# Diagnostic Methods for Optic Nerve Head and Retinal Nerve Fiber Evaluation in Glaucoma

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## ABSTRACT
Glaucoma which is a leading cause of blindness in the world is not a single disease but a group of disorders with diverse clinical manifestations. If not controlled at an early stage, it causes irreversible damage to vision. Proper medication slows down or even halts its growth. Identifying glaucoma at a very early stage is vital and at the same time difficult. Careful evaluation of Optic nerve head structure and its documentation is extremely important for diagnosis of the disease and to monitor its progression. This paper presents a review of diagnostic techniques available for evaluation of optic nerve head.

## General Terms
Engineering in medicine, Bio informatics

## Keywords
Glaucoma, Optic nerve head, Retinal nerve fiber layer, Optical Coherence tomography, Scanning Laser Polarimetry, Confocal Scanning Laser Ophthalmoscopy

## 1. INTRODUCTION
Glaucoma is a disease caused by increased intraocular pressure (IOP). Left untreated, an elevated IOP causes irreversible damage to the optic nerve and retinal fibers resulting in a progressive, permanent loss of vision. Glaucoma is called as silent thief of sight since it causes gradual lack of vision and symptoms are seen only at an advanced stage. According to World Health organization, Glaucoma is the second leading cause of blindness in the world [1, 3]. 66.8 million people in the world are affected with Glaucoma; 6.7 million out of them have blindness [2, 4]. According to a study in southern India, prevalence of glaucoma was found to be 2.6% and 90% of the affected people were never diagnosed before [3]. Glaucoma is a result of an imbalance between aqueous humor secretion and drainage processes within the ocular chambers [5]. Any impairment in the drainage structure causes the IOP to rise. Elevation of IOP beyond the normal limit is a major risk factor for glaucoma. Fibers of the optic nerve are affected, vision deteriorates, and blindness may result. Patients with an increased IOP may not always demonstrate optic nerve damage whereas in some cases patients with normal IOP may have optic nerve damage and visual field loss. However increased IOP is one of the major factors in causing optic nerve damage and visual field loss. Risk factors for glaucoma progression are Increased IOP, age (> 60), family history and race.

## 2. TYPES OF GLAUCOMA
Glaucoma can be divided into two categories, open angle and closed angle glaucoma [6]. The angle refers to the area between the iris and cornea, through which fluid must flow. Open-angle glaucoma arises when the eye's drainage canals become clogged over time. The IOP rises because some amount of fluid cannot drain out of the eye. If not treated early, it causes loss of vision. It develops slowly. If detected at an early stage it can be treated to prevent loss of vision. Angle-closure glaucoma arises when the angle between the iris and cornea reduces. The outer edge of the iris bunches up over the drainage canals, when the pupil enlarges too much or too quickly. This structural problem obstructs circulation of fluid causing rise in IOP.

## 3. GLAUCOMA DIAGNOSIS
Glaucoma diagnosis primarily relies on Tonometry, Perimetry and Optic nerve head (ONH) evaluation. Tonometry involves measurement of IOP. IOP is one of the factors required for primary investigation. Perimetry relies on detection of the functional change that is loss of vision. This test measures side (peripheral) vision. Peripheral vision loss is the result of Glaucoma. ONH evaluation is used for detection of structural changes in ONH. IOP alone is not indicative of Glaucoma unless it is grossly abnormal. Visual Field loss is the late manifestation of the disease. In Glaucoma, structural changes in the ONH precede functional changes in the visual field. Comprehensive examination of the patient's ONH helps in early Glaucoma diagnosis [4, 7]. Optic disc and Retinal nerve fiber layer (RNFL) assessment can be performed according to five rules that include the evaluation of optic disc size, rim shape and area, presence of RNFL loss, presence of parapapillary atrophy and presence of retinal or optic disc haemorrhages. By following these five rules, a thorough and systematic review of the optic disc and RNFL occurs. This improves the ability to diagnose and manage glaucoma [7]. Early treatment reduces rate of progression of the disease thus preventing visual field loss and blindness. Normal eyes show a characteristic configuration of rim thickness. This is called as ISNT rule. The neuroretinal rim is broadest in the inferior rim, followed by superior and nasal rims and is thinnest in the temporal region. The ISNT rule is useful in differentiating normal and glaucomatous optic nerves [8].

## 4. ONH ASSESSMENT METHODS
Clinical examination of ONH includes

### 4.1. Direct Ophthalmoscopy
Direct ophthalmoscope is handheld equipment used for fundus examination. It provides an upright, magnified view of the optic nerve. Its adjustable features help in changing the illumination required for proper examination. Use of the red-free light helps in identifying ONH irregularities.

### 4.2. Slit-lamp Examination
Examination of the optic nerve using slit lamp is ideal and uses hand-held lenses to magnify and control the view of the examination. This method provides a stereoscopic, inverted view of the optic nerve.

Assessment of ONH and RNFL topographies based on clinical evaluation is subject to inter and intra observer variability to some extent [10]. This is because of subjectivity in quantifying ONH parameters. The method may not be sufficiently sensitive to classify normal and glaucomatous optic nerves at an early stage or may not be able to detect subtle changes over a period of time [11]. Thus quantification of RNFL parameters is necessary for improved detection and monitoring of the disease. ONH Analyzers capable of objective documentation and quantification of ONH parameters use methods [9, 11] called as Optical Coherence Tomography (OCT), Confocal Scanning Laser Ophthalmoscopy (CSLO), and Scanning Laser Polarimetry (SLP).

## 4.3. Confocal Scanning Laser Ophthalmoscopy [12]:

A three-dimensional topographic analysis of the retinal structures can be done using CSLO. The system allows the acquisition of two and three-dimensional images. A confocal scanning system has a small diaphragm, which is placed in front of the detector. It is optically conjugated to the focal plane of the optical source. The system consists of a pinhole to which light reflected from the object at the focal plane is focused. The light passing through the pin hole and is detected. Light reflected from layers of the three-dimensional object which is placed above or below the focal plane is not focused to the pinhole. Only a small fraction of it can pass the pinhole which is then detected. This ensures high suppression of the out-of-focus light. Larger is the distance from the focal plane, larger is the suppression. It increases rapidly with the distance. A CSLO system has a high optical resolution along axes perpendicular and parallel to the optical axis. It ensures high resolution along the depth. A two-dimensional image acquired at the focal plane therefore carries only information of the object layer located at or near the focal plane. It can be considered as an optical section of the three-dimensional object at the focal plane. A two-dimensional image is an optical section at the focal plane. When the focal plane is moved and images are acquired at different depth locations, a series of optical section images are obtained. Thus a layer-by-layer three-dimensional image of the three-dimensional object is formed (Figure 4.3.2). This technique is called as scanning laser tomography. The Heidelberg Retinal Tomograph (HRT), which is commercial version of CSLO, is used for quantitative imaging of the posterior segment. It produces a topographical analysis of ONH. Quantification of ONH parameters to find the glaucomatous damage is possible. Also the disease progression can be monitored.

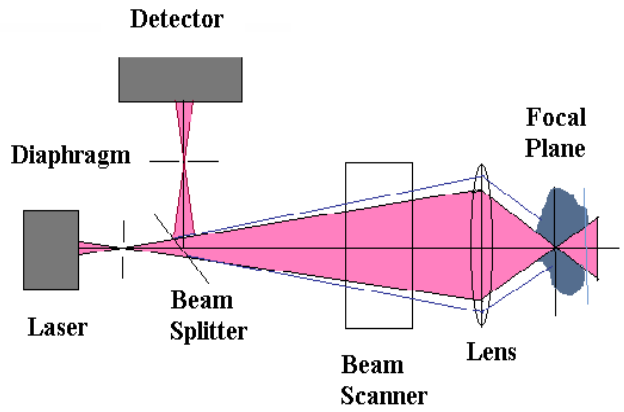



**Figure 4.3.1: A CSLO System [12]**

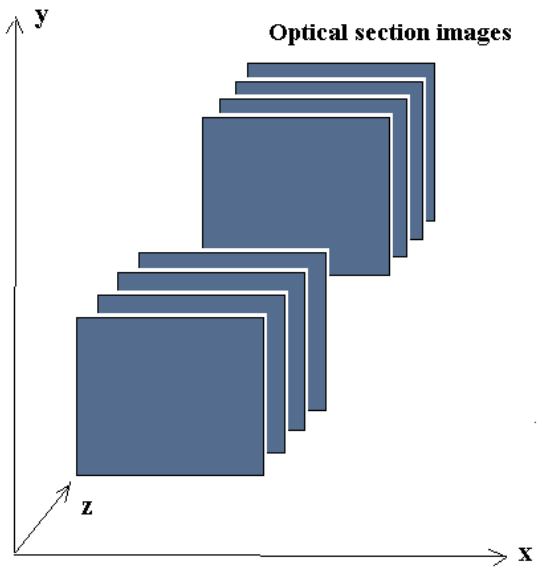



**Figure 4.3.2: Optical section images in CSLO [12]**

The following example demonstrates the interactive measurement using CSLO.

Figure 4.3.3 and 4.3.4 show the topography images and the reflectance images of a normal ONH and that of a glaucomatous ONH. In the topography images, bright colors show depressed structures while dark colors show elevated structures. The cup appears much bigger and deeper in the glaucomatous eye [12].

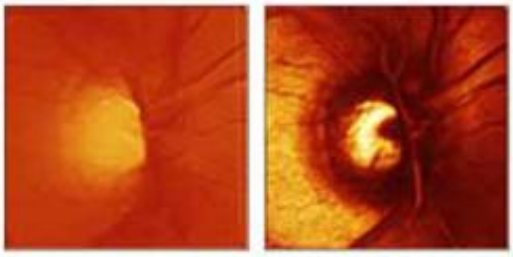


**Figure 4.3.3: The topography and reflectance image of a normal optic disc [12]**

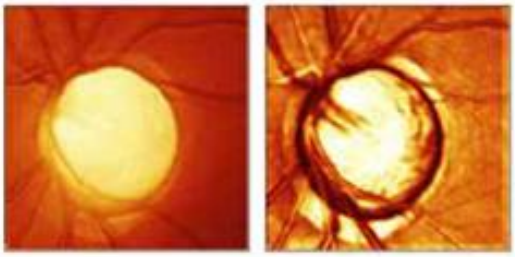


**Figure 4.3.4: The topography and reflectance image of a glaucomatous optic disc [12]**

**Figure 4.3.5: The pseudo 3D topography image of a normal optic disc [12]**

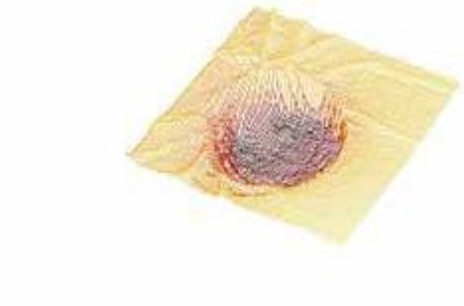
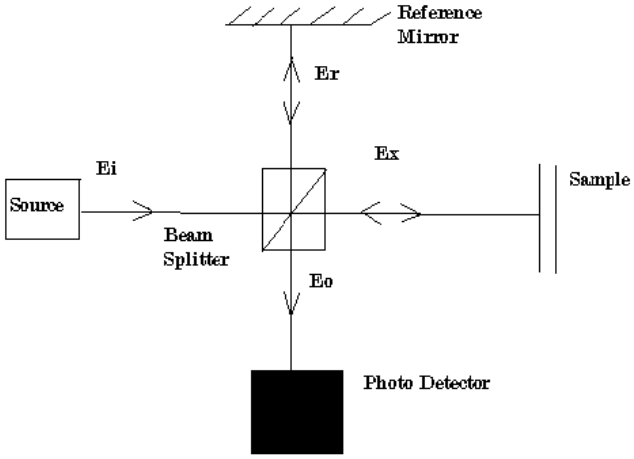


**Figure 4.3.6: The pseudo 3D topography image of a glaucomatous optic disc [12]**

## 4.4. Optical Coherence tomography [13]:

Interference between a split and later recombined broadband optical field is the principle on which OCT works. It is called as interferometric technique. Cross-sectional images of both the RNFL and optic disk can be obtained. A typical OCT schematic is as shown in Figure 4.4.1.




A beam splitter splits the source field, which then travels in two different paths. One path is the reference path, reflecting from a reference mirror, and the other is the sample path where it is reflected from multiple layers within a sample. If the reference and sample arm optical path lengths are matched to the coherence length of the light, interference between the optical fields is observed. The reference mirror is translated to change the reference path length. This is done in order to match multiple optical paths due to layer reflections within the sample. In this way an interference pattern (time domain) is obtained. The intensity peaks in the interference pattern correspond to sharp variations in refractive index which occur in layers of the sample. The temporal coherence of the light source determines the depth resolution of an OCT system. Fourier transform of the output spectrum converts the tome domain information into frequency domain. Frequency domain information is useful in perception of depth. Reference optical path length is kept constant. Frequency components are detected using a spectrometer. The beam scans the object in one or two orthogonal directions and two or three dimensional image is obtained by multiple depth scans. Around 500 depth scans cover a width of 5 mm to obtain a two dimensional cross sectional image. In tissue scans, the depth scan is limited and maximum imaging depths are between 1mm and 3mm for a variety of tissues at wavelengths between 800 and 1300 nm.

Figure 4.4.2 shows OCT images of RNFL segmentation and measurement by the Stratus OCT. Signal strength varies from 5 to 10. If the signal strength increases the average RNFL thickness increases [14]. Figure 4.4.3 shows the RNFL profiles (centered and displaced scans) obtained by displacing the scan circle at an arbitrary distance. The RNFL profile centered at the disk is shown in blue. RNFL profiles with scan circles displaced superiorly (A) and inferiorly (B) are shown in red [14].

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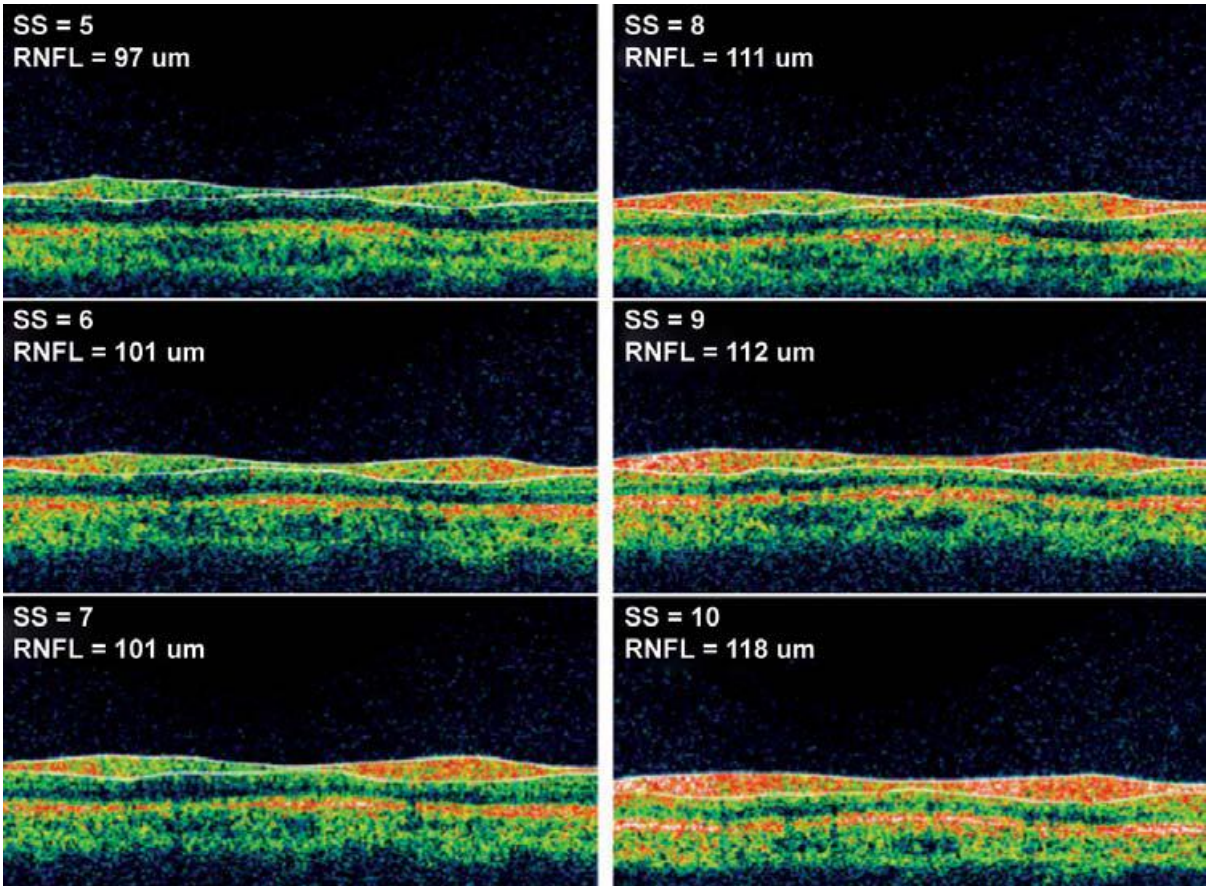


**Figure 4.4.2: OCT images of RNFL segmentation [14]**

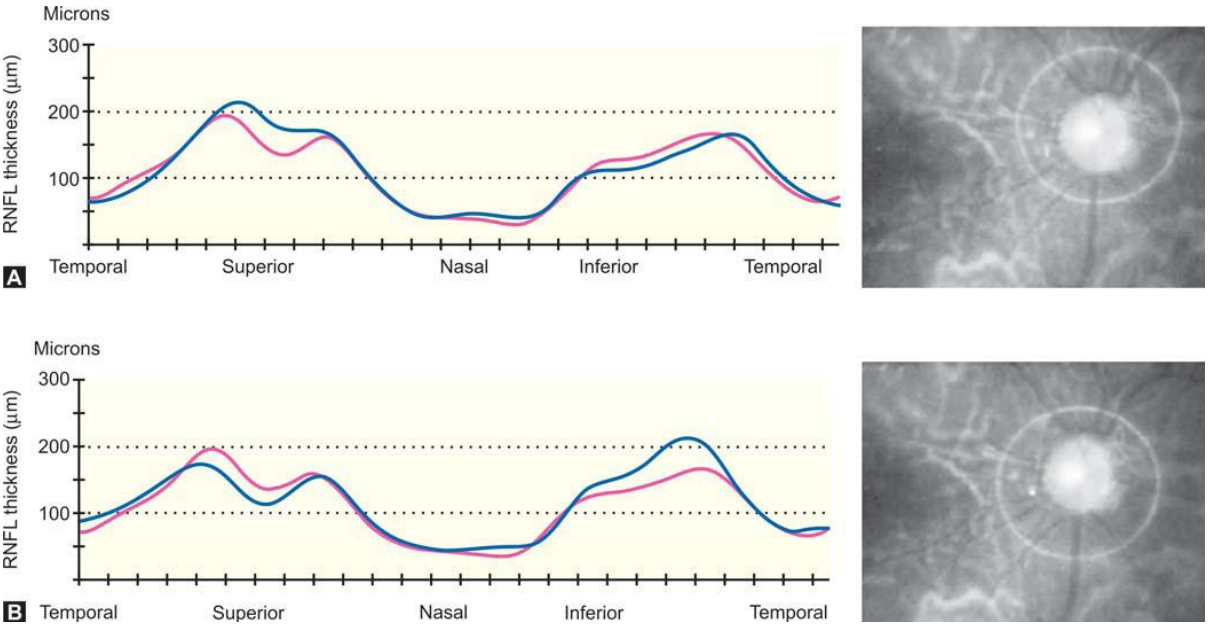


**Figure 4.4.3: RNFL profiles [14]**

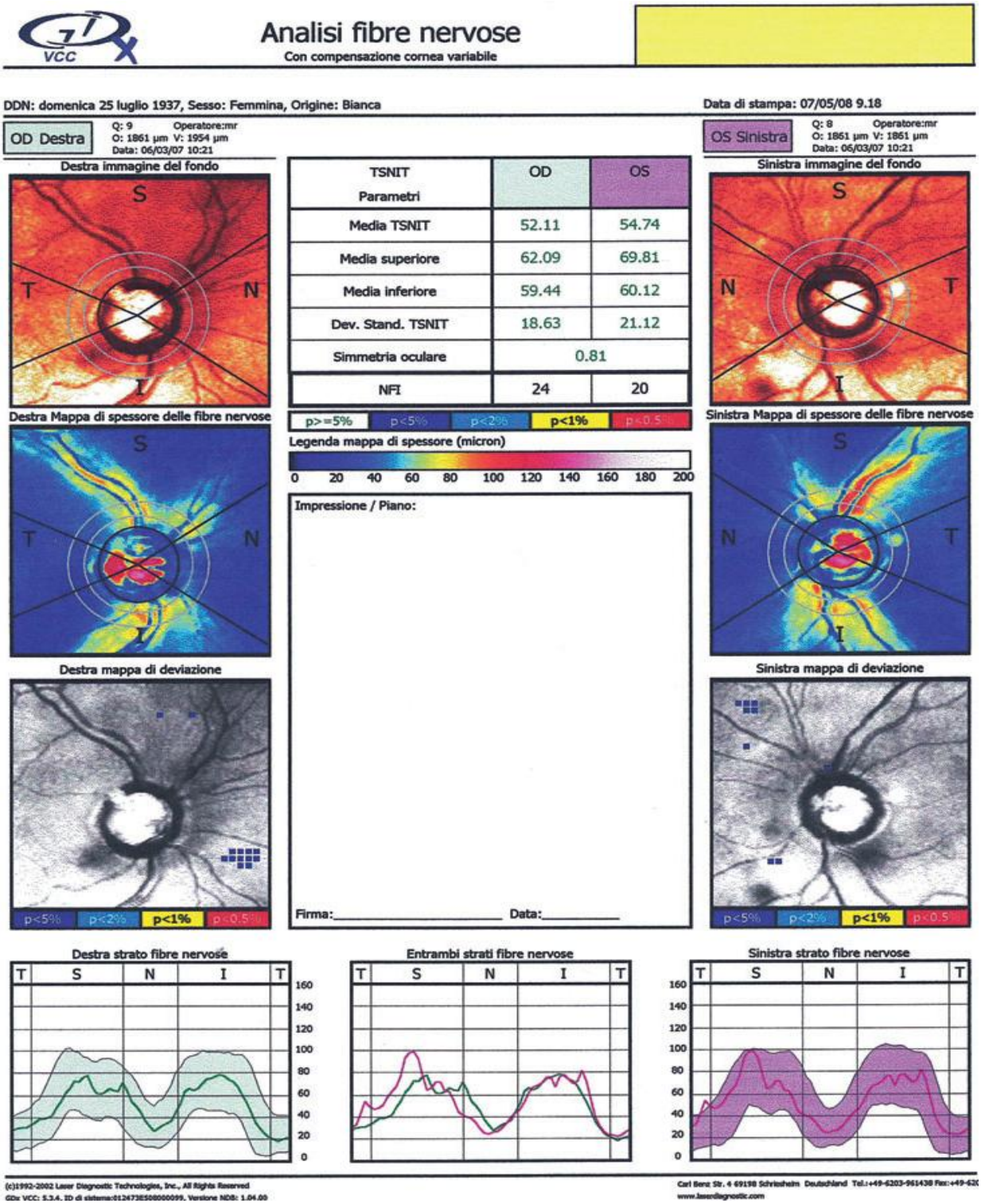


**Figure 4.5.1: SLP analysis of peripapillary RNFL [15]**

## 4.5. Scanning Laser Polarimetry [15]:

SLP produces RNFL measurements using the principle of change in polarization. When a light beam falls on tissues with birefringent properties, such as the RNFL, changes occur in polarization. These are quantified to produce RNFL measurements. The source of RNFL birefringence is parallel arrangement of microtubules within axon bundles. A polarizer splits a polarized light beam (780 nm) into two components before entering the eye. Light projected on the retinal surface crosses the RNFL. The two components travel at different velocities creating a phase shift. This phase shift is proportional to the thickness of the tissue. In other words, the phase shift is smaller for a thinner tissue. RNFL thickness measured using this technique demonstrates an agreement with actual values. Other eye structures like the cornea and the lens also affect this optical property. Hence to obtain accurate RNFL measurements, the RNFL component is isolated and neutralization (compensation) of birefringence components corresponding to the cornea and lens is required. The phase shift values (in nanometers, nm) are then transformed into thickness values (in millimeters, mm). The conversion factor used is 0.67 nm/mm. A fixed corneal compensator (FCC) was included, based on the assumption that the corneal polarization axis (CPA) and magnitude (CPM) both would have the same value in all subjects (CPA) 15° nasally downward. But in nearly 30% of eyes, the axis and the magnitude were found to be different from desired values. This resulted into improper elimination of anterior segment birefringence. Hence RNFL measurements were found to be false for such eyes. The newer version of the instrument, namely GDx-VCC, uses a variable corneal compensator (VCC) which takes eye specific CPA and CPM values. This ensures proper elimination of anterior segment birefringence. GDx-VCC improved significantly in performance pertaining to both, the structure–function relationship and visualization of RNFL defects. Thus ability to predict glaucomatous changes is quite better in GDx-VCC. SLP analysis of peripapillary RNFL is demonstrated in Figure 4.5.1. Splitting of the superior bundle is shown. By examining the RNFL profile on Temporal-Superior-Nasal-Inferior-Temporal graphs, (TSNIT graphs), this feature becomes even more prominent [15].

John R. Trible [16] et al determined the diagnostic accuracy of SLP. The best algorithm tested for SLP demonstrated sensitivities of 57%, 71%, and 81% for early, moderate, and severe glaucoma, respectively. This was associated with a specificity of 89%.

## 5. DISCUSSION

It can often be difficult to distinguish the patient with early glaucoma. Complex issues in the management of glaucoma include both the indications for treatment and the type of treatment. These difficulties lead to the dilemma of, determining which patients should be treated. Patients that do not have glaucoma may be subjected to the inconvenience, expense and possible toxicity of treatment. The unfortunate corollary is that treatment may be withheld from patients who have or may develop glaucoma [17].

In Ha Shin et al [18] have evaluated the relationship between optic disc RNFL measurements obtained with the OCT and HRT in normal, normal tension glaucoma (NTG), and high tension glaucoma (HTG). They concluded that OCT in conjunction with associated HRT variables, not only acts as an adjunct to the traditional triad of visual field, RNFL photography and ONH morphologic studies, but can also be a most useful tool in research analysis.

Felipe A. Medeiros et al [19] have compared the RNFL and optic disc topographic imaging for detection of optic nerve damage in patients suspected of having glaucoma. They concluded that RNFL imaging with GDx-VCC had a superior performance versus topographic optic disc assessment with the HRT for detecting early damage in patients suspected of having glaucoma. For glaucoma diagnosis, these results suggest that GDx-VCC may offer advantage over the HRT when these tests are combined with clinical examination of the optic nerve.

ONH Analyzers capable of objective documentation and quantification of ONH parameters play a vital role in diagnosis and monitoring of glaucoma. Michael Greaney et al [11] have compared the ability of qualitative assessment of different modalities used for ONH evaluation. A combination of imaging methods significantly improves the ability of assessment because different methods assess different aspects of ONH and RNFL and are therefore likely to complement each other. There is no single imaging device that outperforms the others in distinguishing patients with glaucoma [20].

## 6. CONCLUSION

The ultimate aim in the management of Glaucoma is to avoid further damage in ONH structure and subsequent vision loss. Thus early diagnosis is the key for the disease management. Comprehensive examination of the patient's ONH and RNFL helps in early Glaucoma diagnosis. Clinical assessment of ONH is subject to inter-observer variability. ONH Analyzers play a vital role in diagnosis of glaucoma since they are capable of offering quantitative evidence. This is useful in eliminating the subjectivity involved in the diagnosis, especially useful for boundary-line cases. Documentation of ONH facilitates the process of monitoring the disease progression. Every ONH evaluation method works on a different principle and has its own merits. No single method outperforms others in all respects. A combination of these modalities improves the diagnostic capability. Clinical assessment along with the aid of ONH analyzers improves the accuracy and specificity of the disease diagnosis.

## 7. REFERENCES

[1]. R R A Bourne, Worldwide glaucoma through the looking glass, Br J Ophthalmol, (2006) 253-254

[2]. Harry A. Quigley, Number of people with Glaucoma worldwide, British journal of Ophthalmology, 80 (1996) 389-393

[3].Glaucoma is the leading cause of blindness globally, Bulletin of World Health Organization, (2004) 887-888

[4]. Dr. Medha Prabhudesai, Atlas of Optic Nerve Head Evaluation in Glaucoma, First Edition, Jaypee Brothers Medical Publishers (P) ltd, New Delhi

[5]. Glaucoma, an insight into disease and therapy, Karen Long, CphA 2006, Home study program, Canadian Pharmasists association Online learning centre

[6]. Jagdish Nayak, Rajendra Acharya P. Subbanna Bhat & Nakul Shetty & Teik-Cheng Lim, Automated diagnosis of glaucoma using fundus images, Journal of Medical Systems, 33 (2009) 337-346

[7]. Murray Fingeret, Felipe A. Medeiros, Remo Susanna, Robert N. Weinreb, Five rules to evaluate the optic disc and retinal nerve fiber layer for glaucoma, Optometry, 76 (2005) 661-668

[8]. Noga Harizman, MD; Cristiano Oliveira, Allen Chiang, Celso Tello, Michael Marmor, Robert Ritch, Jeffrey M. Liebmann, The ISNT rule for differentiation of normal with glaucomatous eyes, Arch Ophthalmol., 124 (2006) 579-1583

[9]. Pooja Sharma, Pamela A. Sample, Linda M. Zangwill, Joel S. Schuman, Diagnostic tools for glaucoma detection and management, Survey of ophthalmology, 53 (2008) 17-32

[10]. Douglas E. Gaasterland, Beth Blackwell, Leonard G. Dally, Joseph Caprioli, L. Jay Katz, Fred Ederer, FACE ,The AGIS Investigators , The advanced glaucoma intervention study (AGIS):10. Variability among academic glaucoma subspecialists in assessing optic disc notching, Tr. Am. Ophth. Soc, 99 (2001) 177-185

[11]. Michael J. Greaney, Douglas C. Hoffman, David F. Garway-Heath, Mamdouh Nakla,Anne L. Coleman, Joseph Caprioli, Comparison of optic nerve imaging methods to distinguish normal eyes with those of Glaucoma, Invest Ophthalmol Vis Sci, 43 (2002) 140-145

[12]. Quantitative three dimensional imaging of the posterior segment with Heidelberg retina tomograph, Heidelberg Engineering GmbH, Heidelberg, Germany

[13]. P.H.Tomlins, R.K.Wang, Theory, development and applications of optical coherence tomography, Journal of Physics. D: Applied Physics, 38 (2005) 2519–2535

[14].Carol Yim Lui Cheung, Christopher Kai-shun Leung, A practical guide for interpretation of Optical Coherence Tomography retinal nerve fiber layer measurement, Journal of Current Glaucoma Practice, 3(1) (2009) 9-13

[15]. Stefano Da Pozzo, Roberta Marchesan, Giuseppe Ravalico, Scanning laser polarimetry – a review, Clinical & Experimental Ophthalmology, 37 (2009) 68–80

[16]. John R. Trible, Richard O. Schultz, James C. Robinson, Terri L. Rothe, Accuracy of Scanning Laser Polarimetry in the Diagnosis of Glaucoma, Arch Ophthalmol, 117 (1999) 1298-1304

[17]. David A Infeld, John G O'Shea, Glaucoma: diagnosis and management, The Fellowship of Postgraduate Medicine, 74 (1998) 709-715

[18]. In Ha Shin, Sung Yong Kang, Samin Hong, Seung Kab Kim, Gong Je Seong, Kyoung Tak Ma, Chan Yun Kim, Comparison of OCT and HRT findings among normal, normal tension glaucoma, and high tension glaucoma , Korean Journal of Ophthalmology, 22 (2008) 236-241

[19]. Felipe A. Medeiros, Gianmarco Vizzeri, Linda M. Zangwill, Luciana M. Alencar, Pamela A. Sample, Robert N. Weinreb, Comparison of Retinal Nerve Fiber Layer and Optic Disc Imaging for Diagnosing Glaucoma in Patients Suspected of Having the Disease, Ophthalmology, 115 (2008) 1340-1346.

[20]. Shan C. Lin, Kuldev Singh, Henry D. Jampel, Elizabeth A. Hodapp, Scott D. Smith, Brian A. Francis, David K. Dueker, Robert D. Fechtner, John S. Samples, Joel S. Schuman, Don S. Minckler, Optic Nerve Head and Retinal Nerve Fiber Layer Analysis : A Report by the American Academy of Ophthalmology, 114 (2007) 1937-1949