treatment is warranted . Treatment is aimed at halting the progression and preserving the residual vision . Diagnosis is usually delayed till the advanced stages as in the earlier stages patient is symptomless till prominent central fields are preserved ²². Diagnostic modalities used till present date like the visual field is subjective based on patients response and the clinicians interpretation of the result . These modalities can detect glaucomatous damage only after significant nerve tissue lost (~40% or beyond) ^{.92-95} present modifications in the diagnostic methods like the scanning laser polarimetry, confocal scanning laser ophthalmoscopy, and time domain optical coherence tomography (OCT) helps in early and objective

assessment of the the optic nerve head (ONH) and the retinal nerve fiber layer (RNFL) changes in glaucoma .

These methods have reported structural changes that can be seen before the clinical changes. Rnfl changes are seen to be more sensitive than ONH parameters on OCT .⁹⁶ thinning of RNFL seen in glaucoma correlates with the ganglion cell loss indicating glaucomatous pathology .⁹⁷ RNFL loss seen in red free photographs can be detected 6 years before the clinical manifestation .⁹⁸ Interestingly, Deleon-Ortega et al. has quoted that the current modalities that are used to diagnose glaucoma are better in ONH imaging as compared to RNFL imaging.⁹⁹ The Ocular Hypertension Treatment Study (OHTS) concluded that the ophthalmologist can diagnose glaucoma based on the serial fundus photographs taken over 5 years time before they developed any field defect.¹⁰⁰ So the early diagnosis is very important to provide apt treatment, but according to the surveys conducted very few patients were diagnosed early and received prompt treatment^{6,7,100}.

Longitudinal follow up of glaucoma is essential in detecting the rate of progression of the disease, as glaucoma is a slowly progressing disease.¹⁰¹ Appropriate treatment can be offered and the vision can be restored if we had a better imaging modality.

WHY COMPARE WITH AGE MATCHED INDIVIDUALS?

To evaluate the Retinal nerve fiber layer thickness, the disc area, age of the patient and the neuroretinal rim should be considered, because it was found that the nerve fiber layer thickness increases with an increase in NRA. As age advances the retinal nerve fiber layer thickness decreases. Patients with large disc had a thick peripapillary retinal nerve fiber layer as compared to patients with a normal disc size.

AIMS AND OBJECTIVES

PURPOSE

To assess the peripapillary retinal nerve fiber layer (RNFL) thickness and optic nerve head (ONH) parameters measured with SD-OCT in glaucomatous eyes.

AIM

- To evaluate the efficacy of spectral domain OCT in detecting the glaucomatous ONH and RNFL changes in patients with early to moderate glaucoma
- To compare the retinal nerve fiber layer thickness and ONH changes in early to moderate glaucoma with their age matched individuals using SD OCT

MATERIALS AND METHODOLOGY

An observational prospective case control study to evaluate the retinal nerve fiber layer thickness and the optic nerve head changes in early to moderate glaucoma patients and compare them with age matched controls using spectral domain optical coherence tomography. The study was undertaken in the Department of Glaucoma Services, Aravind Eye Hospitals, Madurai. The study was conducted from Oct 2010 to Mar 2012.

SUBJECTS

INCLUSION CRITERIA

- Diagnosed cases of Primary open angle glaucoma.
- Age 18 to 70 years.
- Early to moderate glaucoma on disc evaluation.

EXCLUSION CRITERIA

- Secondary glaucoma
- Angle closure glaucoma
- Advanced glaucoma
- Media opacities like significant cataract, corneal opacity etc

- Congenital Developmental glaucoma
- Refractive error $> - 6.0D < +3.0 D$ Sph.
- Astigmatism $> 3.0D$
- congenital anomaly of the anterior chamber
- concurrent active eye disease in the study eye that may affect intraocular pressure
- Eyes with proliferative or severe nonproliferative retinopathy
- Eyes with field loss attributed to a nonglaucoma condition
- Eyes with dilated pupil diameter of less than 3 mm.

The study participants include 59 patients diagnosed with Primary open angle glaucoma in the case group and 51 normal patients attending the out patient department for a routine checkup taken as controls.

All the study participants including both the cases and the control group underwent the following investigations:

- BCVA using Snellen's chart
- Slit lamp biomicroscopy
- Gonioscopy
- Perimetry (Humphrey visual field Analyzer ,central 24-2 test, size III ,white stimulus, SITA-standard strategy).

- IOP measurement using Goldmann Applanation Tonometry
- Central Corneal Thickness measurement
- Spectral domain OCT
- Dilated Fundus examination using 90D lens
- Informed consent

Glaucomatous appearance of the optic disc defined by the presence of neuroretinal rim thinning, disc haemorrhage, notching, excavation, presence of RNFL defect seen with red free image or asymmetry of the vertical cup to disc ratio of greater than 0.2 between the two eyes. Glaucomatous eyes were classified as early to moderate glaucoma on the basis of the following classification.

GRADING OF GLAUCOMATOUS DAMAGE¹²²:

Mild damage (grade 1) is characterized by minimal cupping, a nasal step or paracentral scotomas and a MD <-6dB.

Moderate damage (grade 2) is characterized by thinning of the neuroretinal rim, an arcuate scotoma and a MD <-12dB.

Severe damage (grade 3) is characterized by marked cupping, extensive visual field loss including defects within the central 5 degree and a MD >12dB.



SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY

CIRRUS™ HD -OCT



Figure – A patient getting Spectral domain optical coherence tomography done

SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY:

The study was conducted Using Cirrus™ HD-OCT software for analysis. Cirrus HD-OCT provides qualitative and quantitative data both in 2D and 3D . The wavelength of the light used is 840nm and can acquire 27,000 A-scans per second and about 200-512 B-scans per second, and constructs a 3D retinal map by aligning the B-scans. The Cirrus™ HD-OCT of the optic disc scans 6x6 mm cube which is formed from 200 A scans for each of 200 B scans. The machine detects segmentation of this 6x6 mm area and analyses the 3.46mm circle around the optic disc area. The RNFL thickness around this peripapillary area analyzed is compared to the normative database. This normative database is available for patients over 18 years of age. This normative database is color coded. 90 % of normal population will fall below the green zone, 5% or less will fall below the yellow zone and 1% falls below the red line. The signal strength is mentioned from 0 to 10. 10 is the maximum limit, values below 6 are considered poor quality. The RNFL thickness maps are also color coded which is studied in the 6x6 mm cube. Thicker RNFL areas represented by the warm colors and the thinner areas by the cool colors. The optic disc is excluded which is displayed in dark blue. The color code expresses the thickness from 0 in blue color to 350 μ in

white color. The deviation map compares the patients values with the normative data.

Statistical Methods

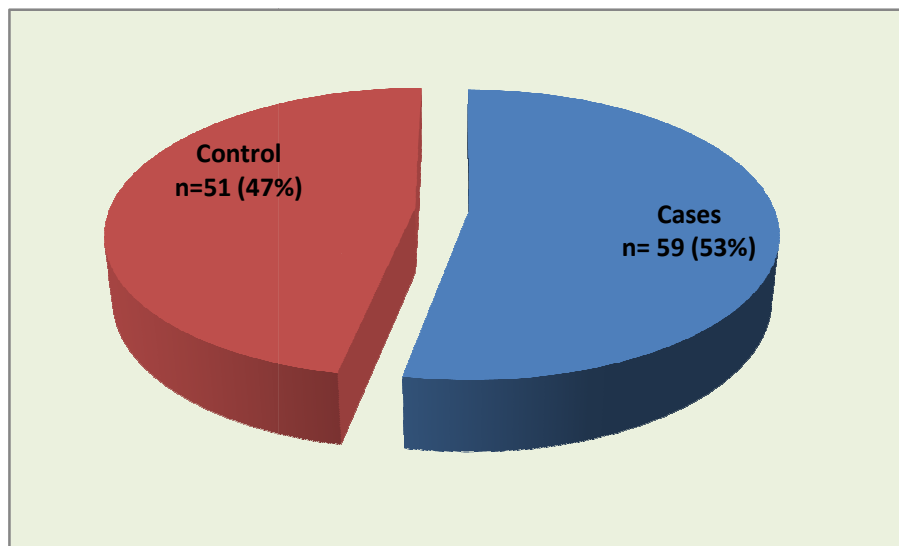
The Statistical analysis was performed by STATA 11.1 (Stata corp college station TX USA). The continuous variables were described by mean, Standard deviation, median and interquartile range. And the categorical variables were described as frequency and percentage. Student's Independent sample t-test or Mann Whitney test was used to analyze the age, ONH parameters and RNFL thickness parameters compared with POAG and controls groups. Receiver operating characteristic (ROC) curves were used to describe the ability to discriminate glaucomatous from healthy eyes for each RTVue values software-provided parameter. The ROC curve provides the trade-off between the sensitivity and 1 -specificity. An area under the ROC curve (AUC) of 1.0 represents perfect discrimination, whereas an area of 0.5 represents chance discrimination. Sensitivities at fixed specificities of 80% and 95% were determined for all the parameters.

OBSERVATION & RESULTS

Table 1 : Case and Control

	Eye	No. Of Patients
Cases	118	59
Control	102	51
Total	220	110

Graph 2: Percentage of Cases

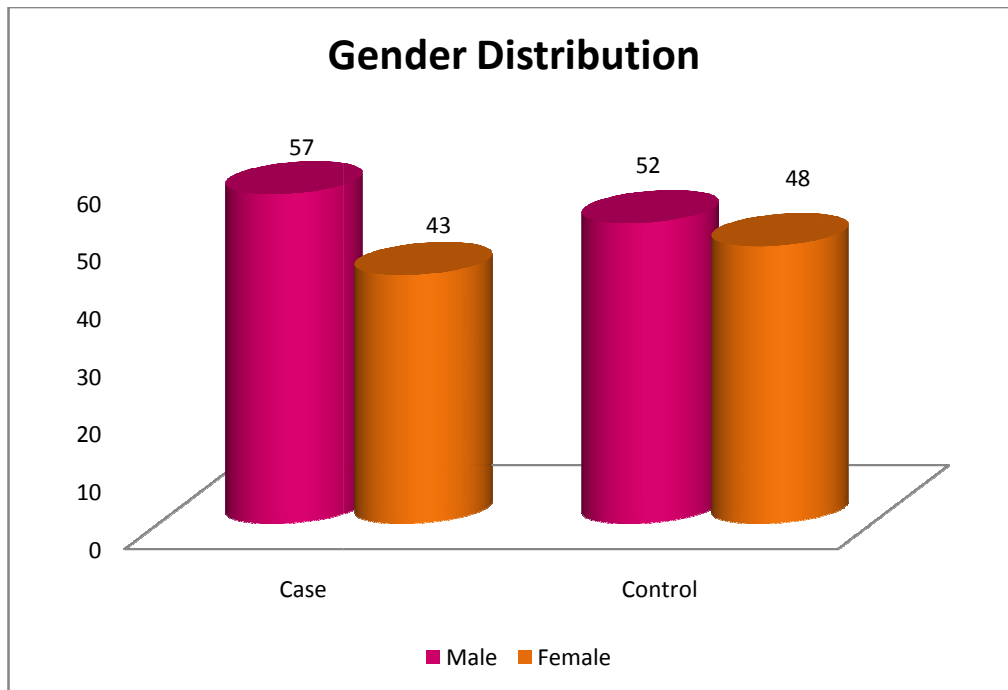


The study included 118 eyes of 59 patients diagnosed with Primary open angle glaucoma and 102 eyes of 51 patients taken as controls. (Table 1)

Table 2 : Demographics

	Case	Control	P-Value
Male	39 (57%)	29(52%)	0.320
Female	29(43%)	22(48%)	
Age (yrs)	54.13 ± 11.9	53.54 ± 7.37	0.565

Graph 2: Gender Distribution



The gender ratio was 39(57%) males and 20(43%) females in cases and 29(52%) males and 22(48%) females in controls. The case group with the mean age of 54.13 ±11.9 was age matched with the control group in which the mean age of the patients was 53.54±7.3. (Table 2)

Table 3 : Visual field variables

	Cases	Control	
	Median (1st & 3rd Quartile)	Median (1st & 3rd Quartile)	P-Value
MD(dB)	-7.82 (-10.7 , -4.57)	-2.175 (-2.98,-1.39)	<0.001
PSD(dB)	5.565 (2.99, 8.18)	2.47 (1.95 ,3.31)	<0.001

The visual field parameters analyzed were mean deviation and pattern standard deviation. The median of mean deviation in the case group was -7.82 and that of Pattern standard deviation was 5.565. The median in the control group for mean deviation was -2.175 and that of Pattern Standard deviation was 2.47. Significant differences were found for the parameters in the two groups ($p < 0.001$). (Table 3)

Table 4 : ONH Parameters

	Cases	Control	P-Value
C D Ratio	0.76 ± 0.07	0.48 ± 0.11	<0.001
VCD Ratio	0.74 ± 0.08	0.48 ± 0.09	<0.001
Rim area(mm ²)	0.89 ± 0.25	1.21 ± 0.28	<0.001
Disc Area (mm ²)	2.07 ± 0.50	2.28 ± 0.43	0.001
Cup Volume (mm ³)	0.59±0.31	0.33±0.16	<0.001

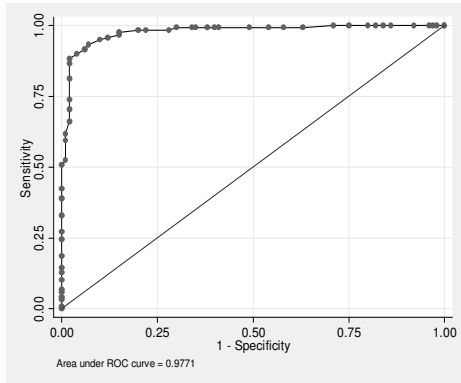
The mean values of the Optic Nerve Head parameters in the two groups are shown in Table 4. Significant differences were observed between the two groups for all the parameters.

Table 4a: ONH parameters : AUC and sensitivities at fixed specificity

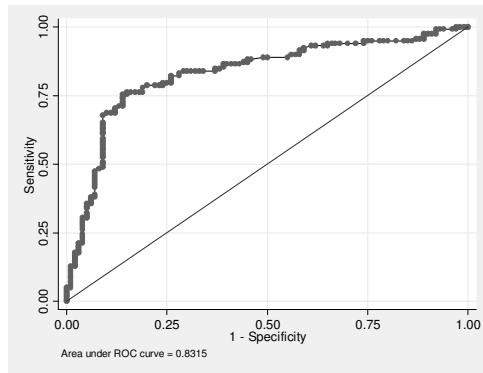
	Sensitivity at 95% Specificity	Sensitivity at 80% Specificity	AUC	95 %. C.I
Vertical CD Ratio	91.53	98.31	0.98	0.96 – 0.99
Cup Volume	35.59	78.81	0.83	0.77 – 0.89
Disc Area	4.0	25	0.65	0.57 – 0.72
Rim Area	39.0	65	0.82	0.76 – 0.87

All ONH parameters showed significant area under the curve (AUC) values in the ROC curve analysis . The best parameters from the optic nerve head analysis were the vertical Cup to Disc Ratio (AUC 0.98), the cup volume (0.83) and the rim area (AUC 0.82) , least AUC value was observed for the disc area (AUC 0.65) The parameter with the greatest sensitivity at 80 % specificity was the vertical Cup to Disc Ratio (98.31%) followed by cup volume (78.81 %) . (Table 4 a) .

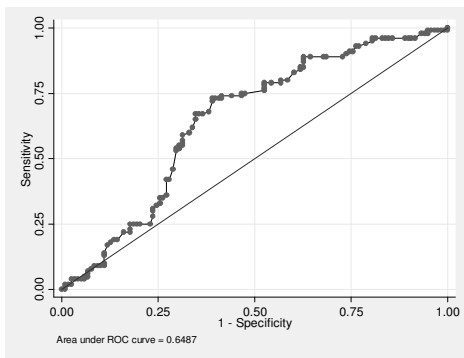
Graph 1 : Vertical CD Ratio



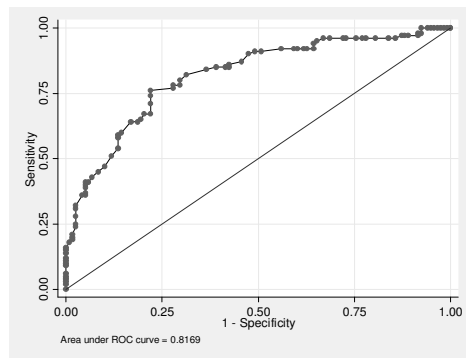
Graph 2 : Cup Volume



Graph 3 : Disc Area



Graph 4 : Rim Area



The mean average Retinal thickness for the case group was 76.84 ± 11.29 and for the control group was 91.76 ± 10.69 , the difference between the two group was statistically significant ($p < 0.001$). In the case group, the average thickness in inferior quadrant was 90.69 ± 23.9 , 94.19 ± 17.96 in superior, 63.68 ± 14.81 in nasal, 60.66 ± 12.91 in temporal quadrant, as compared to the control group which was 118.44 ± 14.89 in the inferior, 116.78 ± 14.35 in superior, 74.30 ± 13.91 in nasal and 71.54 ± 13.98 in temporal quadrant respectively. (Table 5)

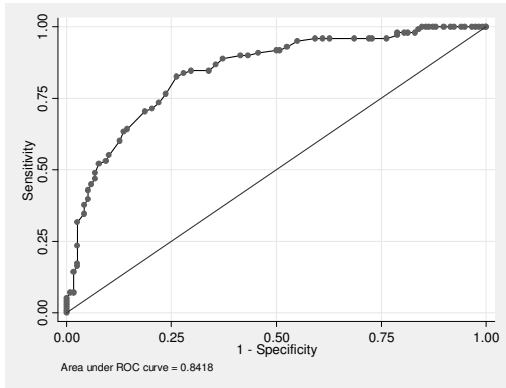
All RNFL parameters showed statistically significant reductions in RNFL thickness in the case group as compared with the control group. The parameter with the largest AUC among the RNFL thickness parameters was the average RNFL thickness (0.87). The temporal (0.72) and nasal quadrants (0.69) showed lower AUC values as compared to the superior (0.84) and inferior quadrants (0.83). The parameter with the greatest sensitivity at 80% specificity were the average RNFL thickness (74%) and RNFL thickness in inferior quadrant (74%).

Table 5 : RNFL parameters in microns

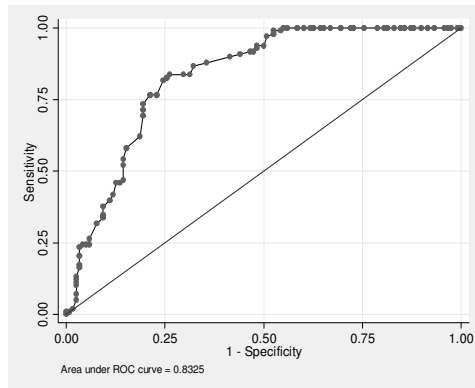
	Cases	Control	P-Value
Inferior	90.69 ± 23.9	118.44 ± 14.89	<0.001
Superior	94.19 ± 17.96	116.78 ± 14.35	<0.001
Nasal	63.68 ± 14.81	74.30 ± 13.91	<0.001
Temporal	60.66 ± 12.91	71.54 ± 13.98	<0.001
Mean Average Thickness	76.84 ± 11.29	91.76 ± 10.69	<0.001

Table 6 RNFL Thickness parameters - AUC and sensitivities at fixed specificity

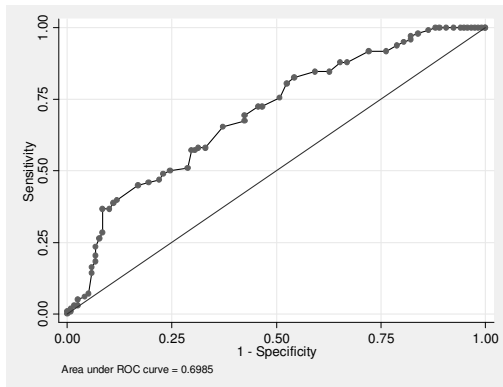
	Sensitivity (%) at 95% Specificity	Sensitivity (%) at 80% Specificity	AUC	95 %. C.I
Superior	38	71	0.84	0.79 – 0.89
Inferior	25	74	0.83	0.78 – 0.89
Nasal	7	43	0.69	0.63 – 0.77
Temporal	21	54	0.72	0.65 – 0.79
Average	50	74	0.87	0.82 – 0.91



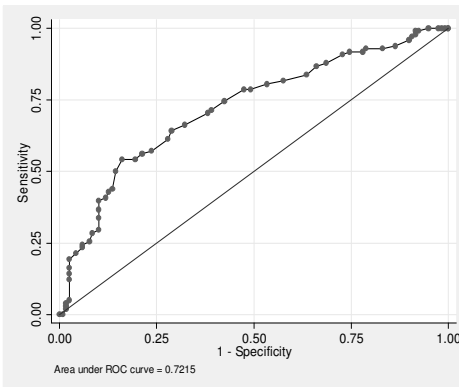
Graph 5 :AUC for Superior quadrant



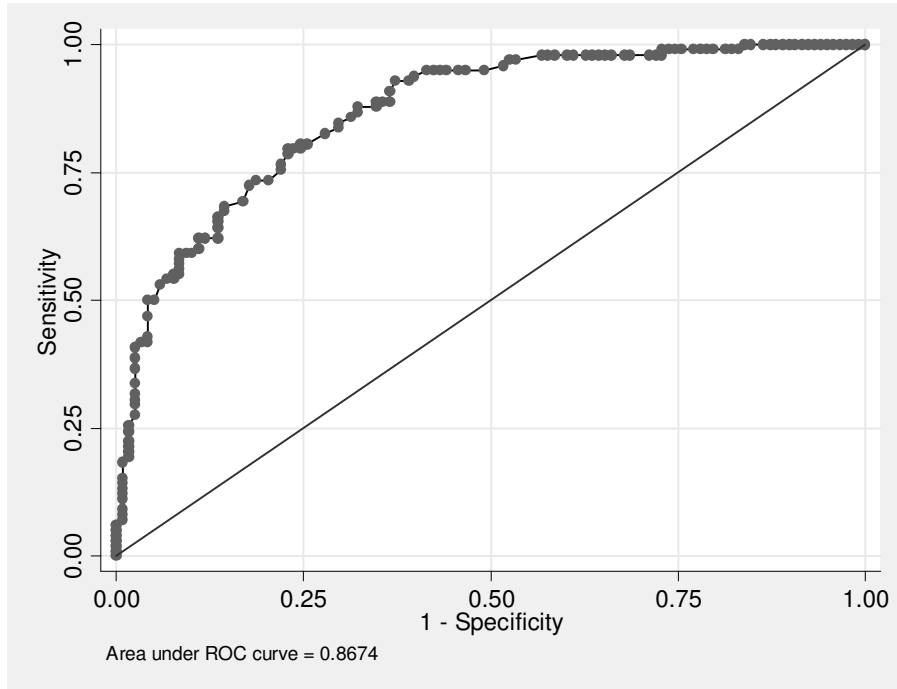
Graph 6 :AUC for inferior quadrant



Graph 7 : AUC for Nasal quadrant



Graph 8 : AUC for temporal quadrant



Graph 9: AUC for Average Thickness

DISCUSSION

The study was done to evaluate the efficacy of spectral domain OCT in detecting the glaucomatous ONH and RNFL changes in patients with early to moderate glaucoma and compared with their age matched controls. Optical coherence tomography works under the principle of low-coherence interferometry to determine the echo time delay and magnitude of backscattered light reflected off an object of interest. which can be used to scan through the ocular structures with very high axial resolution (3 to 15 μm) providing images demonstrating in 3 dimension. Retinal nerve fibre layer (RNFL) thickness measurement and ONH parameters has become a widely used clinical tool for glaucoma assessment. Optical coherence tomography (OCT) is a technology providing RNFL thickness measurements and ONH parameters in a non-contact and non-invasive fashion.

The visual field parameters analyzed in the study were mean deviation and pattern standard deviation. The median of mean deviation in the case group was -7.82 and that of Pattern standard deviation was 5.565, which confirmed early to moderate

glaucoma in the case group .The absence of any glaucomatous changes in the control group were confirmed by their visual field parameters . The median in the control group for mean deviation was -2.175 and that of Pattern Standard deviation was 2.47. Significant differences were found for the parameters in the two groups

OCT can also be used to analyze optic nerve head (ONH) parameters, such as disc area, rim area, or cup-to-disc ratio, with good repeatability and reproducibility^{103,104} . The role of ONH parameters in early detection of glaucoma has been controversial in various studies , and this feature has received less attention. In this study ONH parameters measured were CD Ratio, VCD Ratio, Rim area,Disc area, and Cup volume. Significant differences were found between the ONH parameters in the control and case group . Several other studies have shown similar results, demonstrating that ONH analysis improves our ability to discriminate between healthy and glaucomatous eyes¹⁰⁵⁻¹⁰⁸ .

The AUC represents, in a single number, the diagnostic accuracy of a test wherein a value of 1 represents perfect discrimination, while a value of 0.5 represents random discrimination. OCT parameters with AUC values above 0.80 are

generally considered to have good discriminating ability for a diagnostic test. Parameters with AUCs ranging from 0.70 to 0.80 are only fair, and those with AUCs below 0.7 are considered poor.

In this study, all ONH parameters showed significant area under the curve (AUC) values in the ROC curve analysis . The best parameters detecting glaucomatous damage from the optic nerve head analysis were the vertical Cup to Disc Ratio (AUC 0.98), the cup volume (0.83) and the rim area (AUC 0.82) , least AUC value was observed for the disc area (AUC 0.65) . The most reliable parameter for glaucoma detection was vertical cup to disc ratio in our study .This parameter had the greatest sensitivity at 80 % specificity (98.31%) followed by cup volume(78.81 %) .In glaucoma, the neuroretinal rim loss is initially seen at inferior pole followed by superior pole.This explains why the vertical cup to disc ratio is a better diagnostic parameter than the horizontal cup to disc ratio in diagnosing pre-perimetric glaucoma .A recent study by Medeiros et al.¹¹⁰ demonstrated that all ONH topographic parameters except for disc area were significantly different between normal individuals and those with glaucoma. In that study, the best individual parameter for glaucoma detection was found to be vertical cup-to-disc ratio (AUC = 0.83, sensitivity of 45% at a

specificity of 95%) which is similar to our study . Although disc area was found as poor indicator to detect glaucomatous damage in our study , study by Barbara C. Marsh et al has quoted its importance in differentiating an glaucomatous cup from physiological large cup. An increase in OCT-determined rim area is to be expected with larger disc size as this parameter is directly derived from disc area and cup area. Comparative analysis of cup area and horizontal integrated rim width in relationship to overall disc size may prove useful in the clinical distinction of ONHs with physiologically large optic cups or optic discs with glaucomatous changes .¹¹¹. Interestingly, in another study it was seen that the vertical cup-to-disc diameter ratio corrected for disc size was one of the best variables¹²³ . Hence In our study , the reliability of the various parameters could have been best detected if it was adjusted for the disc area.

RNFL thickness, in contrast to ONH parameters, is less controversial, and numerous reports have arrived at the consistent conclusion that it is a useful marker for assessment of structural damage in glaucoma.¹¹²⁻¹¹⁵

In our study statistically significant difference in the mean average retinal thickness was seen in the case and control

group, indicating glaucomatous process affecting the RNFL thickness. It was seen that in the control group ISNT rule of RNFL thickness was followed. Normal RNFL thickness values follow the ISNT rule with decreasing RNFL thickness values starting from the thickest quadrant inferiorly to the thinnest quadrant temporally. In the control group RNFL thickness was 118.44 ± 14.89 in the inferior, 116.78 ± 14.35 in superior, 74.30 ± 13.91 in nasal and 71.54 ± 13.98 in temporal quadrant respectively. However considering the average RNFL thickness in the glaucomatous patient, it was seen that there was a violation of ISNT rule in the case group, the average thickness in inferior quadrant was 90.69 ± 23.9 , 94.19 ± 17.96 in superior, 63.68 ± 14.81 in nasal, 60.66 ± 12.91 in temporal quadrant. Hence, ISNT rule for RNFL thickness can give a clue to Glaucomatous damage. Though its statistical significance was not studied in this study, studies have demonstrated the usefulness of The ISNT rule in differentiating normal from glaucomatous optic nerves^{116,117}.

In this study, the parameter with the largest AUC among the RNFL parameters were the average RNFL thickness (0.87) followed by superior (0.84) and inferior (0.83) quadrants. The temporal (0.72) and nasal quadrants (0.69) had lower AUC

values as compared to the superior and inferior quadrants . The parameter with the greatest sensitivity at 80 % specificity were the average RNFL thickness (74%) RNFL thickness in inferior quadrant (74%) . Hence, among the RNFL parameters, average RNFL thickness and inferior quadrant RNFL thickness remained the best parameter with the highest AUC, followed closely by the superior quadrant average . These OCT parameters had also been identified by previous study by Joseph Anthony et al as being the best for the diagnosis of glaucoma, however they quoted other parameters like clock-hour sectors, the best were the 7 o'clock and 11 o'clock sectors, followed closely by the 6 o'clock and 12 o'clock sectors 109 , which was not studied in this study .

Studies by Sihota et al identified the average thickness and the inferior quadrant as having the highest AUC.118 Medeiros credited the inferior quadrant with having the highest AUCs of 0.92 in patients with early to moderate glaucoma ¹¹⁹.

In our study too, we identified that among the RNFL parameters, both average RNFL thickness and inferior quadrant thickness Average RNFL Thickness as having highest AUC, it was closely followed by superior quadrants like other studies (superior(AUC = 0.84 , C.I = 0.79 – 0.89) and inferior (AUC

=0.83 , C.I =0.78 – 0.89) , the difference however were not statistically significant.

As all the optic nerve fibers finally converge toward the ONH, one would expect a corresponding change in neuroretinal rim area/volume when there is reduction in RNFL thickness. Hence this study proves that besides the average RNFL thickness, the superior and inferior quadrant RNFL thickness were better indicators of the glaucomatous damage in early to moderate glaucoma .This can be correlated with the vertical cup to disc ratio acting as a better ONH parameter to detect early glaucomatous damage than the horizontal Cup to disc ratio , as the pattern of glaucomatous loss of neuroretinal rim usually starts predominantly in the inferior and superior optic disc regions. AUC for ONH parameters and RNFL thickness in detecting glaucomatous changes is hence significant .Similar results has been seen in study by Christopher Kai-shun Leung et al, which reported both RNFL thickness and most of the ONH measurements attained similar performance in diagnostic sensitivity for glaucoma, however the performance of these two parameters in monitoring the progression of glaucoma was not evaluated in this study¹²⁰ . Demonstration of progressive optic disc changes requires

longitudinal follow-up and serial documentation of optic disc appearance.

LIMITATION

The study was undertaken only on known cases of glaucoma to evaluate the glaucomatous changes but the efficacy of these parameters in detecting the progression of these changes were not studied. The glaucoma suspects were not included in the study, hence the efficacy to predict future glaucomatous changes with these parameters is not known. The ONH parameters would have been better if they were corrected for disc area. The RNFL parameters were not studied for the clock hourwise distribution, hence focal glaucomatous changes could have been missed.

CONCLUSION

In conclusion, SD OCT is an effective tool in evaluating the ONH and RNFL thickness to detect early to moderate glaucomatous changes. In the ONH parameters, the best predictor to detect these changes were Vertical cup to disc ratio. The average RNFL thickness and the Superior and inferior RNFL quadrant thickness are the most sensitive parameters to detect glaucomatous changes. Both the ONH and RNFL parameters are equally reliable as a diagnostic tool but their role in detecting the progression needs to be studied further with the long term study. The study also shows that as age advances the RNFL thickness decreases and hence were comparable.

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ABBREVIATIONS

OCT	-	Optical Coherence Tomography
SDOCT Tomography	-	Spectral Domain Optical Coherence
TDOCT	-	Time Domain Optical Coherence Tomography
RNFL	-	Retinal nerve fiber layer
ONH	-	Optic nerve head
POAG	-	Primary open angle glaucoma
PACG	-	Primary angle closure glaucoma
AUC Curve	-	Area Under the Receiver Operating
IOP	-	Intraocular pressure
RGCL	-	Retinal ganglion cell layer
NTG	-	Normal tension glaucoma
HTG	-	High tension glaucoma
PXEG	-	Pseudoexfoliation glaucoma
EMGT	-	Early manifest glaucoma trial
CNTGS	-	Collabarative normal tension glaucoma study
SLP	-	Scanning laser polarimetry
SLO	-	Scanning laser ophthalmoscope
NRA	-	Neuroretinal rim area
MD	-	Mean deviation
PSD	-	Pattern standard deviation
DB	-	Decibel

PROFORMA

Name M.R.No.:

Age

Sex

Diagnosis: RE

LE

OCULAR EXAMINATION

BEST CORRECTED VISUAL ACUITY

RE

LE

Anterior segment:

- Lens
1. Clear
 2. Cataract
 3. Pseudoexfoliation
 4. Subluxation/Dislocation

Intraocular Pressure

Time:

FUNDUS

Vertical cup to disc ratio

Notching/Thinning of Neuroretinal rim

1. Absent
2. Superior pole
3. Inferior pole

Disc Haemorrhages

1.Absent

2.Present

Nerve Fiber Layer Defects

1.Absent

2.Inferior

3.Superior

4.Nasal

5.Temporal

HFA 24-2

Mean Deviation

Pattern Standard Deviation

CENTRAL CORNEAL THICKNESS

ANALYSIS OF SD-OCT

ONH PARAMETERS

ONH PARAMETERS	RE	LE
Cup to Disc ratio		
Vertical Cup to disc Ratio		
Disc Area		
Rim Area		
Cup Volume		

RNFL THICKNESS PARAMETERS

RNFL PARAMETERS	RE	LE
Average RNFL Thickness		
Inferior Quadrant		
Superior Quadrant		
Nasal Quadrant		
Temporal Quadrant		

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