

**CORRELATION BETWEEN PERIMETRIC INDICES AND  
RETINAL NERVE FIBRE THICKNESS BY OCT AND GDx VCC  
IN PRIMARY OPEN ANGLE GLAUCOMA**



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## **CERTIFICATE**

This is to certify that **Dr.Suma Elangovan**, Post Graduate student in ophthalmology, Regional Institute of Ophthalmology, Government Ophthalmic Hospital, attached to Madras Medical College, Chennai, carried out this Dissertation titled, **CORRELATION BETWEEN PERIMETRIC INDICES AND RETINAL NERVE FIBRE LAYER THICKNESS BY OCT AND GDX VCC IN PRIMARY OPEN ANGLE GLAUCOMA** by herself under my guidance and direct supervision, during the period April 2004 – March 2007. This dissertation is submitted to the Tamil Nadu Dr. MGR Medical University, Chennai in partial fulfillment of the award of M.S Degree in Ophthalmology.

**Prof. V.VELAYUTHAM, M.S., D.O.,**

Chief, Glaucoma clinic,  
Regional Institute of Ophthalmology,  
Govt. Ophthalmic Hospital,  
Egmore, Chennai- 600 008.

**Prof. V.VELAYUTHAM, M.S.,D.O.,**

Director and Superintendent,  
Regional Institute of Ophthalmology,  
Govt. Ophthalmic Hospital,  
Egmore, Chennai- 600 008.

**Prof. Dr. KALAVATHY PONNIRAIIVAN, B.Sc, M.D**

Dean, Madras Medical College &  
Government General Hospital,  
Chennai-600003.

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# INTRODUCTION

Glaucoma is defined as a disturbance of the structural and functional integrity of the optic nerve that can usually be arrested or diminished by adequate lowering of the intraocular pressure<sup>1</sup>. It is among the leading causes of blindness in the developing world<sup>2-3</sup> and a major health problem in the developed world. World Health Organization Statistics, published in 1995 indicates that glaucoma accounts for blindness in 5.1 million persons or 13.5% of global blindness<sup>4</sup>.

Glaucoma is a progressive optic neuropathy in which morphological changes occur in the optic nerve head and retinal nerve fibre layer and are associated with functional deficit measurable as visual field loss<sup>5</sup>. Functional loss is recorded with visual field analysis by automated static perimetry which is both sensitive and specific to detect field loss and it is a widely used technique that is arguably the gold standard to evaluate glaucomatous neuropathy and to monitor disease progression. However it is prone to variability as it requires the subjective input of the tested individual<sup>6</sup>. It has been documented that up to 40 percent of the RNFL may be lost before a defect is apparent on the visual fields<sup>7,8</sup>. Also, numerous studies have shown that glaucomatous field abnormalities may be preceded by structural changes of the ONH<sup>9-11</sup> and NFL<sup>8,12-14</sup>.

Because glaucomatous damage is largely irreversible, it is imperative to identify accurately eyes with early structural changes, because they are at risk of continued injury. Structural damage is still largely dependent on clinical assessment with an ophthalmoscope where the detection of change relies on professional judgement. Standard techniques to diagnose and monitor structural changes in glaucoma include serial stereoscopic photographs of the optic disc and monochromatic photographs of the RNFL. While these methods provide objective

information for comparisons, the interpretation of photographs remains subjective, and variation in photographic assessment among even experienced observers is well documented<sup>15-17</sup>.

Furthermore, qualitative assessment of photographs may not be sensitive to small changes over time, and it is difficult to pick up diffuse damage on these photographs. Newer technologies such as confocal scanning laser ophthalmoscopy (HRT), scanning laser polarimetry with fixed and variable corneal compensator (GDxVCC), optical coherence tomography (OCT) and the retinal thickness analyzer (RTA) have become available that provide quantitative reproducible, and objective measurements of RNFL thickness.

As visual field assessment has been considered as the gold standard for glaucoma diagnosis, all structure based investigatory modalities need to compare with automated perimetry. The purpose of this study is to evaluate the relationship between structural changes by OCT and GDx VCC and functional alteration by automated perimetry.

## REVIEW OF LITERATURE

### VISUAL FIELD ANALYSIS IN GLAUCOMA:

The visual field is that portion of space in which objects are simultaneously visible to the steadily fixating eye. Traquair has compared the visual field to “an island hill of vision surrounded by a sea of blindness”.

The word perimetry means measurement of periphery and is used almost interchangeably with visual field testing. The peripheral limit of the visual field varies:

Nasal field	60-65 <sup>0</sup>
Temporal	90-110 <sup>0</sup>
Inferior	70-75 <sup>0</sup>
Superior	50-60 <sup>0</sup>

### ***Glaucomatous visual field defects:***

Glaucomatous visual field damage results from damage to the intraocular portion of the optic nerve extending from the retinal ganglion cells to just position to the lamina cribrosa. The field defects may be generalized depression seen in kinetic methods as a generalized constriction of peripheral & central isopters or a localized defect corresponding to the NFL loss.

Generalized loss (early, nonspecific):

- diffuse loss of sensitivity
- increased variability
- hemifield asymmetry

Localized loss (more specific):

Early defects:

- paracentral scotoma
- nasal step
- temporal wedge defect (rare).

Late:

- Arcuate scotoma
- Annular scotoma
- altitudinal defect

Advanced field loss:

- Retained central vision and /or temporal island
- split fixation
- Loss of Central Island and/ or temporal field.

***Basic Aspects & Analysis of computerized Static perimetry:***

Computerized static perimetry provides numbers that represent the patient's responses to stimuli in various areas of the retina. These numbers can be manipulated mathematically and statistically to provide information about the reliability of the patient response and test results.

Mostly static with standardized testing conditions. Data retrieval and storage is possible. It is useful in monitoring the progression of the disease. Inbuilt fixation monitoring techniques are provided.

The drawbacks are:

Time consuming - expensive, tedious & cumbersome

***Basic Machine Design considerations:***

There are three fundamental hardware features that help distinguish the various computers from one another. They are

- 1) Stimulus source
- 2) Fixation control and
- 3) Data storage<sup>22</sup>

***Stimulus source:***

- Projecting system - as in Goldmann perimeter & Octopus 201.
- Light emitting diode system.
- Video monitor system to prevent dark & light combination of stimuli on a diffuse background - patient fixates on a pseudo infinite target.

***Fixation control:***

3 basic systems have been used

- Eye movement sensors

- Closed circuit TV monitor
- Blind spot projection technique (Heijl-Krakau method)

Most sensitive system is one that uses eye movement sensors to detect even minute shifts in eye position. Unfortunately, the level of sensitivity achievable with these devices is so great that unavoidable insignificant physiology fixation shifts could be registered as fixation loss. An advantage of the video signal monitoring type system is that it monitors fixation continually throughout the test, whereas in the blind spot projection, fixation is monitored in sequence and not in parallel with the rest of the visual field examination and the fixation monitoring procedure in and of itself require time.

***Data Storage:***

- Internal or external hard disc storage
- Floppy disc storage - more cumbersome

**TERMINOLOGY IN VISUAL FIELD TESTING**

***Basic software design consideration:***

There are three basic testing strategies used to explore the visual field.

- i) Suprathreshold screening
- ii) Threshold related screening
- iii) Full threshold determination examination

### ***Supra threshold screening:***

Each stimulus presented is intense enough to be seen easily by nearly all normal subjects. The same level stimulus is used across the entire visual field area being tested, and the patient has simply to respond (or not) to the presence of the target.

Supra threshold screening is perhaps the least valuable strategy available to the computerized perimeter. It is almost exclusively confined to screening examinations to exclude gross pathology.

### ***Threshold related screening:***

This screening varies the intensity of the test object at different points throughout the field. The intensity of the stimulus presented at a given point is related to the normal threshold at the stimulus site. Hence all stimuli are supra threshold. At best, threshold related supra threshold tests can only approximate the true sensitivity of the visual field. Once scotoma is detected, the computer follows either zone level testing where missed point is retested with brighter stimuli or spatially adapted testing where missed points are surrounded by additional test points to determine the extent of field defect.

### ***Full threshold determinations:***

It is the most accurate and most time consuming way to evaluate the visual field. It determines the visual sensitivity at each and every point tested by means of a “repetitive bracketing” or “stair case” procedure.

## TERMINOLOGY IN VISUAL FIELD TESTING:

### 1. **Luminance:**

Physical counterpart of the psychological term 'brightness' represented by non-logarithmic units called apostilbs. It is a measure of differential light threshold measured in units of brightness/ unit area. On this scale, the higher the numeric value, the brighter the target e.g. 1000 asb is brighter than 315 asb. On octopus and Goldman perimeter: 1000 asb; On Humphrey field analyzer: 10,000 asb

### 2. **Decibel:**

The decibel scale is a logarithmic scale that is reciprocally related to luminance. The decibel is simply 0.1 log unit. Thus 5 db - 0.5 log units. The higher the dB number the dimmer the stimulus.

### 3. **Differential light threshold:**

Refers to the ability of the visual system to detect a difference in contrast between two areas of different contrast.

### 4. **Target size**

(Goldmann's target scale)

(I = 0.25 mm<sup>2</sup> ;II = 1.00 mm<sup>2</sup>;III = 4.00 mm<sup>2</sup>;IV = 16.00 mm<sup>2</sup>;

V = 64.00 mm<sup>2</sup>)

The most frequently used stimulus with the Humphrey & Octopus perimeter is Goldmann stimulus size III (4.00 mm<sup>2</sup>)<sup>21</sup>

### 5. **Threshold:**

Threshold is defined as the intensity of the stimulus that is perceived 50% of the times it is presented.

**6. *Suprathreshold:***

It is defined as the intensity of the stimulus that is perceived 95% of times it is presented. It is the dimmest target that is always seen at a given point of retina when presented.

**7. *Infrathreshold:***

It is the intensity of the stimulus that is seen only 5% of times it is presented. In other words, it is the brightest target that is not always seen/ missed at a given point of retina when presented.

**8. *Fluctuation:***

It is an estimation of the variability in results if the measurements were repeated. The variability in repeated measurements in the same testing is short term fluctuation and the changes between different testing sessions are long term fluctuation.

**FACTORS AFFECTING PATIENT'S RESPONSES DURING VISUAL FIELD EXAMINATION:**

**1. *Age:***

Increased age is associated with increased variability. There is an average decrease of approximately 0.5dB of sensitivity per decade. So, most automated perimeters compare the results of visual fields in patients with glaucoma with large sets of age-matched normal population baseline data.

**2. *Psychological Effects:***

Fatigued or ill patients perform less well. Stress and anxiety influence patient response; effect of learning curve.

### 3. ***Refractive Error:***

Refractive errors results in the formation of a blurred image on the retina. These errors usually cause a generalized reduction in sensitivity. For each diopter of uncorrected refractive error, there is a 1.26 dB decrease in visual sensitivity within the central 6° of the visual field.

### 4. ***Pupil size:***

The amount of light entering the eye is proportional to the area of the pupil. A small pupil (<2.4mm) causes

- a) A reduction in the amount of light entering the eye, which alters the level of dark adaptation, and
- b) Reduction in the resolving power of the eye because of diffraction at the edge of the pupil.

A pupil larger than 5 mm is associated with mild generalized contraction. Ideal pupil size = 3mm

### 5. ***Media Opacities:***

Causes localized depression/ defect (e.g. corneal opacity) or generalized depression (cataract)

### 6. ***Testing variable:***

Technician, inter and intra technician variability.

### 7. ***Background Luminance:***

The visibility of target depends upon the contrast between the target and background luminance. The background intensity also affects the degree of light or

dark adaptation of the retina. The background luminance is darker (4 asb) in Octopus than in Humphrey & Goldmann where it is brighter 31.5 asb.

**8. Target intensity and size:**

The visibility of a stimulus relates to its size. The target size in Octopus in III (Goldmann's targets); for low vision, it may be increased to size V.

**9. Duration of stimulus:**

Octopus - 0.1 seconds / Humphrey- 0.2seconds.

**Reliability indexes:**

False positive and false negative response

Fixation reliability.

False positive responses occur when the patient indicates that he or she has seen a stimulus when one was not presented. This is usually a reaction to a random noise generated by the perimeter.

False negative response occur when the patient fails to respond to a stimuli that is at least as bright or brighter than one that he or she had previously recognized in that position.

False positive or false negative scores in excess of 20% to 30%, indicate a test of questionable reliability.

**Fixation reliability:**

Fixation losses exceeding 20% are considered poor in most circumstances.

***Global Indexes:***

The global indexes, which reflect the result of the visual field examination, are mathematic summaries of the actual sensitivity data produced by the examination.

***Mean Sensitivity:***

It is the average of the patient's responses for all of the points tested. i.e., average of all measured value of retinal sensitivity in dB.

***Mean deviation or defect:***

It is the weighted average deviation from the normal reference field. It is a statement of generalized depression of the visual field and is useful in recognizing early diffuse visual field loss in glaucoma.

***Standard Deviation Vs. Variance:***

The standard deviation of the mean of the patient's response is the same as the square root of the variance. The Humphrey perimeter analysis program reports standard deviation (pattern standard deviation) whereas Octopus reports loss variance. Thus the pattern standard deviation is a weighted standard deviation of the point wise differences between the measured and the normal, age-corrected reference fields. It is an index of localized change in the field.

Loss variance measures the scatter or non-uniformity of the threshold by calculating the variance of sensitivity determination. It is a good measure of localized defects. Corrected loss variance and corrected pattern standard deviation are the indexes obtained when loss variance and PSD values have been corrected for short term fluctuation.

### ***Short term fluctuation:***

It is a weighted mean of the standard deviation at ten test points where the threshold is determined twice. The SF value is usually between 1.1 and 2.5 dB in reliable normal fields.

### **OCTOPUS PERIMETERS:**

#### ***Evolution:***

The pioneering work of Dr. Franz Fankhauser and his associates in developing the original octopus model 201 in the early and mid 1970's established the standards for today's computerized perimetry.

The Octopus family perimeters are all projection system perimeters with a capacity to perform full threshold examinations and to store or transmit data for sophisticated presentation and statistical analysis. Three original perimeters the model 201 (1970s), 2000 series (1980s) and 500 series (1985) all project their stimuli on a bowl or cupola with a background illumination of 4 asb.

The newer octopus 1-2-3 perimeter introduced in 1988 uses an entirely different projection system, which consists of a screen in which the patient looks into the machine through a small (roughly 3 inch diameter) "port hole". The stimulus source is a single light emitting diode whose output appears to the patient to originate from infinity. Using a separate white halogen light, a background illumination of 31.5 asb is used. Because the unit's optical system is arranged so that the patient appears to see light coming from infinity, no correction for myopia is needed. Correction is however, required for hyperopes or patients with significant astigmatism.

### ***Fixation control:***

Infra red photograph of pupil is recorded in the memory of the computer and if the eye deviates or the eyelid is closed, the machine registers loss fixation and disregard any patient responses that occur until fixation is reestablished.

### ***Octopus software Programs:***

Currently divided into three basis categories:

- Screening tests
- Grid perimetry programs
- Diagnostic programs

### ***Screening Tests:***

The traditional octopus screening programs are #03 and #07.

Program #03: explores the central 30° with 132 test points.

Program #07: uses the same number of points to explore the entire visual field out to 70° temporally and inferiorly.

Based on the age matched values, targets are presented 6 dB brighter and the responses are tested in order to define the extent and depth of any scotoma.

Screening tests are not particularly useful for patients with glaucoma or other optic nerve diseases but they have found some utility for evaluating dense neurological defects.

## THRESHOLD TESTS:

### ***Test Pattern:***

Grid perimetry programs were the hallmark of the original octopus software. The commonly used programs were program #31 & #32.

Program #31 tested the central  $30^{\circ}$  with a full threshold strategy, using  $6^{\circ}$  spacing from the initial point located at fixation.

Program #32 tested the same region with the same strategy, but the points were offset up and over by  $3^{\circ}$  - i.e. no point at fixation or along XY axes.

### ***Threshold strategies:***

- Choice of either
  - normal thresholding test strategy
  - fast thresholding strategy

Normal thresholding test strategy (repetitive bracketing):

Machine presents a test target 5dB brighter than the expected. If the patient sees the stimulus, intensity is decreased in brackets of 4 dB till it is not perceived. Then the intensity is increased by 2dB until stimulus is seen. If patient does not see the stimulus, the intensity is increased by 4dB till he sees it. Then the process is reversed i.e., intensity is decreased in brackets of 2dB till patient stops seeing. Depending on the brightest target that is not seen and the dimmest target seen – infra threshold and supra threshold are determined. Average of these two is taken as threshold.

### ***Fast threshold strategy:***

The initial projection is 4dB supra threshold. If the patient seen the initial stimuli, the machine moves to other areas of the field and than returns to the original point and retests with the identical db Supra threshold stimulus. If the

patient sees the light the second time also, the machine assumes the sensitivity here to be approximately normal and prints a value halfway between the test value and the age - matched normal. The fast strategy allows for an error of  $\pm 2$ dB at each normal point.

### ***Diagnostic Programs:***

The G1 program is designed specifically for testing patients with confirmed or suspected glaucoma.

The G1 program has an asymmetric distribution of target (56 test points). There is a test point at fixation, four points in the oblique meridians that are  $2.5^{\circ}$  from fixation, and four additional points within  $6^{\circ}$ . The region around fixation is thus covered with nine test points. The arcuate region is covered by 11 points and the nasal step region is examined by 12 points.

The G1 test take place in 2 phases. A phase is defined as a segment of the visual field test in which each test point is measured. The two phase examination means that all 56 central test points are thresholded fully once, and then the same test points are tested again. It is possible to interrupt the test after phase 1. Such multistage programs include 'X' in their designations. The most commonly used one the G1 x (G1 program), the M2x (the macular program), and the STX (a screening program).

A phase 1 test can calculate the mean sensitivity and loss variance. Because each point is tested only once in phase 1, there is no determination of short-term fluctuation and hence corrected loss variance can not be tested.

A newer innovation on some of the octopus programs is to divide the phases into stages. A stage is a specified fraction of a phase.

For example: G1 x program has 3 phases.

Phase 1: Measures full threshold at each of the central test points.

Phase 2: Determines these thresholds for a second time

Phase 3: Two zone screening test performed in the mid-peripheral field.

Phase 1&2: Divided into 4 stages

Stage 1: Tests 1/6 points (full threshold) over central 30°  
60% of information of field is revealed.

Stage 2: 16 additional points and reveals upto 80% of information contained in the field.

Stage 3: 12 additional points are tested and 90% of information is obtained.

Stage 4: Final 14 points are tested and increases the sensitivity to 95%

### ***Octopus Machines - Tendency oriented Perimetry (TOP):***

Conventional threshold tests are often long and uncomfortable for patients. They tire them out thus decreasing test reliability. The TOP strategy was designed to collect as much information as the standard tests in half the time without sacrificing test accuracy. TOP reduces test time to about 3 minutes. It uses answers from surrounding visual points to calculate the threshold at the point being tested because, in a visual field all neighbouring points are interconnected. TOP works by investigating consecutively 4 intermingled matrices. Initially the first matrix is tested under the assumption that the threshold is equal to half the normal age corrected value (NV). A positive answer draws the field up and the negative answer pulls it down. The bracketing step taken to approach the threshold is 4/16 NV. The machine then goes on to test the second matrix with a step of 3/16 NV dB and for the third and fourth matrix it is step of 2/16 and 1/16. Visual field data

obtained with TOP correlates well with the normal threshold tests with a high specificity and positive predictive value.

***Specialized Programs:***

M1 Program → tests within central 10°

M2 X program

Profile program FM → performs a static profile cut through a specific area of visual field.

Program #62 and #64 - uses focus programs can be used to focus attention on a specific small area anywhere within the central 6° with 3° resolution.

Program #35, #45 and #25 termed low vision programs using Goldmann size V target

Program NT → screening test for neurological disease.

Program BJ → Visual disability test.

The components of the octopus 1-2-3 printouts and their interpretation:

***Patient data:***

Name, age, sex, date of birth , Date of examination, program and strategy used, eye examined, pupil size, refraction & visual acuity.

***Reliability factors:***

***False positive and false negative catch trials:***

The number of false positives is expressed as a percentage of the total positive trials .False negative catch trials are also expressed in number and in a percentage

of the total questions asked. Recommended false positives and negatives <10%.  
Patient with a higher rate than 10-15% may need closer surveillance because they lost attention or are not in a good condition.

***RF (reliability factor) index:***

False positive to false negative ratio: should be <10%.

***Grey Scales:***

This is a crude representation of visual field defect. The lighter the shades or colours, the better and higher is the retinal sensitivity. Conversely, darker areas indicate areas of depressed sensitivity and black areas indicate absolute loss of sensitivity.

***Numerical Data:***

Consists of patient's threshold values at each location tested in decibels. The other graphs, plots and presentations are derived from this data by calculations based on normative data and statistical methods.

***Bebie Curve:***

Also known as cumulative defective curve. Consists of graphical representation of field defect; if it is in between 2SD it is taken as normal. It helps examiner to assess the visual field at a glance. Test points are ranked in order of least deviation from the expected normal and plotted in the form of a graph. The least deviated points lies to the left and the most deviated point lies to the right.

***Numerical Difference Scale:***

Consists of difference between age matched values and patients threshold values at each test locations.

## VISUAL FIELD INDICES:

### ***Mean sensitivity:***

This is the average of all measured values of retinal sensitivity in dB called the mean sensitivity. The normal MS value depends on the patient's age and therefore, there cannot be a range of normality for this index. It is useful to detect diffuse change.

### ***Total loss:***

It is the sum of the difference between age corrected normal value and measured threshold for each location.

### ***Mean Defect:***

Mean defect is the most important index related to global damage. It is the average difference between age corrected value and measured test value at each location. It is sensitive to generalized depression. The MD is independent of age; there is a tolerance range from  $-2$  to  $+2$  dB for normality. A loss of 1 dB in MP corresponds to approximately 10% loss of visual function.

### ***Loss variance:***

This index is calculated from the individual deviation of all measured locations with the mean defect value. Therefore, the LV index is sensitive to irregularity and is the early indicator for localized damage.

### ***Short term fluctuation:***

It is the measure of the variability of the patient's response during a single visual field.

### ***Corrected Loss Variance:***

This index is obtained after correcting the loss variance due to fluctuation by subtracting the SF factor which results in an even more sensitive value than loss variance for the detection of early local defects.

### **ANALYSIS OF THE NERVE FIBER LAYER IN GLAUCOMA:**

#### ***Recent concepts:***

In recent years, various studies have established the importance of visualizing and quantifying the optic nerve head and retinal nerve fiber layer parameters in glaucoma. Research has shown that 40% of ganglion cell loss may result in only a 10 dB visual field defect, a relatively shallow scotoma. A study by Sommer et al<sup>14</sup> found that 88% of ocular hypertensives who converted to glaucoma has retinal nerve fiber layer defects at the time when visual field defects were detected by perimetry. 6% of these converters had RNFL defects present 6 years prior to the visual field defect. It has also been documented that RNFL changes can occur prior to optic nerve head changes<sup>11,12</sup>.

A study by Quigley et al found that RNFL changes were detected more frequently than ONH changes in eyes that converted from ocular hypertension to glaucoma<sup>25</sup>. In a sample of 813 ocular hypertensives followed for over 5 years, they found that of the 37 eyes that developed abnormal visual field tests at the end of the 5 years period, 73% had either a RNFL defect initially or developed one during follow up. Progressive RNFL atrophy was observed in 49% of eyes, while optic disc change was observed in only 19%. Several studies have found evidence that RNFL is a better and easily predictor of glaucomatous damage and visual field loss<sup>25-27</sup>.

A study by Arakinsen found that RNFL defects developed in 83% of early glaucoma patients, while only 42% developed an abnormal CD ratio<sup>28</sup>, the clinical assessment of the ONH & NFL highly subjective and prone to variability. Hence, it is essential that new objective tools be created to permit the early diagnosis of the disease and the early detection of its progression. In response to this demand, technologies have been developed to allow objective measurement of the ONH & RNFL.

***The retinal nerve fiber layer and its changes in glaucoma:***

The nerve fiber layer of the retina is composed primarily of ganglion cell axons, some astrocytes, retinal vessels and Muller cell processes. The normal nerve fiber layer has a striated appearance better appreciated when examined under red free light with an ophthalmoscope. The striations are formed by bundles of axons compartmentalized in glial tunnels formed by muller cell processes.

The normal temporal pattern from above to below is composed of bright reflexes superiorly, dark towards the fovea, and bright again inferiorly, reflecting the thicker NFL superiorly and inferiorly .

***Pattern of retinal nerve fiber layer abnormalities:***

***Slit like or groove like defects:***

- Can be seen in healthy NFL
- Slit defects are narrower than the diameter of adjacent vessels.
- Likely to be abnormal if they extend all the way to the optic disc margin.

### ***Wedge - Shaped defects:***

- It is a highly localized injury often located in superior and inferior actuate areas.
- A wedge is dark and at least twice as wide as an arteriole. Its width narrows near the disk and broadens towards the periphery.

### ***Diffuse loss:***

The retinal vessels are covered only by the inner limiting membrane, resulting in better visibility and sharper image of the retinal vessels.

### ***Imaging of RNFL in Glaucoma:***

Ganglion cell death is the cause of visual field loss in glaucoma. The goal of NFL evaluation is the early diagnosis of glaucoma and its progression. Conventional NFL evaluation involved the use of red free or green light. Optimal visibility is obtained with a stereoscopic image of the NFL at the slit-lamp biomicroscope optimally using a Goldmann or other fundus contact lens or non contact lens. The use of NFL photography provides the clinical with the opportunity for more relaxed evaluation and comparison between eyes.

### ***The nerve fiber analyzer:***

The NFA measures the rotation of polarized light reflected from the retina to determine the NFL thickness, using the birefringence of the NFL to change the polarization. The change in polarization is termed as “retardance” - The assumption used by the NFA is that the polarized light rotation is proportional to the NFL thickness and this retardance is measured by Fourier ellipsometry<sup>34</sup>.

### ***Scanning Laser Ophthalmoscope:***

Digital image processing can be used to enhance the contrast of the NFL using confocal scanning laser ophthalmoscope. The SLO can display NFL striations with increased lateral resolution and contrast. Advantages include ease of use with small pupil and less clear media.

### ***The retinal thickness analyzer (RTA) :***

The RTA is based on the principle of slit lamp biomicroscopy in which a green 540nm. He-Ne laser is projected on the fundus at an angle and its intersection with the retina is imaged. The distance between the vitreo-retinal interface and retina-RPE interface is directly proportional to the retinal thickness. A 2x2 mm area is scanned by 10 cross sections optically in 400 ms. Unlike OCT, The RTA maps rapidly larger areas, but is limited by pupil size and is difficult in eyes with media opacities<sup>35</sup>.

### ***Confocal Tomographic angiography:***

This combines confocal laser scanner and indocyanine green to visualize vascular pattern of ONH.

### **SCANNING LASER POLARIMETRY:**

The scanning laser polarimetry is an imaging technology that uses the birefringent properties of the retinal nerve fiber layer to quantify its thickness. The parallel arrangement of the microtubules within the retinal ganglion cell axons causes a quantifiable change in the polarization of light that passes through them. This change is called “retardation” and this is proportional to the RNFL thickness.

A scanning laser polarimeter has an integrated ellipsometer to measure retardation. The amount of retardation is captured by a detector and converted into thickness (in microns).

***Importance of corneal compensation:***

The total retardation of a subject's eye is the sum of the cornea, lens and the RNFL birefringence. Hence, compensation of anterior segment birefringence is necessary to isolate the RNFL birefringence.

Early scanning laser polarimeter (e.g. The GDx NFA (nerve fiber analyzer I & II) and the GDx access) compensated for anterior segment birefringence based on fixed values of the axis and magnitude of the anterior segment birefringence. Studies of Greenfield<sup>29</sup> et al and Knighton<sup>30</sup> et al revealed a large variation in polarization properties of the cornea in different subjects.

The GDx VCC(variable corneal compensator) individually compensates for the anterior segment birefringence for each eye. First the eye is imaged without compensation. The uncompensated image presents the total retardation from the eye. The macular region is imaged and the non-uniform retardation profile around the macula is analyzed. Using the radial birefringence of the Henle's layer in the macula as control, the VCC is adjusted for each eye.

***Device fundamentals & Data Acquisition:***

The currently available unit is the GDx VCC (Laser diagnostic technology, San Diego, California) is a fourth commercial generation SLP. The light source used is a diode laser (780 nm wavelength). A 15x15 degree area is measured with an acquisition time of 0.7 seconds. A complete scan consists of 65,536, individual retinal locations (256x256 pixels). Immediately after acquiring the data, a computer algorithm calculates the amount of retardation at each

measured retinal position. The map consists of 256x256 pixels and the value of each pixel represents the amount of retardation at that particular location.

The nerve fibre layer retardation is assessed by means of positioning a peripapillary band (a 10 pixel wide circle or ellipse) around the inner margin of the peripapillary scleral ring (1.7 disc diameter, default setting) Thus approximating the optic disc margin. The retardation along this band sup 120<sup>0</sup>, inf 120<sup>0</sup>, nasal 70<sup>0</sup> and temporal 50<sup>0</sup>) is measured and the result is represented graphically.

***Measurement techniques:***

It is performed with an undilated pupil of at least 2 mm diameter . Time of acquisition is 0.8 seconds. Total time for the examination and output is less than 3 minutes for both eyes. The test is objective and reproducibility of images is 5 to 8 micron per measured pixel. The diameter of the ellipse is displayed in microns and gives an idea about the actual disc diameter.

***Sources of error/variability with GDx:***

Varies with ethnicity and age - requires wider Indian data base affected by anterior and posterior segment pathology:

- Ocular surface disorders.
- Macular pathology (basis for corneal compensation is intact Henle's layer in macula)
- Cataract and refracting surgery (alters corneal birefringence)
- Refractive errors (False positive in myopes)

- Peripapillary atrophy (Scleral birefringence interferes with RNFL)

***Other Limitations:***

- Does not measure actual RNFL thickness (inferred value)
- Measures RNFL at different location for each patient
- Does not differentiate true biological change from variability.

***Advantages:***

- Easy to operative
- Good reproducibility
- No dilatation required.
- Independent of optical resolution of the eye.
- Age matched normative database.
- Does not require a reference plane.
- Early detection before visual field exam.

***Clinical Interpretation of a GDx VCC printout:***

For each GDx VCC scan, an age matched comparison is made to the normative database and any significant deviation from normal limits one flagged as abnormal with a p value.

There are 4 key elements of the printout:

1. Thickness map
2. Deviation map
3. TSNIT graph
4. Parameter table.

***Thickness map:***

It shows a colour -coded format of the RNFL thickness. Thicker regimens are coloured yellow to red while dark blue, light blue and green area are regions of thin RNFL. The colour scale follows the colour spectrum (blue to red) upto 120 microns.

***The Deviation map:***

This analyzes a 128x128 pixel region ( $20^0 \times 20^0$ ) centered on the optic disc. To reduce variability due to anatomical deviations, the 128x128 region is averaged into 32x32 square grid where each square is the average of 4x4 pixel region (Super pixels). The RNFL thickness at each super pixel is compared to age matched database and are colour coded based on the probability of normality. Dark blue squares represent  $<5^{\text{th}}$  percentile of normative database i.e., only a 5% probability exists that the RNFL in this area is within normal limits. Similarly, light blue is used for deviation below 2%, yellow for deviation below 1% and red represents deviation below 0.5%. Thus, the deviation map reveals the location and magnitude of RNFL defects over the entire thickness map.

### ***The TSNIT Map:***

This map displays the RNFL thickness values along the calculation circle starting temporally and moving superiorly, nasally, inferiorly and ending temporally.

In the normal eye, the TSNT, plot follows the typical 'double-hump' pattern with thicker RNFL superiorly and inferiorly.

The TSNIT graph shows the curve of the actual values for that eye along with a shaded area which represents 95% normal range for that age. In the centre of the printout at the bottom the TSNIT graphs for both eyes are displayed together. A dip in the curve of one eye relative to another indicates RNFL loss.

### ***The parameter table:***

The TSNIT parameters are based on RNFL thickness values within the calculation circle. The parameters are displayed in a table in the centre of the printout. These parameters are automatically compared to the normative database and are qualified in terms of probability of normality (Colour coding - same as the deviation map).

The calculation circle is a fixed circle center on the ONH. The band is 0.4 mm wide and has an outer diameter of 3.2 mm and an inner diameter of 2.4 mm

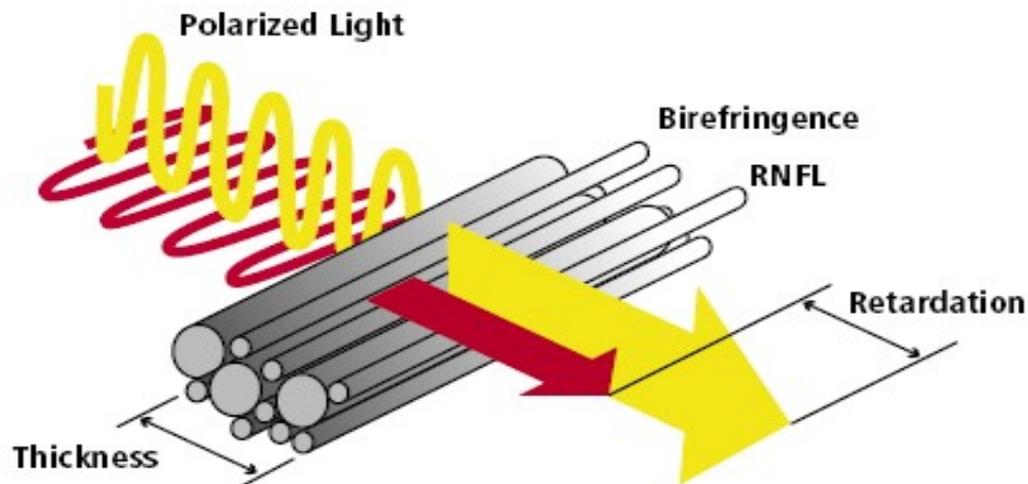
The parameters are as follows:

- |                   |  |
|-------------------|--|
| TSNIT Average:    | The average RNFL thickness around the entire calculation circle.           |
| Superior Average: | The average RNFL thickness in the superior 120° of the calculation circle  |
| Inferior average: | The average RNFL thickness in the inferior 120° of the calculation circle. |

TSNIT SD: This measure captures the modulation (peak to trough difference) of the double hump pattern the eye; normal eye: High modulation; glaucomatous eye: low modulation in the double hump pattern.

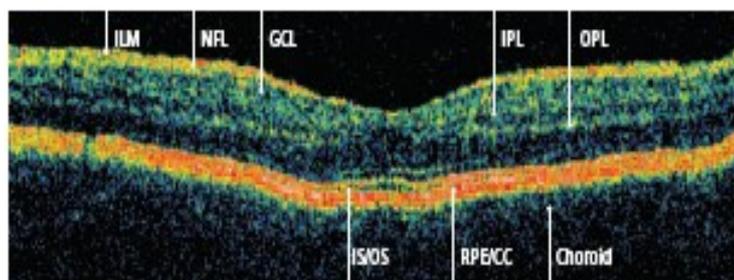
Inter-eye symmetry: Correlates the TSNIT function in both eyes & measures the symmetry. Range:  $-1$  to  $1$ . Normal eyes have good symmetry with values around  $0.9$ .

**Principle of GDx: Two orthogonal components of polarized light pass through the RNFL (a birefringent medium) and one component is retarded proportional to the RNFL thickness**



### Stratus OCT Image of Normal Retinal Layers

**ILM:** Internal Limiting Membrane  
**NFL:** Nerve Fiber Layer  
**GCL:** Ganglion Cell Layer  
**IPL:** Inner Plexiform Layer  
**OPL:** Outer Plexiform Layer  
**IS/OS:** Junction of Inner and Outer Photoreceptor Segments  
**RPE/CC:** Retinal Pigment Epithelium/Choriocapillaris



### ***The nerve fiber indicator:***

It is a global measure based on entire RNFL thickness map calculated using an advanced neural network called SVM - support vector machine. Value ranges from 1 to 100: values between 1-30 classified as normal, 31-50 as borderline, and 51+ abnormal.

Research shows NFI is the best parameter for discriminating normal from glaucoma<sup>31</sup>. The sensitivity and specificity of NFI is 89% and 98% respectively. In general, TSNIT average, superior average, inferior average and TSNIT SD, nerve fiber indicator and inter eye symmetry are abnormal if  $p < 1\%$  and considered borderline at  $p < 5\%$  level.

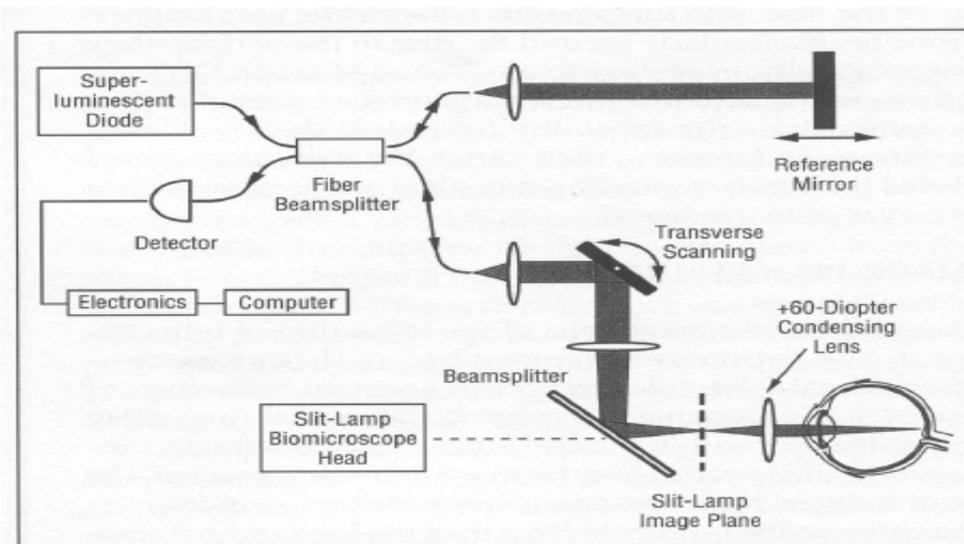
### **RNFL ANALYSIS BY OPTICAL COHERENCE TOMOGRAPHY:**

OCT is a non contact noninvasive imaging technology that uses light to create high-resolution, real time, cross-sectional tomographic images. It shows cross sectional living histology of retina with a higher resolution of approximately  $10\mu$  and has a high reproducibility<sup>32, 33</sup>. It is the optical equivalent of B mode ultrasound wherein light reflection from the scanned area is detected.

### ***Basic Principle:***

The OCT is based on the principle of Michelson's interferometry.

## Optics and principle of OCT Michelson interferometer



Low coherence infrared (830nm) light coupled to a fiberoptic travels to a beam splitter and is directed through the ocular media to the retina and to a reference mirror, respectively. Light is reflected by the different retinal tissue layers. When the distance between the light source and retinal tissue is equal to the distance between the light source and reference mirror, the reflected light between the retinal tissue and reference mirror interacts to produce an interference pattern which is detected and then processed into a signal. A two-dimensional image is built as the light source is moved across the retina.

The presently available model is stratus OCT (OCT 3, Version 4, Carl Zeiss Inc., Dublin, California, USA).

***RNFL Image acquisition and analysis protocol:***

The newer stratus OCT can be used in the absence of dilatation and usually requires atleast a 3mm pupil for adequate visualization. An operator determined circular or linear path centered on the optic disc is scanned, to generate a series of 100 axial reflectance profiles. From these, a two dimensional image is constructed.

The first reflection measurement is the vitreous internal limiting membrane interface. The highly reflective interface posterior to this is the retinal pigment epithelium-Photoreceptor interface. The retinal thickness is measure between the two interfaces. Mean RNFL thickness is calculated using inbuilt RNFL thickness average analysis protocol. The boundaries are defined by first determining the thickness of the neuro sensory retina. Average measurements are given for 12, 30

degree sectors. These depth values are independent of the optical dimensions of the eye and no reference plane is required.

***OCT 3 gives a variety of RNFL analysis protocols:***

- RNFL thickness protocol (3.4 mm) - scans an area of radius 1.73 mm, centered on the optic disc
- Fast RNFL thickness protocol (3.4mm) - acquired three fast circular scans.
- Proportional circle: Allows RNFL measurement around the optic disc along a circular scan, the size of which can be varied.
- Concentric 3 rings. RNFL thickness measured along 3 defect circular scans of 0.9 mm, 1.81 mm & 2.71 mm radii.
- RNFL thickness (2.27 x disc): Scan size is 2.27 times the optic disc radius
- RNFL map: Comprises of six circular scans of 1.44mm, 1.69 mm, 1.90mm, 2.25 mm, 2.73 mm and 3.40 mm radii.

***Components of the print out:***

- Patient data
- Red free photograph to denote position of the scan circle
- Individual TSNIT curves for each eye

- Clock hour wise and quadrant wise distribution of RNFL thickness; Various ratios, average thickness, quadrant averages and difference among quadrants between the two eyes can be arrived out.
- The nerve fiber layer thickness is colour coded according to the age related normal of the population. 95% of normal population falls in or below green band, 90% falls within green band, 5% of normal population falls within or below yellow band, 1% falls within red band and is considered outside normal limits.

Schuman et al<sup>34</sup> in 2003 have attempted to measure the average RNFL thickness in normal is diseased condition their results are as follows:

Normal:  $95.9 \pm 11.4$  ; Early glaucoma:  $80.3 \pm 18.4$ ; Advanced glaucoma:  $50.7 \pm 13.6$

***Advantages of OCT:***

- Provides objective, quantitative & reproducible measurements.
- Not affected by axial length reflection
- Automatic definition of ONH margin.
- High axial resolution
- Provides cross-section view of examined tissues.

***Limitations:***

- High cost factor
- Presence of cataract impairs performance
- Limited transverse sampling
- Pupillary dilatation may be required for acceptable peripapillary measurements.

***AIMS AND OBJECTIVES OF THE STUDY:***

- To evaluate the correlation between the Retinal nerve fibre layer parameters(RNFL) analysed by OCT and GDx VCC and the global perimetric indices obtained with octopus perimetry
- To establish whether structural parameters provided by optical coherence tomography (OCT ) and GDx VCC can be used to reflect functional damage in the visual field
- To evaluate the relationship between the RNFL parameters measured using OCT and GDx VCC.

## ***MATERIALS AND METHODS:***

This was a cross sectional study, prospectively planned. 67 eyes of 34 glaucoma patients attending glaucoma clinic were included in this study. The study was carried out in Glaucoma clinic, Regional Institute of Ophthalmology and Government Eye Hospital, Chennai between March 2005 and July 2006.

### **Inclusion criteria:**

- Established primary open angle glaucoma patients on medical treatment and routine follow up were chosen for the study .The patients were diagnosed as glaucomatous by the following criteria: at least three or more occasions of elevated intra ocular pressure  $>21$  mm Hg now on medical control and significant optic nerve head changes with or without visual field defects.
- All patients had open angles  $>2$  by Shaffer's grading on gonioscopy
- Refractive errors : Hyperopia  $\leq +2.50$ D
  - Myopia  $\leq -3.00$  D
  - Astigmatism  $\leq \pm 2.00$  D
- Best corrected visual acuity 6/ 12 or better
- Pupil size 3.0-5.0 mm
- Relative intelligence to understand the test and patients co-operative for visual field analysis.

**Exclusion criteria:**

- Closed angles /narrow angles by gonioscopy
- All patients who had secondary glaucomas, juvenile and congenital glaucomas
- Primary open angle glaucoma patients who undergone surgical or laser therapy for glaucoma
- Patients with media opacities; for example – cataract, vitreous haemorrhage etc.
- Patients who had evidence of other retinal pathology like retinitis pigmentosa, diabetic or hypertensive retinopathy, age related macular degeneration
- Patients who had other ocular diseases like neurological diseases which could present with visual field damage were excluded from this study.

All subjects underwent a complete ophthalmologic examination including refraction , Slit lamp biomicroscopy for anterior segment evaluation and fundus examination with +90 D lens, gonioscopy, Intra ocular pressure measurement using Goldmann applanation tonometry and also direct ophthalmoscopy. Glaucomatous appearance of the Optic disc was defined as an increased C: D ratio, asymmetry of the C:D ratio of  $>0.2$  between the two eyes, Neuro retinal rim thinning , disc haemorrhage , notching and excavation.

**RNFL analysis performed by Optical coherence tomography:**



**Visual field analysis by Octopus perimetry:**



**The GDx VCC Nerve fibre analyzer:**



***Visual field analysis with Octopus perimeter:***

Visual field analysis was performed with Octopus Interzeag1-2-3 perimeter. The tendency oriented perimetry strategy was used. The target size used was Goldmann size III (4.0mm<sup>2</sup>). All the patients were subjected to the test under standardized lighting conditions, and in the same room. The tests were administered between 8.00 am and 9.30 am by the same well trained technician. The refractive error correction was done with Trial lenses of 40mm diameter. No near correction was given. Intra ocular pressure was normalized using medication and pupil size was maintained at 3-5 mm during visual field testing.

All the study patients were briefed about the procedure and the tests were repeated if necessary. All patients showed reliable and reproducible results on the perimetric evaluation.

An abnormal visual field was defined as:

Field plotting with mean deviation > 4, Loss variance > 6 , a local dip in the Bebie's curve outside 2 SD normal limits, Points of depressed sensitivity especially in the arcuate areas, paracentral areas , nasal step region or advanced tubular fields.

All fields were reliable with false positive and false negative catch trials < 15%.

### ***RNFL analysis with Optical coherence tomography:***

Retinal nerve fibre layer measurements were obtained with Stratus OCT (Zeiss) version 4.0.1. To measure the RNFL thickness, OCT measures the difference in temporal delay of backscattered low coherence light (840nm) from the anterior and posterior RNFL. Software is then used to determine RNFL based on reflectance difference between the layers. All scans were performed by well trained technicians who were masked to the patient diagnosis and characteristics. For each patient three 3.4 nm diameter circular scans was obtained, judged to be of acceptable quality and averaged by trained technicians to provide mean measurements of RNFL thickness. Total scan acquisition time was 1 sec. The Pupil size was 3-5 mm and all patients had relatively clear media for adequate image quality. The OCT parameters analyzed in this study were Total average nerve fibre layer thickness (OCT T Avg), superior average (OCT S Avg) and inferior average thickness (OCT I Avg) and superior (OCT S Max) and inferior maximum (OCT I Max) thickness.

### ***RNFL analysis with GDX VCC:***

The GDX VCC (Version 5.2.3) is a scanning laser polarimeter that measures RNFL thickness using polarized light.

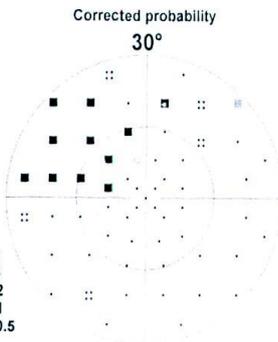
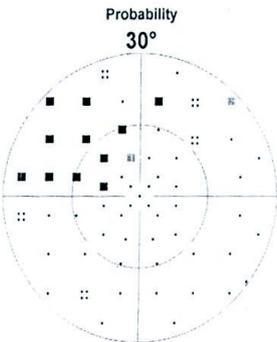
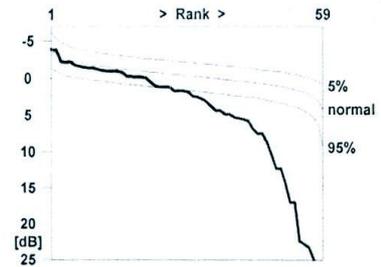
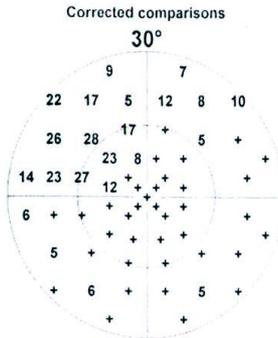
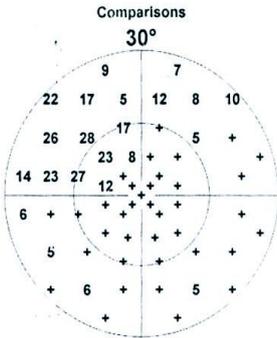
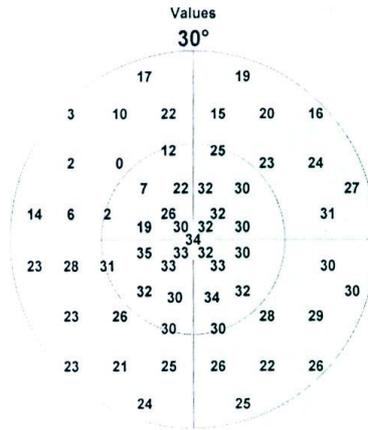
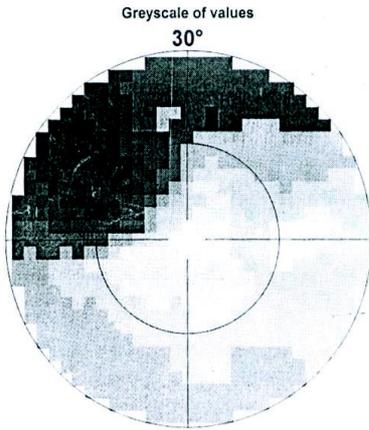
This uses the near infrared laser 780nm polarized light source. A complete scan consists of  $128 \times 256$  pixels. The field of view used by the system was  $40^\circ \times 20^\circ$ . Total scan acquisition time was 0.8 sec. All scans were performed by the same well trained technician. The pupil size was 3-5mm. Three High quality images per eye were taken in one sitting. The quality of the image was assessed by the experienced technician and with the aid of the GDx Software. The best images were used to generate an overall mean image. The mean image was clear and had a clearly definable disc margin. The disc margin on the image was established with

an ellipse whose parameters were adjusted by the experienced technician who was masked to the patient diagnosis and characteristics. A series of RNFL parameters were generated by the software for this study, the parameters TSNIT average thickness, Superior Average thickness, Inferior average thickness and Nerve Fibre Indicator (NFI) were considered.

All these three investigating modalities were carried out within a period of 3 weeks to obtain the best cross sectional comparison and to nullify the effect of any temporal lag.

Statistical analysis was carried out using SPSS™ software. Correlation analysis was done by Pearsons' correlation coefficient and the statistical significance ascertained by two tailed significance test. Students t test was used to derive the significance of the difference between the means .

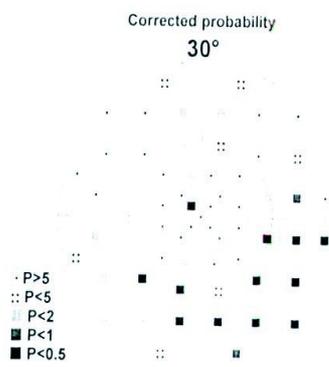
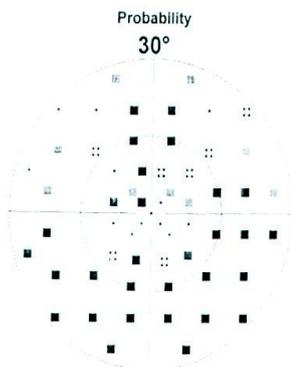
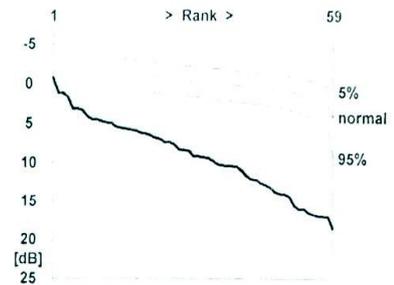
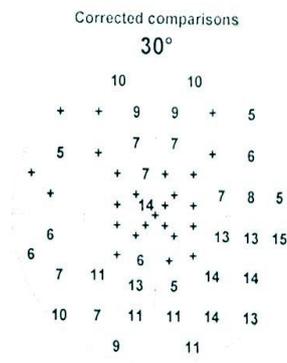
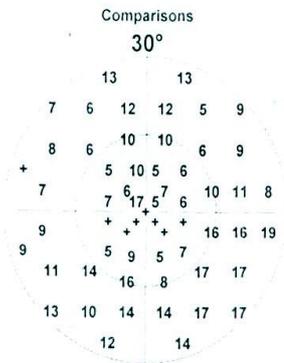
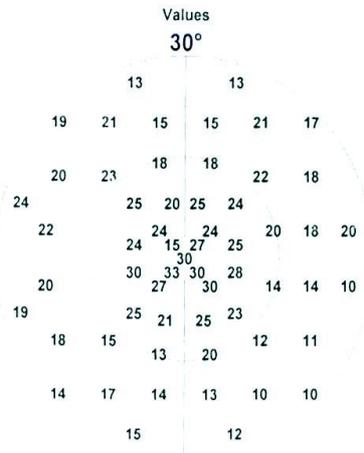
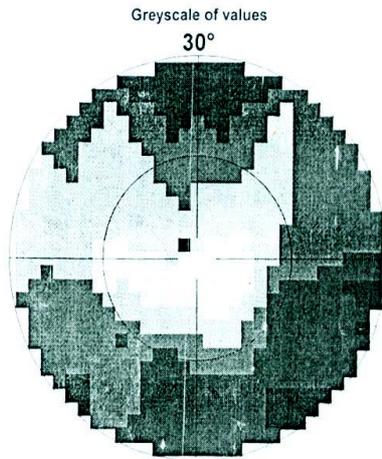
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 First name: **B** Date / Time: **12/26/2005 08:19 AM**  
 ID #: **1128/05** Test duration: **2:22**  
 Birthdate: **11/16/1974** Program / Code: **tG1 / 0**  
 Age: **31** # Stages / Phases: **/ 1**  
 Sex: **male** Strategy / Method: **TOP / Normal**  
 Refr. S / C / A: **/ /** Test target / duration: **III / 100 ms**  
 Acuity: **6/6** Background: **31.4 asb**  
 IOP: **17.3** # Questions / Repetitions: **70 / 0**  
 Diagnostics: **pos 1 / 3, neg 0 / 4**  
 Patient file: **E:\Octopus\ExDat\DEMO.PVD**



Deviation [dB] 0.0

	Phase 1	Phase 2	Mean
#	59	0	0
MS	23.7		
MD	5.1		
LV	68.7		
CLV			
SF			
RF			14.3

Name:	RANJIT KUMAR	Eye / Pupil[mm]:	Left (OS) / 3
First name:	B	Date / Time:	12/26/2005 08:24 AM
ID #:	1128/05	Test duration:	2:38
Birthdate:	11/16/1974	Program / Code:	tG1 / 0
Age:	31	# Stages / Phases:	/ 1
Sex:	male	Strategy / Method:	TOP / Normal
Refr. S / C / A:	/ /	Test target / duration:	III / 100 ms
Acuity:	6/6	Background:	31.4 asb
IOP:	33	# Questions / Repetitions:	74 / 2
Diagnostics:		# Catch trials:	pos 1 / 4, neg 2 / 4
Patient file:		E:\Octopus\ExDat\DEMO.PVD	



Deviation [dB] 3.1

	Phase 1	Phase 2	Mean
#	59	0	0
MS	19.7		
MD	9.2		
LV	22.5		
CLV			
SF			
RF			37.5



# Nerve Fiber Analysis

With Variable Corneal Compensation

Glaucoma Services - Prems' Eye Clinic  
 120 A, Bazaar Road, Saidapet  
 Chennai, Tamil Nadu 600015 India  
 24321517, 18, 24327736

**RANJITH KUMAR B**

DOB: Tuesday, November 12, 1974, Gender: Male, Ancestry: Indian

**ID: 365607**

Print Date: 12/28/05 2:05 PM

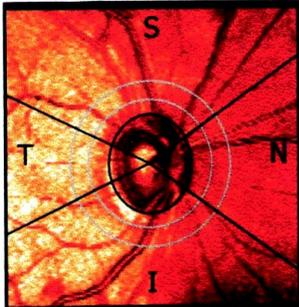
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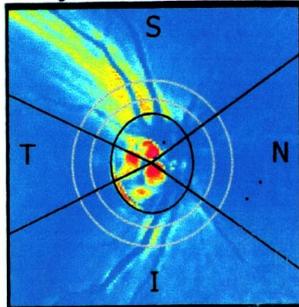
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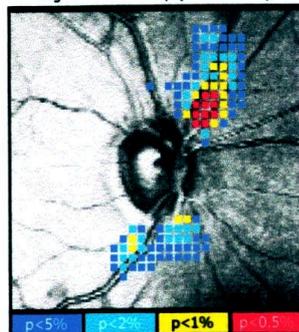
Right Fundus Image



Right Nerve Fiber Thickness Map



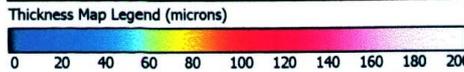
Right Deviation Map (from Normal)



p<5% p<2% p<1% p<0.5%

TSNIT Parameters	OD Actual Val.	OS Actual Val.
TSNIT Average	39.1	31.1
Superior Average	52.4	37.0
Inferior Average	42.6	31.7
TSNIT Std. Dev.	16.1	9.0
Inter-Eye Symmetry	0.81	
NFI	48	77

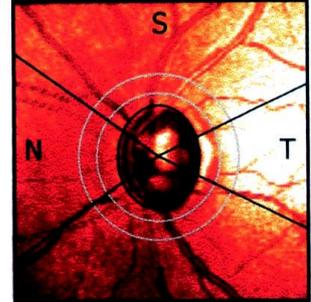
p>=5% p<5% p<2% p<1% p<0.5%



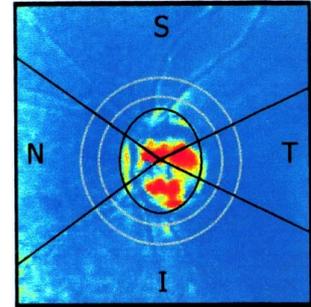
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Signature: \_\_\_\_\_ Date: \_\_\_\_\_

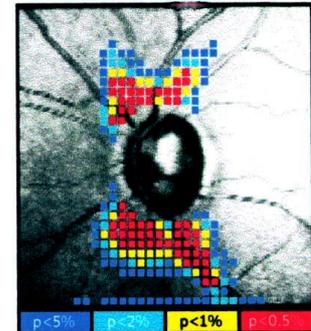
Left Fundus Image



Left Nerve Fiber Thickness Map

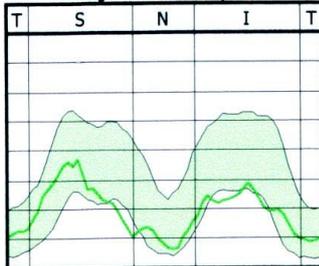


Left Deviation Map (from Normal)

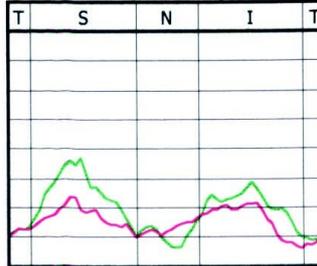


p<5% p<2% p<1% p<0.5%

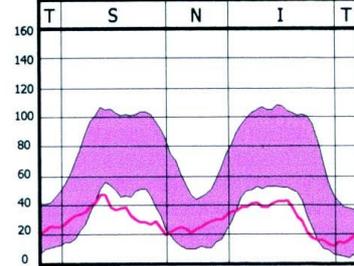
Right Nerve Fiber Layer

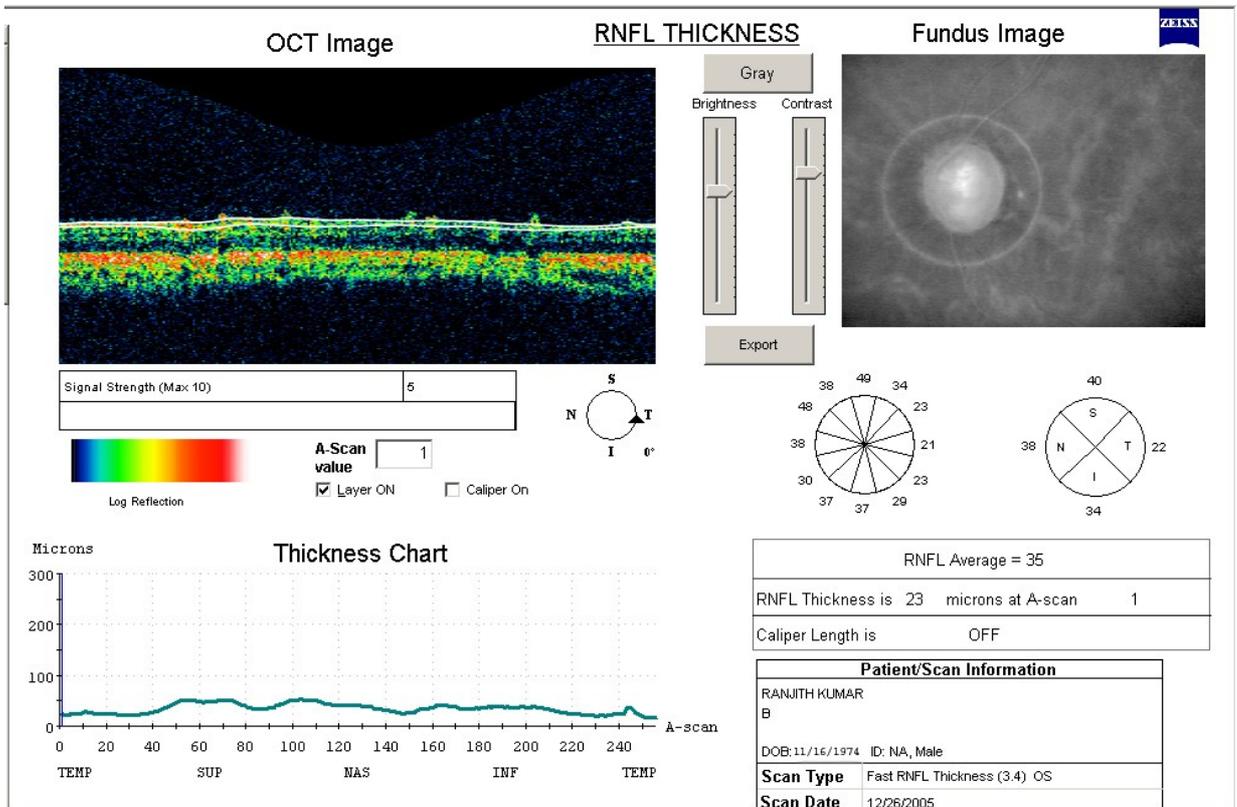
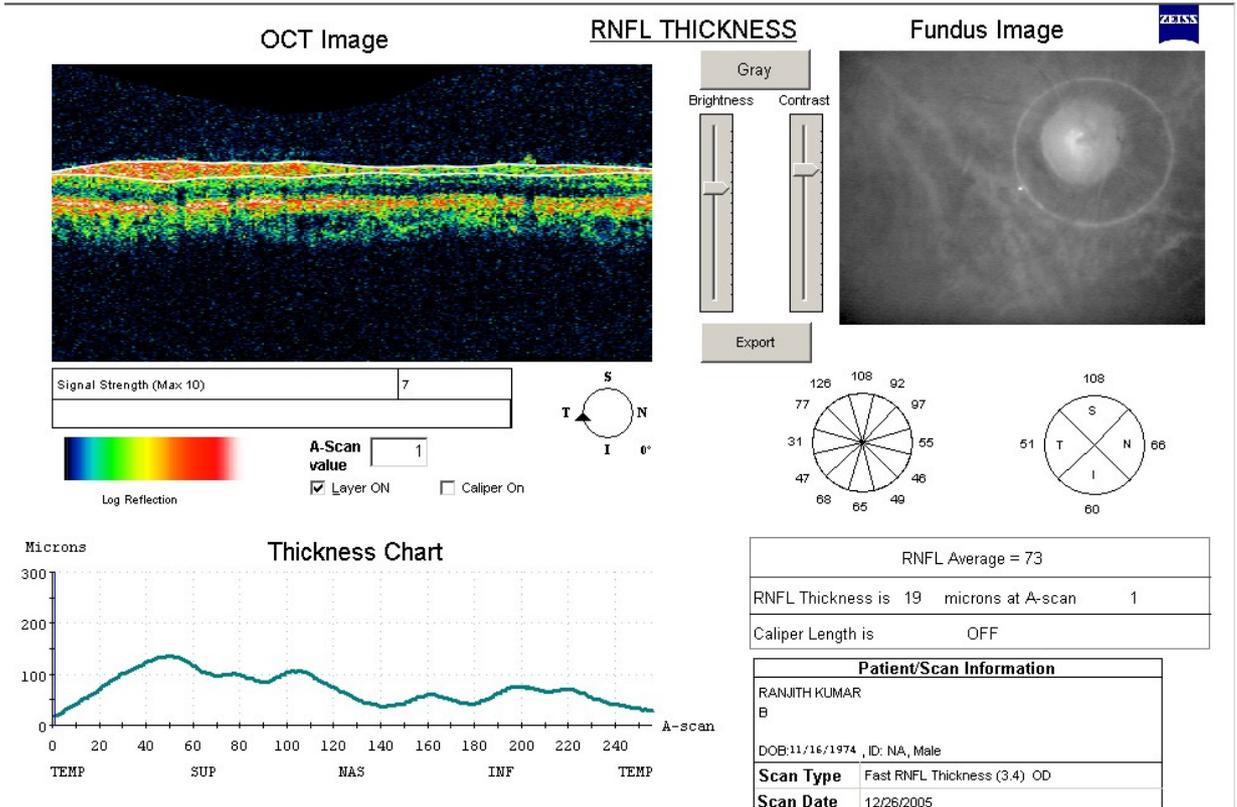


Both Nerve Fiber Layers



Left Nerve Fiber Layer





**Results of the study:**

67 eyes of 34 established Primary open angle glaucoma patients were analysed in this study. The mean age of the patients of this study was 46.911 years (SD±13.531) .The ages of these patients ranged from 26 to 70 years.

**Descriptive analysis of the study population:**

**Age distribution:**

Age(yrs)	n =34			
	Mean	SD	Min	Max
	46.911	13.531	26	70

**Sex distribution:**

Group	Frequency	Percentage
Male	24	70.58%
Female	10	29.41%
Total	34	100%

Out of the 34 patients, 10 patients were females accounting for about 29.41%.

**Octopus Interzeag 1-2-3 perimetry: Global indices:**

The global visual field indices obtained from octopus perimetry were mean defect (MD) and loss variance (LV).

The mean MD for our group of patients was 5.140 (SD + 5.853) and the mean LV was 22.551(SD ± 20.793)

Global indices	Primary open angle glaucoma			
	n = 67			
	Mean	SD	Min	Max
MD	5.140	±5.853	-1.4	24.9
LV	22.551	±20.793	1.8	88.4

**Optical coherence tomography RNFL parameters:**

The Retinal nerve fibre layer thickness was analysed by Optical coherence tomography and the parameters which were obtained were Total average nerve fibre layer thickness (OCT T Avg) , superior average(OCT S Avg) and inferior average thickness (OCT I Avg) and superior (OCT S Max) and inferior maximum(OCT I Max) thickness.

OCT parameters:	Primary open angle glaucoma			
	n = 67			
	Mean	SD	Min	Max
Total average thickness	87.74627	22.218	20	129
Superior average	112.806	32.328	0	164
Inferior average	103.507	32.671	34	159
Superior maximum	143.597	36.860	22	203
Inferior maximum	137.388	36.077	40	208

**GDX RNFL parameters:**

The GDX VCC RNFL analysis parameters studied were the TSNIT average (TSNIT Avg), superior (GDXSAvg) and inferior averages (GDXIAvg) and the nerve fibre indicator (GDX NFI)

GDX parameters:	Primary open angle glaucoma			
	n = 67			
Total average thickness	Mean	SD	Min	Max
	48.216	9.026	24.160	64.710
Superior average	58.425	13.289	23.800	79.201
Inferior average	54.476	11.629	26.860	73.300
Nerve fibre indicator	32.463	25.367	9	98

*Correlational analysis was carried out between the functional global visual field indices obtained with octopus perimetry and the global RNFL parameters as obtained by OCT and GDX.*

**Correlation between MD and LV and OCT Total average nerve fibre layer thickness:**

Global perimetric index		n =67
		OCT RNFL parameter
		OCT T Avg
Mean defect	r	-0.5860
	p	0.000**
Loss Variance	r	-0.2762
	p	0.024*

r = Pearsons correlation coefficient; p =p value

\*  $p \leq 0.05$  (0.01 to 0.05) –significant at 5% level

\*\*  $p \leq 0.01$ - significant at 1% level

\*\*\*  $p > 0.05$  – not significant at 5% level

The above table shows that mean defect obtained from visual field analysis shows strong negative correlation with the OCT total nerve fibre thickness . The correlation was found to have a high statistical significance with a p value of 0.000 (significant at 1% level). When the Loss variance was correlated with the OCT parameter, a negative correlation was obtained as higher the loss

variance, larger the defect/depression in the visual field. This correlation was statistically significant with a  $p$  value  $\leq 0.05$  – significant at 5% level.

The correlations are negative because in the Octopus system a positive number indicates a depression whereas in Humphrey systems, a negative number indicates a depression or a defect.

**Correlation between MD/LV and GDX VCC TSNIT average:**

Global perimetric index		n =67
		GDX TSNIT Avg
Mean defect	r	-0.6288
	p	0.000**
Loss Variance	r	-0.3134
	p	0.01**

r = Pearsons correlation coefficient; p =p value

\*  $p \leq 0.05$  (0.01 to 0.05) –significant at 5% level

\*\*  $p \leq 0.01$ - significant at 1% level

\*\*\*  $p > 0.05$  – not significant at 5% level

According to this table, the GDX nerve fiber thickness correlates negatively with mean defect and loss variance. This correlation had a high statistical significance with a  $p$  value of 0.000 ( $p \leq 0.01$ - significant at 1% level) .

**Correlation between MD/ LV and GDX NFI:**

Global perimetric index		n =67
		NFI
Mean defect	r	0.7218
	p	0.000**
Loss Variance	r	0.4288
	p	0.000**

r = Pearsons correlation coefficient; p =p value

\*  $p \leq 0.05$  (0.01 to 0.05) –significant at 5% level

\*\*  $p \leq 0.01$ - significant at 1% level

\*\*\*  $p > 0.05$  – not significant at 5% level

The Nerve fibre indicator was found to have a higher and a positive correlation with Mean deviation and loss variance with a correlation coefficient of 0.7218 and 0.4288 respectively (p value of 0.000 - significant at 1% level).

***Correlational analysis was carried out between RNFL parameters as obtained by OCT and GDXVCC.***

The OCT parameters correlated were the Total average nerve fibre layer thickness (OCT T Avg) , superior average(OCT S Avg) and inferior average thickness (OCT I Avg) with the GDX VCC parameters TSNIT average (TSNIT Avg), superior (GDXSAvg) and inferior averages (GDXIAvg) respectively. A high positive correlation was obtained with a p value  $\leq 0.01$ - significant at 1% level.

Correlation between	n = 67	
OCT T Avg & GDX TSNIT Avg	r	0.7925
	p	0.000**
OCT S Avg & GDXSAvg	r	0.8123
	p	0.000**
OCT I Avg & GDXIAvg	r	0.7341
	p	0.000**

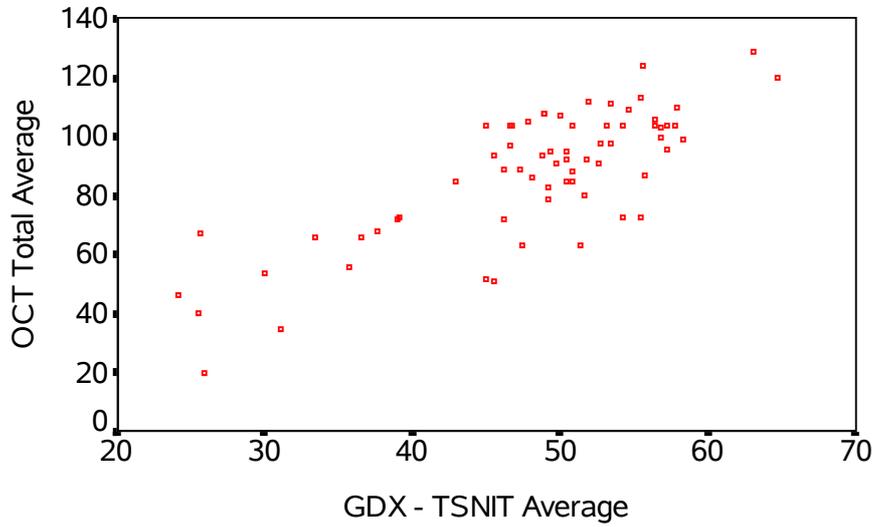
r = Pearsons correlation coefficient; p =p value

\*  $p \leq 0.05$  (0.01 to 0.05) –significant at 5% level

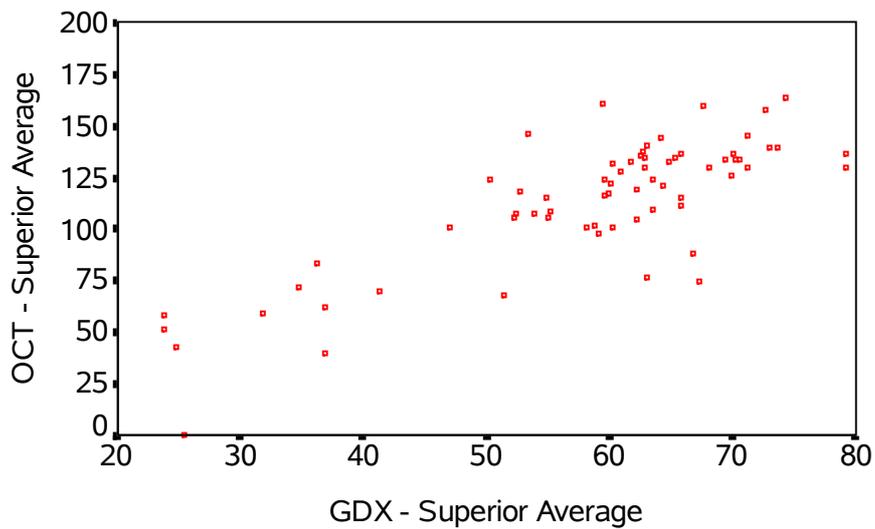
\*\*  $p \leq 0.01$ - significant at 1% level

\*\*\*  $p > 0.05$  – not significant at 5% level

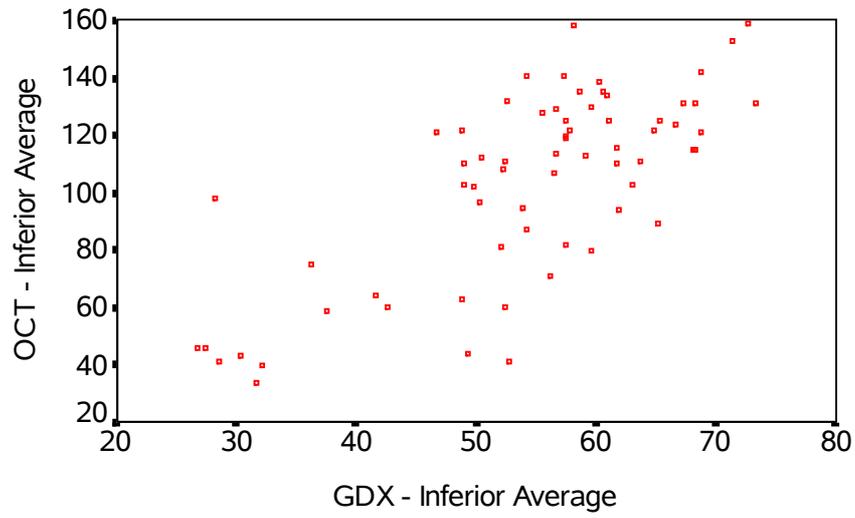
**Scatter plot showing the positive correlation between the total average nerve fibre layer thicknesses obtained with GDx and OCT.**



**Scatter plot showing the positive correlation between the superior average nerve fibre layer thicknesses obtained with GDx and OCT.**



**Scatter plot showing the positive correlation between the inferior average nerve fibre layer thicknesses obtained with GDx and OCT.**

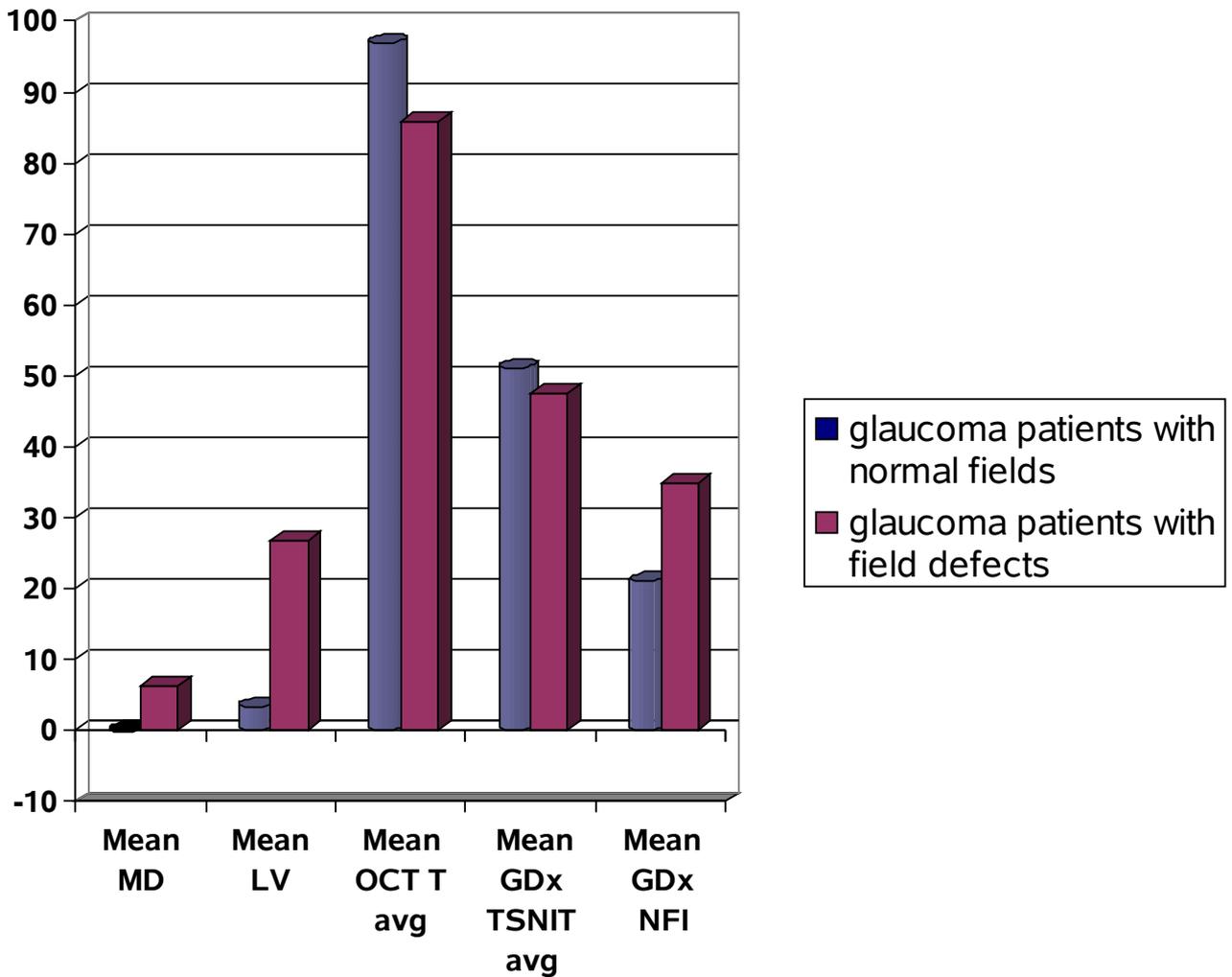


The data was split on the basis of presence or absence of visual field loss and analysed . Out of the 67 eyes ,12 eyes did not show any field defect whereas the rest had significant visual field loss .

Parameter	Group				Significance of difference between the means ( <i>Students t Test</i> ) P value
	Normal fields n=12		Abnormal fields n=55		
	Mean	SD	Mean	SD	
MD	-0.10	0.90	6.28	5.85	0.000**
LV	3.48	1.32	26.71	20.73	0.000**
OCTT Avg	96.92	11.95	85.75	23.48	0.023*
GDX	51.18	5.10	47.57	9.59	0.075***
TSNIT					
NFI	21.08	8.63	34.95	27.13	0.003**

r = Pearsons correlation coefficient; p =p value  
 \*  $p \leq 0.05$  (0.01 to 0.05) –significant at 5% level  
 \*\*  $p \leq 0.01$ - significant at 1% level  
 \*\*\*  $p > 0.05$  – not significant at 5% level

**Bar chart showing the difference between the mean values among the two subgroups – glaucoma patients with normal fields and glaucoma patients with field defects:**



The mean MD, LV, OCT total average thickness, GDx TSNIT average and NFI were calculated and were found to be different among the groups. Student's t test was used to determine the significance of difference between the means.

According to the above table, significant ( $p \leq 0.01$ ) differences between the means were found among the two subgroups for MD( $-0.10 \pm 0.90$  dB for the POAG subgroup without visual field damage and  $6.28 \pm 5.85$  dB for the POAG subgroup with visual field damage) and LV( $3.48 \pm 1.32$  and  $26.71 \pm 20.73$  in both the groups respectively).

Lesser significant difference ( $p \leq 0.05$  (0.01 to 0.05) – significant at 5% level) was obtained for the OCT Total average thickness ( $96.92 \mu\text{m} \pm 11.95$  in the normal field group and  $85.75 \mu\text{m} \pm 23.48$  in the group with abnormal field)

When the GDx parameter, TSNIT average was analysed, no significant difference was appreciated between the two subgroups ( $51.18 \pm 5.10$  in the normal field subgroup and  $47.57 \pm 9.59$  in the other subgroup;  $p$  value = 0.075 ( $p > 0.05$  – not significant at 5% level)).

Significant difference was obtained ( $p \leq 0.01$ ) between the two subgroups for the GDx parameter, NFI ( $21.08 \pm 8.63$  in the normal field subgroup and  $34.95 \pm 27.13$  in the subgroup with field changes; The  $p$  value obtained was 0.003).

## ***DISCUSSION:***

This study was designed with the major objective to evaluate the relationship between perimetric indices and structural changes brought out by optical coherence tomography and GDX VCC RNFL parameters and to compare the results obtained by these two methods for quantitatively assessing the RNFL(OCT and GDX VCC).

Although, stereophotography and standard visual field testing are the current standards used for glaucoma diagnosis in research, it is possible that newly developed instruments are better at detecting glaucoma<sup>35-42</sup>.

The primary strength of this study is that the instruments were compared in a single population. The advantage of examining the performance of these instruments in a single population is that population characteristic based variables are eliminated, thus allowing direct comparison of the results obtained with the different instruments.

This study attempts to correlate the visual field indices obtained with Octopus perimeter with the RNFL analysis, while most of the recent studies analyzed the indices obtained with Humphrey perimeter. Also, all tests were completed within a period of three weeks. This is to obtain the best cross sectional comparison of different diagnostic techniques. However, longitudinal studies offer the only way to truly determine the sensitivity and specificity of these tests.

Limitations of this study include small number of subjects. Another limitation, inherent in any comparable study is that different diagnostic techniques evaluated in this study are currently at different stages of development. More established techniques (SAP and SLP) were compared with newer technologies (OCT). In general, established technologies benefit from robust normative

databases and more sophisticated analysis strategies. Also, different techniques may identify different characteristics of glaucomatous damage.

In this study, the mean defect obtained from visual field analysis showed strong negative correlation with the OCT and GDx RNFL parameter- total average thickness and TSNIT average. The correlation was found to have a high statistical significance with a p value of 0.000 (significant at 1% level).

When the Loss variance was correlated with the OCT total average thickness, a negative correlation was obtained which was statistically significant with a p value  $\leq 0.05$ —significant at 5% level. When the Loss variance was correlated with the GDx RNFL parameter TSNIT average, a negative correlation was obtained. This correlation was statistically significant with a p value  $\leq 0.01$ —significant at 1% level. Here, the correlations are negative because in the Octopus system a positive number indicates a depression whereas in Humphrey systems, a negative number indicates a depression or a defect. Similar results were shown by Sanchez-Galeana et al<sup>44</sup> and Hoh et al<sup>45</sup> who showed significant correlations between OCT total thickness and SWAP MD and PSD and SAP MD and PSD respectively. Zangwill et al<sup>46</sup> reported association between mean OCT measured RNFL thickness and Superior and Inferior thicknesses and mean SAP MD and inferior and superior SAP MD with an r value of 0.35, 0.35, 0.43 respectively.

The GDx Nerve fibre indicator was found to have a high positive correlation with mean defect with a correlation coefficient of  $r = 0.7218$  (p value of  $\leq 0.01$ - significant at 1% level). The Nerve fibre indicator was found to have a positive correlation with loss variance with a correlation coefficient of 0.4288 (p value of  $\leq 0.01$ - significant at 1% level). Studies by Lester<sup>43</sup> et al also showed that though all GDx parameters correlated with perimetric indices, the strongest correlation was with NFI.

When the OCT parameters, the Total average nerve fibre layer thickness (OCT T Avg), superior average (OCT S Avg) and inferior average thickness (OCT I Avg) were correlated with the GDx VCC parameters TSNIT average (TSNIT Avg), superior (GDXS Avg) and inferior averages (GDIX Avg) respectively, a high positive correlation was obtained with a p value  $\leq 0.01$ - significant at 1% level. The data were split into two subgroups on the basis of presence or absence of visual field defect and analysed. A gross difference was observed between the mean values of MD, LV, OCT T Avg, TSNIT Avg, and NFI in the two subgroups. Students t test was used to analyse whether this difference between the groups was significant. The difference between the mean values of MD and LV and NFI were highly significant with a p value  $\leq 0.01$ - significant at 1% level. Also, the OCT parameter, Total average nerve fiber layer thickness differed significantly between the two subgroups (p value  $\leq 0.05$ —significant at 5% level). The mean GDx TSNIT average did not differ significantly between the two subgroups. These data could suggest that while using the GDx the NFI is a higher predictor of visual field damage, than the GDx TSNIT average thickness. Also, among the Total average nerve fibre layer thickness measured by OCT and GDx (TSNIT average), the OCT parameter seems to correlate better with visual field damage than the GDx parameter.

In this study though all correlations were found to be statistically significant, a higher correlation was obtained with mean defect and a slightly lesser degree of correlation of all parameters with loss variance. The following reasons could be attributed for this:

Firstly, the sample size may not have been large enough in this study. Tole et al<sup>47</sup> found all the significant correlations disappeared when the analysis was confined to the glaucoma patients with MD of  $<10$  dB. They supposed it reflected

the statistical effect of reducing the numbers from 106 eyes to 67 eyes. In addition, correlations were better for MD than for CPSD.

Secondly, this study included only glaucoma patients. According to various studies, correlations were found to be better for combined healthy and glaucoma subjects than in glaucoma subjects alone. This may be due to the larger range of values in combined groups.

Thirdly, our data demonstrated that advanced cases have a greater influence on the relation between RNFL parameters and visual field indices. Moreover for a specific value of visual field index there was a larger degree of variability in the RNFL parameters. Two explanations can be reasoned out for this: one is the large variation of these parameters within the normal population and the other reason is individual differences in the amount of RNFL damage necessary for the visual field loss to occur. The study of Kwon et al<sup>48</sup> also mentioned this problem. A normal visual field can be associated with a wide range of RNFL thicknesses. When the RNFL thickness was greater than 70  $\mu\text{m}$ , the visual field mean sensitivity was nearly normal or changed little. When the RNFL thickness was below this level, it was associated with a rapid decrease in the visual field sensitivity. Longitudinal analysis is a good method of removing the influence of individual variations.

Fourthly, in this study, only the global parameters were correlated. For all RNFL parameters measured by the various instruments, the relations were better and more parameters were found to have correlation with visual field indices for sectors than for the whole area. A certain amount of ONH damage or RNFL damage must occur before the global parameters showed significant changes. Thus, interpretation of global parameters may overlook focal damage of ONH and RNFL. This may be the reason why sectoral parameters and sectoral visual field indices

had a better association than the global parameters and global visual field indices. Schuman et al<sup>49</sup> and Pieroth et al<sup>50</sup> illustrated case studies in which OCT measured focal RNFL defects corresponded to quadrant specific SAP defects.

Finally, large amount of normative database for the various investigatory modalities are currently not available for the Indian population.

This is a Pilot study carried out in an attempt to establish the relationship between the Visual field indices and RNFL parameters in glaucoma patients in our south Indian population. This study brings out statistically significant correlations in spite of the above limitations. This finding validates both techniques as indicators of glaucomatous damage. A similar study, if undertaken, with a larger sample with inclusion of normal population as age matched controls and carried out longitudinally would possibly make the results much more specific. Also, inclusion of glaucoma suspects, ocular hypertensives and early glaucoma patients in subsequent trials would serve to establish the utility of these newer diagnostic technologies in glaucoma management and research.

## ***CONCLUSION:***

Outcomes of the study:

- In established glaucoma patients a significant correlation exists between the global perimetric indices and the RNFL thickness .
- The RNFL thicknesses measured by two different investigatory modalities OCT and GDx are well correlated.
- Among the GDx parameters, the NFI was found to be a better indicator of visual field damage than the average thickness.

In conclusion, though visual field testing is subjective, at present it cannot be replaced by imaging modalities. The newer instruments are valuable tools that have become available to provide quantitative reproducible and objective measurements of RNFL thickness.

Thus, structural information provided by the OCT and GDx and functional information provided by the field analysis are both important and complementary to each other.

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## PROFORMA

### CORRELATION BETWEEN PERIMETRIC INDICES AND RETINAL NERVE FIBRE THICKNESS BY OCT AND GDx VCC IN PRIMARY OPEN ANGLE GLAUCOMA

Name: Age: Sex:

Address: Occupation:

OP/IP.No Glaucoma.no:

Diagnosis:

#### HISTORY:

History of systemic illness: DM /HT /asthmatic / cardiovascular / cerebrovascular  
disease / others/H/o prior non ocular surgeries

Current systemic medical therapy:

Ocular history:

H/O presenting illness: Defective vision/ headache/ routine screening

Age of onset of complaints:

Duration:

Right eye

Left eye

Defective vision

Pain

Redness

Field loss

Coloured haloes

Frequent change of glasses

H/o previous eye disease/trauma

H/O ocular surgeries/ medications:

Family H/O glaucoma:

**Systemic examination:** general condition:

Pulse:

B.P:

## OCULAR EXAMINATION

Right eye

Left eye

### VISUAL ACUITY

Without correction

With correction

### CONJUNCTIVA

### CORNEA

### ANTERIOR CHAMBER

### IRIS

### PUPIL

Size

Shape:

1. Normal, regular
2. Altered
3. others ,Pseudoexfoliation etc

Reaction to light

1. Reacting briskly
2. RAPD
3. Sluggish

### LENS

1. Clear
2. Cataract
3. Pseudoexfoliation
4. Subluxation/ Dislocation
5. Pseudophakic

GONIOSCOPY: Shaffer's grading

INTRA OCULAR PRESSURE

(By Goldmann Applanation tonometry)

Time \_\_\_\_\_

FUNDUS (90 D EXAMINATION)

Vertical cup/ disc ratio

Bayonetting/Nasalisation

Laminar dot sign

Notching/ Thinning of Neuroretinal rim

1. Absent
2. Superior Pole
3. Inferior Pole

Disc Haemorrhages

1. Absent
2. Present

Nerve Fibre Layer Defects

1. Absent
2. Wedge
3. Diffuse atrophy

VISUAL FIELD DEFECTS (By Octopus perimetry)

Visual field group: 1-normal fields

2-abnormal fields

Field defects

1. Absent
2. Superior Arcuate Scotoma
3. Inferior Arcuate Scotoma
4. Nasal Step
5. Double Arcuate Scotoma
6. Paracentral Scotoma
7. Generalized Reduction of Sensitivity

Mean defect

Loss variance

## OPTICAL COHERENCE TOMOGRAPHY

Parameter	RE	LE
Total average thickness		
Superior average		
Inferior average		
Superior maximum		
Inferior maximum		

GDx VCC parameters:

Parameters:	RE	LE
TSNIT average thickness		
Superior average		
Inferior average		
Nerve fibre indicator		

### **Key to master chart:**

UCVA: Un corrected visual acuity

BCVA: Best corrected visual acuity

IOP: Intra ocular pressure

C:D ratio: Cup:Disc ratio

MD: Mean Defect

LV: Loss Variance

OCT Tavg: OCT Total Average Thickness

OCT Savg: OCT Superior Average Thickness

OCT Iavg: OCT Inferior Average Thickness

OCT Smax: OCT Superior maximum Thickness

OCT Imax: OCT Inferior maximum Thickness

GDx TSNIT AVG: GDx TSNIT Average Thickness

GDx S avg: GDx Superior Average Thickness

GDx I avg: GDx Inferior Average Thickness

GDx NFI: GDx Nerve Fibre Indicator

**LIST OF SURGERIES PERFORMED:**

S.no	Name	age/sex	OP/IP no	date of surgery	diagnosis	surgery performed
1	Mr.Janakiraman	63/m	381737	15-06-2004	RE-IMC	LE- ECCE with PCIOL
2	Ms.Tamilarasi	28/f	72845	17-06-2004	RE-chalazion	Incision & curettage
3	Ms.Jagadha	68/f	382247	26-06-2004	LE-IMC	LE- ECCE with PCIOL
4	Mr.Laxminarayanan	29/m	86745	15-07-2004	RE-ptyerygium	Excision-Bare sclera
5	Mrs.Chinnamma	70/f	81979	23-09-2004	RE_dacryocystitis	Dacryocystectomy-RE
6	Mrs. Kuppammal	45/f	386101	28-10-2004	LE-MC	LE- ECCE with PCIOL
7	Mrs.Jayamary	48/f	390542	21-03-2005	LE-Nuclear cataract	LE- ECCE with PCIOL
8	Mrs.Devaki	28/f	32670	20-05-2005	RE-Dermolipoma	Excision
9	Mr.Parthasarathy	54/m	393166	22-06-2005	RE-MC	RE-ECCE with PCIOL
10	Mr.Venkatasubbiah	72/m	56407	08-08-2005	RE-Corneal Ulcer	Paracentesis with AC Amphotericin Wash
11	Mrs.Muniammal	67/f	393872	27-08-2005	RE-PCC	RE-ECCE with PCIOL
12	Mr.Kannan	35/m	60184/9914	22-08-2005	LE-mixed ulcer	LE-TKP
13	Mrs.Raniammal	40/f	331456	25-08-2005	RE-endophthalmitis	RE-Vit Tap/ Intravit Antibiotics
14	Mr.Venugopal	40/m	66211/10018	25-08-2005	LE-mixed ulcer	LE-TKP
15	Mrs.Thulasi	60/f	395669	17-09-2005	LE-MC	LE- ECCE with PCIOL
16	Mrs.Krishnammal	55/f	395991	26-09-2005	RE-IMC	RE-SICS with PCIOL
17	Mr.Muthiah	70/m	395729	21-09-2005	RE-IMC	RE-SICS with PCIOL
18	Mrs.Umayal	60/f	43144/9595	26-08-2005	RE-Panophthalmitis	RE-Evisceration
19	Mrs.Muniammal	60/f	55348	01-09-2005	RE_dacryocystitis	Dacryocystectomy-RE
20	Mr.Gopal	72/m	396124	03-10-2005	RE-Chr ACG	RE-ECCE with Trab
21	Mrs Parvathy	45/f	398891	14-02-2006	RE-Corneal Tear With iris prolapse	Corneal Tear Suturing with Prolapse Repair

