Review article

Use of OCT for Glaucoma Specialists

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Abstract

Primary open-angle glaucoma (POAG) is a chronic and progressive optic neuropathy characterized by retinal nerve fiber layer thickness (RNFLT) loss and neuro-retinal rim tissue thinning with progressive visual field (VF) damage.

The basic pathology is the progressive loss of retinal ganglion cells (RGCs), especially the apoptosis of the axons of ganglion cells, followed by peripapillary retinal nerve fiber layer (RNFL) defects. Glaucoma predominantly affects the inner macular retinal layers: the macular RNFL (m RNFL), ganglion cell layer (GCL) and inner plexiform layer (IPL), where ganglion cell complex (GCC) consists of RNFL, GCL and IPL thickness.

The ability to detect structural loss is fundamental in the diagnosis and management of glaucoma. While glaucomatous structural damage can be assessed clinically by examining the optic nerve head (ONH) and peripapillary retinal nerve fiber layer (RNFL), the introduction of ocular imaging modalities has supplemented the clinical diagnosis and hence it is possible to either slow or prevent the progression of vision loss by adequate early treatment and management of glaucoma.

In recent years, along with visual fields, optical coherence tomography (OCT) has become an important modality for the early diagnosis of glaucoma disease and the monitoring and analysis of glaucoma patients.

Keywords: Glaucoma, Optical coherence tomography, Retinal nerve fiber layer analysis, Anterior segment OCT.

Introduction

Primary open-angle glaucoma (POAG) is a chronic and progressive optic neuropathy characterized by retinal nerve fiber layer thickness (RNFLT) loss and neuro-retinal rim tissue thinning with progressive visual field (VF) damage.

The basic pathology is the progressive loss of retinal ganglion cells (RGCs), especially the apoptosis of the axons of ganglion cells, followed by peripapillary retinal nerve fiber layer (RNFL) defects. Glaucoma predominantly affects the inner macular retinal layers: the macular RNFL (mRNFL), ganglion cell layer (GCL) and inner plexiform layer (IPL), where ganglion cell complex (GCC) consists of RNFL, GCL and IPL thickness.[1]

This loss of axons and ganglion cells cannot be identified with any clinical diagnosis methods before it exceeds a certain critical threshold.[2-5] Research has shown that the earliest sign

that can be detected clinically in glaucoma is the loss or thinning of the RNFL.

The ability to detect structural loss is fundamental in the diagnosis and management of glaucoma. Glaucomatous structural damage is difficult to assess clinically, and hence, the introduction of ocular imaging modalities has supplemented the clinical diagnosis and thereby making it possible to either slow or prevent the progression of vision loss by adequate early treatment and management of glaucoma.

Individuals with glaucoma are usually asymptomatic until the advanced stage of the disease hence early detection is crucial. In recent years, along with visual fields, optical coherence tomography (OCT) has become an important modality for the early diagnosis of glaucoma disease and the monitoring and analysis of glaucoma patients.

Since early detection is essential to prevent visual impairment and blindness[3], efforts have been made to develop methods that allow clinicians to identify mild to moderate disease with adequate sensitivity and specificity.

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Spectral-domain optical coherence tomography (SD-OCT) can provide objective measurement of structural parameters of the optic nerve head and RNFLT.[4,5]

Types of OCT and Their Principles

OCT is a high-resolution imaging device that uses low coherent light from a broadband light source produced from a super-luminescent diode to acquire *in-vivo* images of the retina. Optical coherence tomography applies the principle of Michelson interferometry to interpret reflectance data from a series of multiple side-by-side A-scans combined to form a cross-sectional image. It can be either time domain (TD) or spectral domain (SD).

The operating principle of time-domain OCT is associated with the delay in the reflection time of light. The actual variable in the spectral domain OCT is the change in the optic frequency.

OCT1 was the first OCT device to be developed, followed later by the development of OCT 2 and 3, all belonging to the time domain variant. Nowadays, all OCT devices that are manufactured have the spectral domain technology.

The SD-OCT has high axial resolution, being affected by eye movements at a minimum level and low artifacts. To date, the axial resolution obtained through spectral domain OCT devices has reached up to a value of 3 microns, and these devices are rightfully referred to as OCTs with very high speeds and very high resolutions.[6]

SD-OCT has been reported to have higher sensitivity than TD-OCT in glaucoma screening and may have the potential for early detection in a high-risk population.[7]

The diagnostic capabilities of SD-OCT for discriminating between healthy and glaucomatous eyes using average RNFL thickness have been reported to have an area under receiver operating characteristics curve value of around 0.9.[8] However, the discrimination ability is dependent on the severity stage of glaucoma, with better performance in discriminating between healthy and more advance disease compared with discrimination of early stages of glaucoma.[9]

Acquisition of 3D images of the ONH region enables accurate and reproducible measurements of ONH parameters that include disc and rim area, cup-to-disc ratio, cup volume and others. A diagnostic capability study with SD-OCT of glaucoma and age-matched healthy controls reported that these ONH parameters are able to discriminate between healthy and glaucomatous eyes similar to RNFL thickness.[10] Another study with glaucoma, pre-perimetric glaucoma and healthy subjects demonstrated that RNFL thickness was better than any tested ONH parameter.[11] The contradictory results of these two studies may be attributed to differences in glaucoma severity within the study samples. However, both studies reported similar diagnostic capability with rim area and average RNFL thickness in advanced glaucoma. The role of SD-OCT ONH analysis in glaucoma diagnosis is yet to be determined.

While total macular thickness (TMT) has been associated with glaucoma, the diagnostic capabilities have been reported to be worse than with RNFL thickness. However, SD-OCT segmentation algorithms have enabled quantification of individual layers in the macular region that are particularly impacted by glaucomatous damage, specifically, macular RNFL (m RNFL), ganglion cell layer with inner plexiform layer (GCIPL) and ganglion cell complex (GCC=m RNFL+GCIPL).

SD-OCT diagnostic studies have demonstrated that glaucomatous damage results in the thinning of RNFL and G CIPL as well as ONH structural changes that allow for discrimination between glaucoma and healthy eyes. However, in most of these studies, the diagnostic accuracy may not translate when used in clinical practice for early-stage glaucoma detection because the discrimination studies are usually based on differentiating healthy eyes from eyes with established glaucomatous visual field (VF) loss.

Myopia is a risk factor for glaucoma and a confounder that complicates diagnosis because it presents with structural changes that can progressively lead to glaucomatous-appearing VF defects. Myopic refractive error and longer axial lengths impact RNFL and macular thickness measurements due to the optical projection artifact of the scanning area.

In summary, the literature to date suggests that RNFL thickness remains the most diagnostically accurate parameter for detecting glaucoma. Though there have been some conflicting reports, several studies suggest that the diagnostic performance of segmented macular and ONH parameters is comparable with RNFL parameters. Furthermore, there is a reported difference in RNFL thickness measurement between different SD-OCT devices attributed to variations in optical properties and segmentation algorithms, and therefore, the measurements are not inter-changeable between devices.[12] However, despite these variations, the devices have demonstrated similar diagnostic capabilities.[13]

Glaucoma Screening

Individuals with glaucoma are usually asymptomatic until late in the disease processes and it is possible to either slow or prevent the progression of vision loss if detected early by adequate treatment. Therefore, a glaucoma screening tool for the general population is desirable. Population-based glaucoma screening is currently not cost-effective, but it may be more beneficial and cost-effective in a targeted high-risk population such as older African Americans and Hispanics or those with a family history of glaucoma. Screening for glaucoma in a community-based high-risk population with TD-OCT resulted in moderate sensitivity and high specificity for definitive glaucoma, suggesting that the device does not have adequate sensitivity to be used alone but may have utility in excluding subjects from further evaluation.[14] However, SD-OCT has been reported to have higher sensitivity than TD-OCT in glaucoma screening and may have the potential for early detection in a high-risk population.[15] As of this writing, the use of SD-OCT for glaucoma screening in high-risk populations has not been reported. In summary, OCT currently lacks the necessary diagnostic performance for general-population glaucoma screening.

Glaucoma Progression

Once glaucoma is diagnosed, a sensitive method for detection of progression is essential because appropriately intensifying treatment can slow RGC loss and preserve vision. The detection of glaucoma progression with OCT remains a challenge because when assessing structural changes over time, it is difficult to discriminate between glaucomatous structural damage and measurement variability or age-related structural loss. A prospective study assessing age-related loss enrolled 100 healthy subjects for cross-sectional evaluation and then randomly selected 35 subjects for 30 months of longitudinal evaluation.[16] Cross-sectional analysis of healthy subjects demonstrated a significant negative correlation between age and average RNFL thickness of −0.33 µm/year, while the longitudinal analysis reported a −0.52 µm/year rate of age-related loss of RNFL. Furthermore, the same study reported that age-related structural loss varies as a function of baseline RNFL, where a higher baseline thickness is subject to higher rates of decline.

SD-OCT has been reported to be more sensitive than TD-OCT in detecting RNFL changes in glaucoma progression.[17] SD-OCT glaucoma progression algorithms measure changes based on either event-based or trend-based analysis. Event-based analysis detects progression when a follow-up measurement exceeds a pre-established threshold for change from baseline. This analysis identifies a gradual change over time that eventually crosses a threshold or an acute event that exceeds a threshold. The limitation of this approach is the susceptibility to the effect of outliers that can be inappropriately labeled as progression. Trend-based analysis detects progression by evaluating the slope of measured parameters over time. Trend analysis is less sensitive to measurement variability and identifies a rate of progression that may be extrapolated for time-to-event predictions. The limitation of this approach is the requirement for a large number of tests before the analysis can be considered reliable. Furthermore, trend analysis has an a priori assumption of a linear rate of structural loss, which might not be applicable to all eyes.

The first study to show the potential of OCT in detecting glaucoma progression used an event-based approach to evaluate TD-OCT RNFL thickness measurements over time and reported a mean loss of average RNFL thickness of 11.7 µm over 4.7 years in glaucoma subjects.[18] In a longitudinal SD-OCT study of glaucoma and healthy eyes followed for 3 years. The investigators reported a significantly greater rate of RNFL loss in glaucomatous optic disc progressors compared with non-progressors.[19] A 2-year study of perimetric glaucoma and healthy eyes with SD-OCT scans demonstrated superior detection of early glaucomatous progression with measurement of GCC global loss volume and focal loss volume compared with ONH, RNFL thickness and average GCC parameters.[20]

The three commonly used SD-OCTs that are used in glaucoma diagnosis and treatment are the spectralis (Heidelberg Engineering, Dossenheim, Germany), the Cirrus (Carl Zeiss Meditec, Dublin, CA) and the RTVue (Optovue Inc., Fremont, CA).

Cirrus high-definition (HD)-OCT is widely used to evaluate circumpapillary RNFL (cp-RNFL), the thickness of the RNFL is crucial for the early diagnosis of glaucoma and for being able to have an opinion on its progression. RNFL thickness is depicted in a color scale ranging from zero (blue) to 350 µm (white) is indicated using color codes. The optic disc is recorded within a 6 × 6 mm cube. The center of the optic disc is automatically identified. The value of the signal power is between 0 and 10, with 5 being the threshold. Fundus images can be taken by automatic centering functionality.

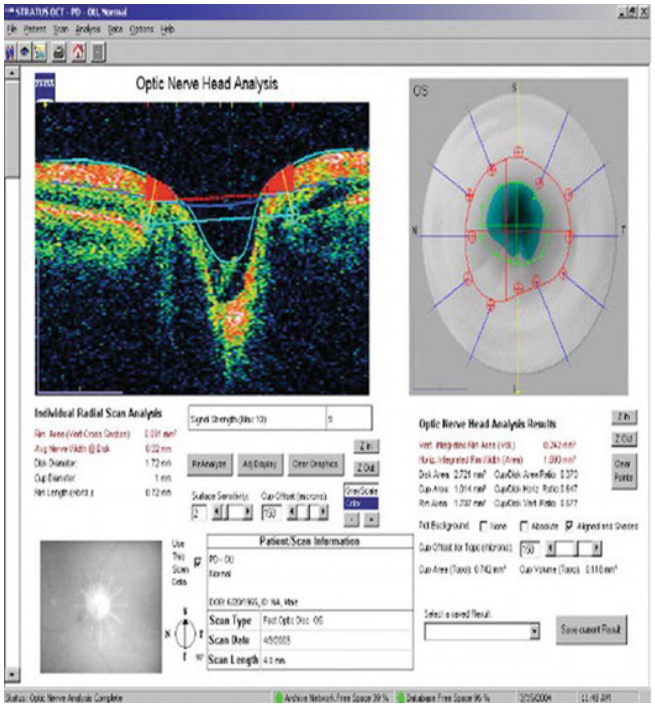
The RNFL normative database is available for glaucoma patients who are older than 18 years of age. The database uses the colors as follows:

Red

Values within the lowest portion of 1% are displayed in red and are considered abnormal (Figure 1).

Yellow

Values within the lowest portion of 5% are displayed in yellow and are considered doubtful.



Source: RNFL thickness map is color-coded, where thinned areas are represented by cold colors and thick areas are shown in hot colors. The thickness map in Cirrus Zeiss ranges from zero (blue) to 350 µm (white). The average thickness values of the patient are depicted in numerical chart format and the values are compared to normative data. The TSNIT thickness profile is displayed in the following color codes (white, green, yellow, and red).

Figure 1: Optic disc scan

Green

Over 90% of all measurements are in this section and should be considered normal.

Anterior Segment Imaging in Glaucoma

The AS-OCT is a non-contact, rapid imaging device that uses low-coherence interferometry to obtain cross-sectional images of the anterior segment.[21]

Izatt *et al*. (61) (1994), for the first time, demonstrated the use of OCT for the anterior segment of the eye.

AS-OCT technology has several types, including time-domain, swept-source, and spectral-domain-based configurations.

SS and SD-based imaging are considered a type of Fourier-domain (FD) OCT. Due to its inherent signal-to-noise ratio advantage, it has a higher imaging speed (up to 20–40 kHz line-scan rate) than those that are based on a TD configuration.

SS-OCT can monitor PAS peripheral anterior synechiae and there development of angle-closure glaucoma.

Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) is an SD AS-OCT. It has enhanced depth imaging (EDI), which increases the imaging sensitivity of the structures at greater depth. The SS-OCT, utilizing an SS laser and is able to capture extremely high-resolution images.

AS-OCT achieves better resolution and does not require contact with the ocular surface (Figures 2 and 3).

These devices play an important role in glaucoma diagnosis and management by aiding in the visualization of the angle, bleb and glaucoma drainage devices. Visualization of the anterior chamber (AC) angle is a crucial step in the diagnosis of glaucoma, more so in cases of angle-closure variants.

Several new AS-OCT parameters have been associated with angle closure (Figure 4), including smaller AC width, area, and volume; larger lens vault; and a greater iris thickness, curvature, and area.[22]

AS-OCT revealed that patients with acute primary angle-closure glaucoma tended to have smaller AC depth and iris curvature.[22]

The AS-OCT also has certain limitations, the visualization of the inferior quadrant is poor due to the variable placement of the scleral spur. The main limitation is the inability of the light energy to penetrate tissues behind the iris pigment epithelium, so AS-OCT cannot visualize any structures posterior to the iris pigment epithelium; therefore, it is not useful in diagnosing plateau iris syndrome or phacomorphic angle-closure.

For evaluation of AC angle, the scleral spur is used as a reference point for parameters such as the iris area and volume, angle opening distance (AOD), angle recess area, scleral thickness, trabecular meshwork-ciliary process

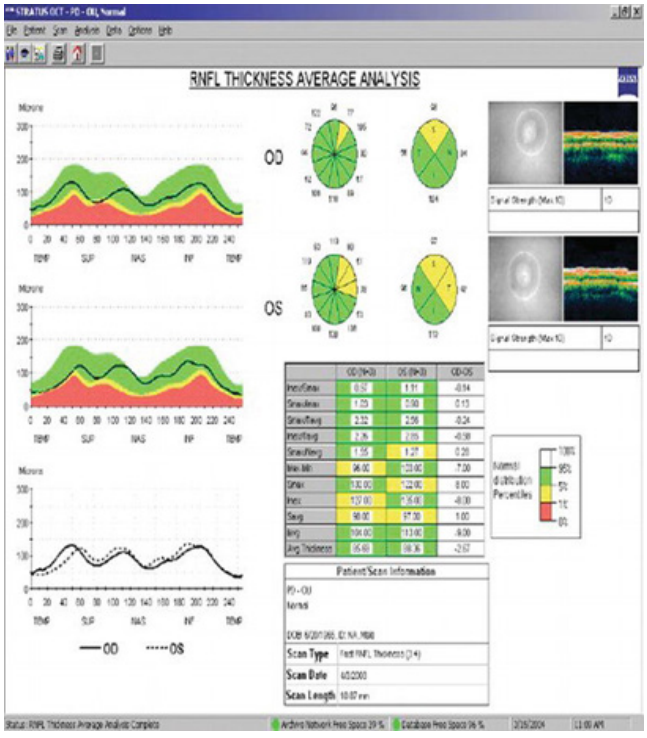


Fig. 2: RNFL Thickness Map

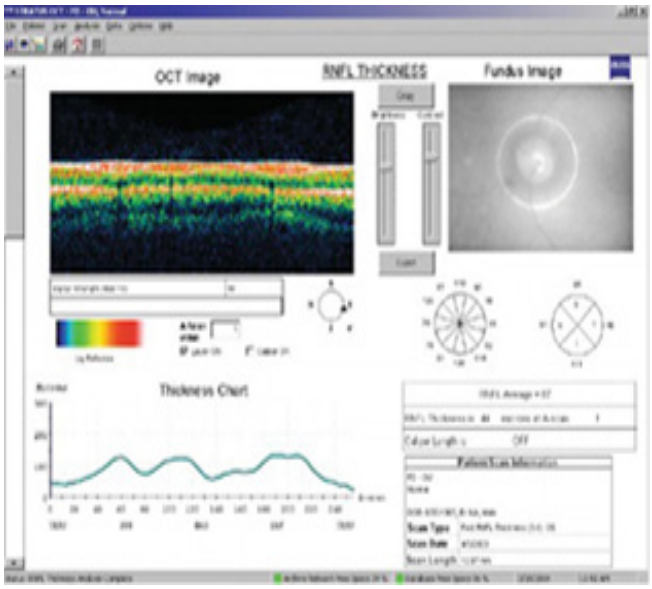


Figure 3: RNFL analysis screen

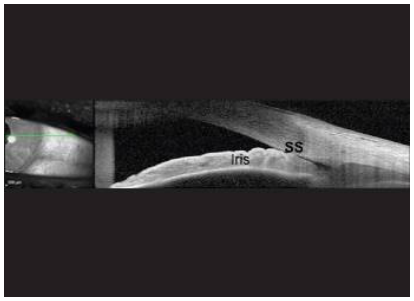


Figure 4: Anterior segment optical coherence tomography photo demonstrates S-type angle-closure with apposition beginning at Schwalbe's line. SS: Scleral spur.

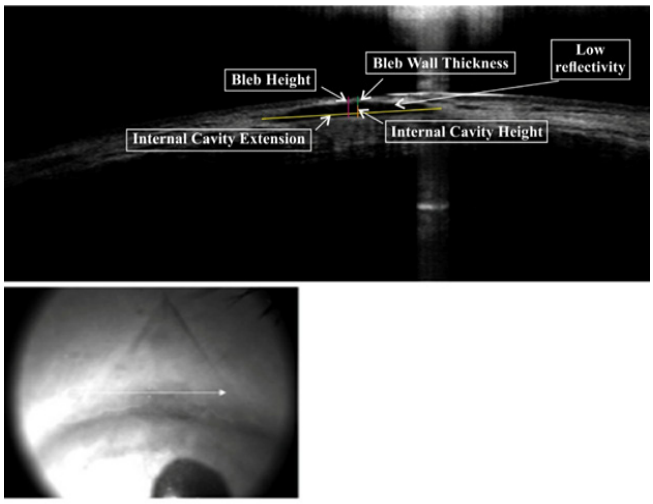


Figure 5: Anterior segment optical coherence tomography photo demonstrates morphology of filtering bleb after trabeculectomy

distance, trabecular iris angle and trabecular iris space area.[22] However, difficulty in identification of the scleral spur has been noticed. Other parameters include iris thickness, iris curvature, AC depth, AC width, and lens vault.[22]

AS-OCT has been used in eyes with narrow angles to demonstrate the widening of the angles after laser peripheral iridotomy (LPI).[23] And also, it helps to demonstrate whether an LPI is patent, which on clinical examination is quiet challenging.

AS-OCT is most commonly used for appositional angle closure. It is being done recently to calculate the irido-trabecular contact (ITC) index with the help of software that can estimate the percentage of angle-closure by manually identifying the scleral spur.

AS-OCT also helps in monitoring the results of trabeculectomy. Morphology of filtering bleb is of paramount importance for IOP control after trabeculectomy.[24]

AS-OCT may be especially useful for fragile (Figure 5) post-trabeculectomy blebs, given the non-contact nature of the test.[24]

As intraocular tissues show different optical properties, hence OCT is capable of defining these in detail.

AS-OCT findings can be recorded under the following parameters- bleb height, bleb wall thickness, internal cavity height, internal cavity extension, and bleb reflectivity pattern.

Conclusion

OCT has become a very important diagnostic tool in ophthalmology. The recent development of better technology in OCT has led to its widespread use in screening and monitoring the progression of glaucoma.

The ability of OCT to detect structural loss due to glaucoma may decrease the morbidity that is caused by the disease worldwide. Also, since it is a non-contact and non-invasive investigation, patient compliance is also maintained.

Nevertheless, early glaucoma detection in myopes still remains a challenge and should be an area of research.

Conflict of Interest

None

Financial Disclosures

None

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