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ROI	All articles are CPD accredited in the Republic of Ireland			12

OCT in Glaucoma

by **Adam Wannell** MSc DipSV DipGlauc DipTp(IP) MCOptom

Outline

This article will examine what OCT can tell us about the structural changes associated with glaucoma and consider how OCT can help in the diagnosis and management of this condition.

About the author

Adam is Specsavers Head of Enhanced Services, module leader for postgraduate glaucoma module, Wales Optometry Postgraduate Education Centre (WOPEC), medical optometrist at the Bristol Eye Hospital and, until recently, was optometrist director of a community practice involved in delivery of a range of enhanced services. He has a postgraduate qualification in clinical teaching, a College of Optometrists Diploma in Therapeutics and Glaucoma and an MSc in Clinical Optometry from City University, London. He has a Diploma in Sports Vision Practice and has been involved with National Sports Vision Screening.

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The learning objectives for this article are:

2.7.2 Optometrists will have an enhanced understanding of the use of OCT for assessment of patients with or at risk of chronic open-angle glaucoma

3.1.3 Optometrists will have an evidence-based understanding of the principles of use of OCT to assess various structures within the retina

6.1.8 Optometrists will have an enhanced understanding of the identification of glaucomatous features of an optic nerve head using OCT

2.1.2 Therapeutic optometrists will have an enhanced understanding of the identification of glaucomatous features of an optic nerve head using OCT

Introduction

Glaucoma stems from a loss of retinal ganglion cells and their axons, giving rise to characteristic functional changes of vision, as shown by visual field defects and structural changes at the optic nerve head (ONH) and surrounding region. The evolution of OCT imaging has made it possible to measure these structural changes with increasing accuracy and has assisted with our understanding of glaucomatous effects on the optic nerve and on the cellular layers of the retina itself. This article will examine what OCT can tell us about the structural changes associated with glaucoma and consider how OCT can help in the diagnosis and management of this condition.

Firstly, in order to be able to interpret OCT images, it is important to appreciate the underlying anatomy of the retina and ONH as shown by OCT. Figure 1 shows a detailed OCT section of a healthy macula with eight of the retinal layers identified. One important layer not present at the fovea is the retinal nerve fibre layer (RNFL) which lies directly above the ganglion cell layer and can be discerned as the thin, top bright layer on the right side of the picture. Looking at Figure 2, the RNFL becomes much thicker and more visible as the nerve fibres gather at the disc.

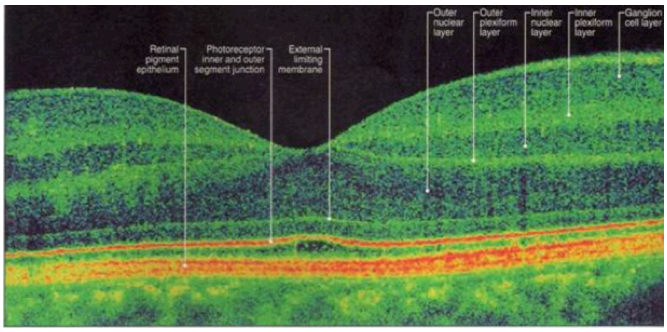

Figure 1: OCT fovea and macula detail

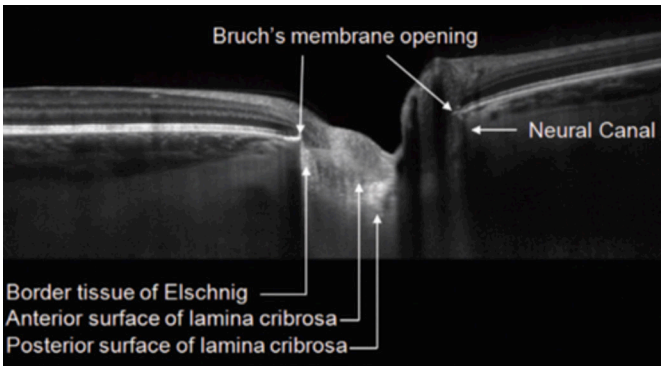

Figure 2: OCT optic nerve head detail

Throughout the retina, just below the retinal pigment epithelium (RPE), is the collagenous Bruch's membrane which separates the retina from the choroid. At the disc margin, Bruch's membrane inserts into the border tissue of Elschnig, thus separating the outer retina and choroid from the axons of the inner retina.[1] It is the termination of Bruch's membrane that forms the anatomical opening of the neural canal containing the optic nerve, as shown in Figure 2. It is essential for OCT algorithms to identify this opening to ensure accurate ONH measurements are captured.

Glaucoma detection: What can OCT tell us?

The information that OCT can provide regarding the glaucomatous status of our patients centres around three anatomical areas: the ONH, the RNFL and the ganglion cell layer. The importance of each of these structures in our assessment of glaucoma is discussed in this section, alongside the respective scanning techniques used to image them.

Optic nerve head: Disc analysis

Variations in optical reflectance along a point through the tissue are combined to depict an axial scan or A-scan; this forms the foundation of any scan. By gathering several A-scans through the tissue, a cross-sectional image can be generated; this is known as a B-scan. Multiple parallel B-scans are then collected to give a three-dimensional or cube scan. A typical scan is made from 128 parallel B-scans, each of which is made from 512 A-scans, making a total of 65,000 scans! With good resolution and reproducible measurements,[2] the 3D scan provides cross-sectional and volumetric data of the ONH and the surrounding region.

The structural changes observed at the ONH in glaucoma form an essential part of its diagnosis. 3D scan parameters include: disc area, cup area, neuroretinal rim area, cup volume, cup to disc ratio (both horizontal and vertical) and the RNFL thickness immediately surrounding the disc (Figure 3).

Item	Value
C/D(Horizon)	0.79
C/D(Vertical)	0.76
R/D(Min)	0.02
R/D(Angle)	184
Disc Area[mm^2]	2.16
Cup Area[mm^2]	1.33

Figure 3: Disc parameter measures displayed by Scan Duo. The minimum rim to disc ratio value is recorded, along with the position at which this occurs in (shown as an angle in degrees akin to the standard notation of a trial frame when looking at the disc)

In order for the software algorithms to make these measurements, fixed reference points must be defined (Figure 4). These are usually taken from the termination or opening of Bruch's membrane, to define the disc edge, together with a horizontal reference plain set typically around 150μm above the RPE. Even with such a wide variation in ONH morphology in individual patients, OCT disc parameters have been shown to be able to distinguish healthy eyes from those with glaucoma.[3] However, they have been found to be inferior to RNFL thickness measurements when used for glaucoma discrimination, especially in patients with early-stage glaucoma and in glaucomatous patients with small optic discs.[4]

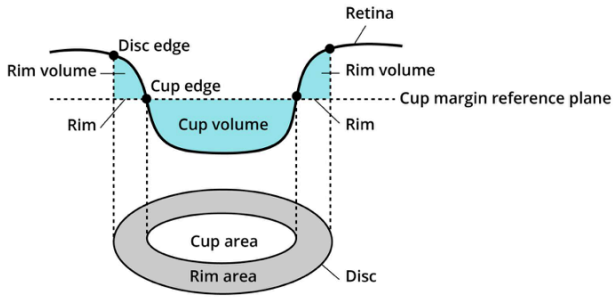

Figure 4: OCT disc analysis. OCT identifies the disc edge and neuroretinal rim edge. By superimposing a reference plane at a set distance below the retinal surface, calculations build a comprehensive topographical dataset.

It is worth noting at this point that both algorithms and reference points vary between OCT manufacturers, thus making scans between machines non-transferable and highlighting the importance of consistent scans over time for individual patients.

Optic nerve head: Radial scans

In any OCT scan there is a slight trade-off between the amount of data captured and the image resolution, due to the way scans are constructed. By eliminating the multiplying effect of scan numbers, as shown in the previous section to achieve the volumetric data via B-scans, more A-scans per area can be performed. This results in a higher axial resolution with more accuracy. Radial scans simply combine line scans through a common point, either the fovea or centre of the ONH, for highly accurate thickness measurements.

Shifting the focus back to ocular anatomy, one of the major difficulties with clinical examination of the ONH has been the accurate identification of both the outer and inner parts of the neuroretinal rim. The optic nerve is encased by scleral tissue forming the scleral canal, which, if seen end-on, is visible as the scleral ring or lip, and surrounded by the retina. When all the retinal layers abut this canal, then the junction between the neuroretinal rim and retina is at the same point and readily distinguished. If, however, the retinal layers do not fully reach the scleral canal, then other layers become visible giving rise to a scleral ring, peripapillary atrophy (PPA) or scleral crescent. This can result in difficulty assessing the disc size and poorer distinction of the outer neuroretinal rim boundary. Conversely, the inner neuroretinal rim can be difficult to distinguish if there is little change of colour from cup to rim, no alteration of vessel path emanating from disc to indicate the cup, or if the cup is very shallow and sloping giving poor stereoscopic depth cues. One or several of these factors may be present in any given individual, thus making disc interpretation difficult.

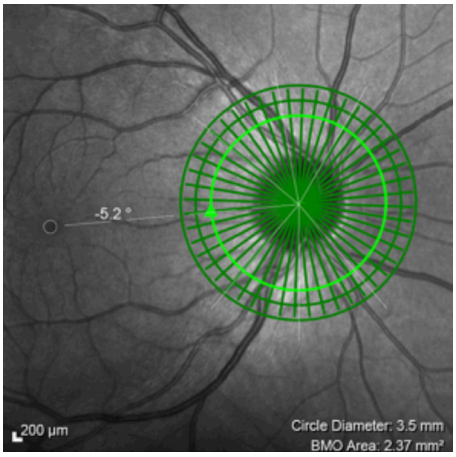

Figure 5: Radial disc scan pattern used by Spectralis to capture Bruch's membrane opening to neuroretinal rim width measurements. The scan also shows fovea-to-disc alignment to improve scan orientation accuracy and reduce errors induced by head tilt.

This has largely been overcome by the recent advancements in OCT enabling the consistent identification of the termination of Bruch's membrane as the edge of the optic nerve, the so-called Bruch's membrane opening (BMO) and width of the neuroretinal rim. The identification of the BMO provides a more consistent measurement of the optic disc's size and rim area.[5] By employing a set of radial scans, image resolution is improved, allowing the multiple measures of neuroretinal rim width (minimal, perpendicular and horizontal width) to be quantified at numerous points around the disc (Figure 5). This in turn enables a direct and anatomically accurate impression of the ONH to be built. As previously mentioned, improved resolution does come at the expense of losing volumetric data, but Bruch's membrane opening–rim width parameters do correlate well with visual field sensitivity (Figure 6).[6] In particular, the Bruch's membrane opening–minimum rim width (BMO-MRW), could offer the best diagnostic performance of OCT parameters including RNFL thickness.[7]

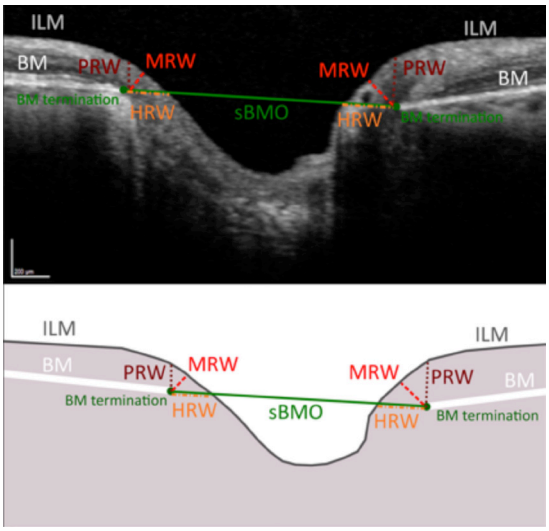

Figure 6: Bruch's membrane opening parameters.[6] Top: Original OCT image with manual measurements done with the built-in software. Bottom: Schematic illustration of measurements: internal limiting membrane (ILM; continuous grey line), Bruch's membrane (BM), Bruch's membrane termination (BM termination; dot), connection line between two BM terminations (sBMO; continuous green line), minimum rim width (MRW; dashed line), perpendicular rim width (PRW; dotted line), horizontal rim width (HRW; dashed-dotted line)

Retinal nerve fibre layer: Circumpapillary scan

The circumpapillary or circle scan is the mainstay of OCT glaucoma diagnostic capability.[8,9] It provides thickness measurements of the RNFL by intercepting all nerve fibres emanating from the disc. By placing the scan at around 3.5mm diameter, inaccurate measurements resulting from sampling through PPA are thereby reduced. The scan data is then rolled out, much like a rug is unrolled, to produce a RNFL thickness map beginning and ending nasally with superior, temporal and inferior quadrants successively between. Thickness is then compared to a normative database and plotted on a probability graph depicting 95%, 5% and 1% confidence limits, as shown in Figure 7. The greater amount of nerve fibres emanating from the superior and inferior sections of the optic disc is highlighted by the double hump of the RNFL thickening at those poles. Absence of this "double-hump sign" is an indicator of preferential nerve fibre loss in these areas and is, therefore, highly suspicious for glaucoma.

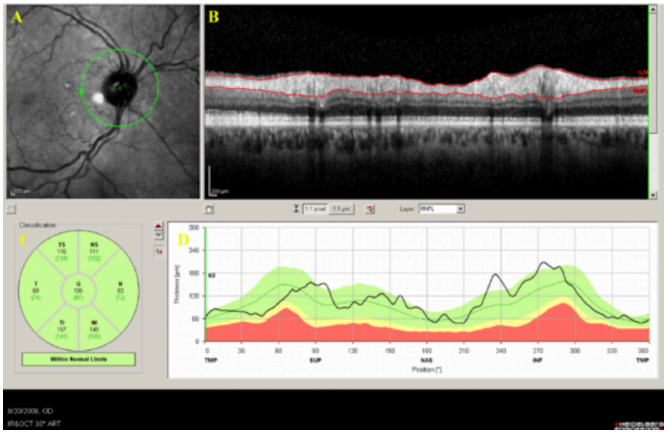

Figure 7: Screen grab from the Heidelberg Eye Explorer software automated analysis of the RNFL thickness. A: Infrared image showing the location of the circular scan (green circle) centred on the optic nerve (green cross) of the right eye. B: Circular optical coherence tomography image of the retina showing the RNFL segmented (red lines). C: RNFL thickness measurements in seven sectors as measured by the software. D: Plot of patient's RNFL thickness (black line) against normative values (coloured lines).

Sectoral averaging of RNFL thickness, (as shown in Figure 7C) is helpful to highlight more localised loss but can still mask very focal defects within these sectors. Thus it is important to trace the whole thickness plot graph, as shown in Figure 7D. Further divisions of sectors can help to avoid this problem.

Macula scan: Raster cube scan

With up to 50% of the total number of retinal ganglion cells present at the macula,[10] it follows that potential exists to employ macular scans to aid glaucoma detection and progression. Together with the intimate link between the RNFL and ganglion cells, and the extension of ganglion cells into the inner plexiform layer, the inner retinal layers are often combined in thickness analysis. The ganglion cell analysis within the Zeiss Cirrus OCT (Carl Zeiss Meditec, Dublin CA) combines both the ganglion cell layer and inner plexiform layer, whilst Topcon Maestro (Topcon Corporation, Tokyo) and Nidek Scan Duo (Nidek Co., Ltd, Japan) combines both of these layers with the RNFL naming it the ganglion cell complex (GCC). OCTs employ several parallel line scans, known as a raster scan, combined together across the macula to produce cross-sectional and volumetric data of the region.

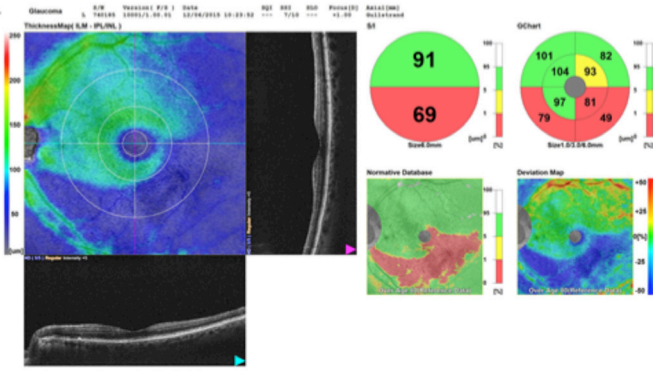

Figure 8: Scan Duo glaucoma macular analysis includes GCC thickness information overlaid onto the fundus image, superior vs. inferior hemifield, nine macular zones based on EDTRS diabetic screening format, comparison to normative database and deviation map. A significant asymmetry is shown, along with depiction of an inferior RNFL wedge defect.

The common element to any macular thickness analysis is a comparison between inferior and superior hemispheres, and between eyes. Although peripheral macular thickness asymmetry does occur between healthy eyes, central macular thickness is highly symmetric both between eyes and between superior/inferior hemispheres.[11] OCT software takes advantage of this by directly comparing superior and inferior hemispheres and central macular thickness zones, either divided into an overlying 3x3 degree grid pattern (as seen in the Heidelberg Spirit), or nine macular zones as dictated by the Early Treatment Diabetic Retinopathy Study (EDTRS) by the Scan Duo – as shown in Figure 8. Any statistically significant differences from normal at the 1% level are highlighted in red and should be investigated. Note that the foveal thickness is ignored due to a lack of inner retinal layers in this area.

In a review of macular assessment by OCT for glaucoma diagnosis, Sung et al[9] concluded that ganglion cell layer measures are generally inferior to RNFL measures in a diagnostic capability, but that they can be useful in specific cases. These include cases of advanced glaucoma where much of the RNFL and neuroretinal rim have been already lost; ganglion cell layer measures may be better indicators of further structural changes. Additionally, in early glaucoma which preferentially affects the central retina, ganglion cell layer measures may serve as an early indicator of structural changes.[12] Furthermore, GCC measurements were shown to be the best parameters for the clinical diagnosis of glaucoma in patients with high myopia[13] due to frequently anomalous ONH and surrounding retinal physiology such as tilted discs and PPA.

Interpretation of reports

OCT provides a wealth of information; therefore, a systematic approach to interpretation of the outcome reports is required to make the most from its utilisation. Across manufacturers, the common element of reporting data is the use of statistical comparison of thickness measures to a normal population database and representing this with green, yellow and red backgrounds. Thickness measures falling within 95% of normal limits are shown in green, measures occurring within 5% of normal limits are in yellow, and those occurring in ≤1% are highlighted in red. When interpreting reports, it is important to initially assess whether the data you have captured are corrupted by any errors or artefacts.

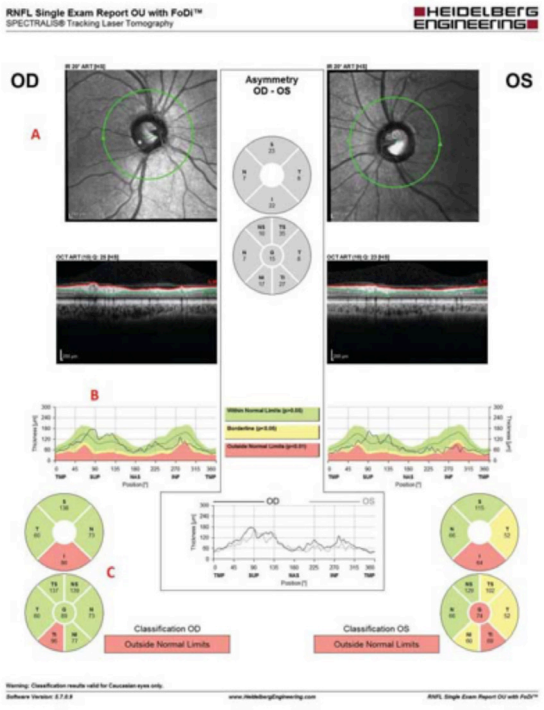

Figure 9: Spectralis RNFL OU Report.
A: Fundus image with RNFL segmentation below and sectoral eye asymmetry shown in microns. B: RNFL thickness profiles. C: Pie charts show the average RNFL thickness of each sector with the global average shown centrally as compared to a normative database. The classification bar displays the worst sector result. The combined RNFL profile for both eyes is shown centrally. Here, both eyes indicate thin inferior-temporal RNFL, which is indicative of early to moderate glaucoma.

When interpreting OCT reports, there are a number of elements to consider, including:

a) Signal strength: Low signal strength causes artificial thinning of the RNFL and significantly affects the diagnostic and monitoring ability of the OCT. Cataract, small pupils and dry eye disease are common causes. It is important to be aware of the recommended minimal signal strength for your machine. The Scan Duo has a minimum SSI score of 7 or above to perform an accurate scan whilst the Spectralis recommends a minimum quality score of 15.

b) Accuracy of segmentation: Segmentation is the process by which the OCT identifies the various retinal layers on which thickness measurements are then based. Generally, the algorithms recognise retinal layers very well, but highly reflective structures, such as an epiretinal membrane or posterior hyloid face, may result in the OCT being unable to distinguish the true retinal layers, giving rise to segmentation errors. Therefore, check the segmentation is correct before interpreting the output.

c) Presence of artefacts: A significant number of scans may contain artefacts which can easily result in the false identification of abnormal scans. Whilst head tilt, blinking, eye movements and scan centration issues are by far the most common artefacts, modern software technology such as eye tracking and anatomical centration are reducing the impact of these issues.

Be particularly mindful of natural variation and cases of myopia. The marked natural variation in ocular parameters between individuals is not reflected in the standard database used by OCTs so caution has to be applied when confronted with an abnormal or "red" scan. Just as most visual field tests highlight thresholds statistically different from normal, the OCT applies statistical analysis to the measured parameters and compares them to its own database highlighting any parameters statistically different from normal. However, this does not necessarily mean that they are abnormal. Normative databases are typically taken from around 200 patients, who may be mostly or exclusively Caucasian in origin. Marked variation in the appearance of the ONH, RNFL thickness variations (especially found in large or small eyes) or anatomical variations in the distribution of RNFL, which result in thickness peaks outside the typical inferior and superior sectors, can all be flagged as falsely abnormal. Fortunately, the latter variation can be easily recognised by the retained existence of the "double hump" sign in the RNFL thickness map which is simply shifted to different quadrants in the analysis.

Moderate to high myopia requires the circumference of the scanning circle around the disc to be larger and RNFL thickness is, therefore, taken further away from the centre of the disc. Given the natural convergence of the retinal nerve fibres at the disc, this results in an apparent reduction in RNFL thickness as the fibres are more dispersed. Together with PPA and possible anomalous disc insertion, caution should be maintained with the interpretation of myopic disc and RNFL scans.

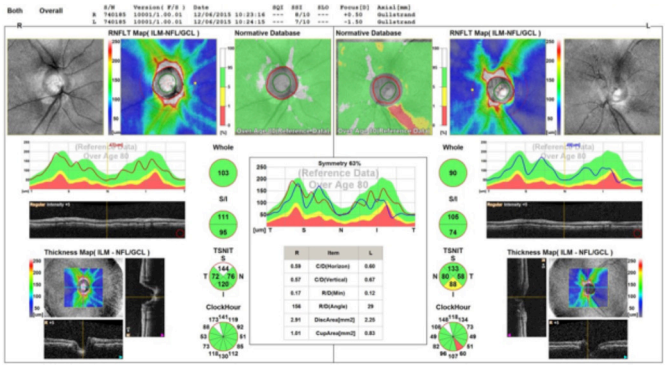

Figure 10: Nidek Scan Duo disc and RNFL analysis report shows fundus image, RNFL thickness map and normative database map (top section); individual and combined TSNIT graphs with analysis charts and table (middle section) with an OCT image of disc circle (lower right and lower left). Results indicate thicker than normal superior RNFL in the RE, but with focal thinning in the inferior-temporal sector of the LE. The LE is highly suspicious for glaucoma and results need to be integrated with fields, IOP and stereo-disc view for diagnosis.

Once signal strength, segmentation accuracy, the presence of artefacts and natural variations have been considered, the scan output becomes more meaningful and reliable. The most effective diagnostic detection is achieved by combining multiple scans of RNFL, ONH and ganglion cell analysis to demonstrate similar outcomes.[14,15] Similarly, the OCT functions best when combined with disc assessment, IOP and visual field testing,[16] so always endeavour to avoid taking OCT results in isolation.

OCT and glaucomatous progression

Structural changes observed at the ONH are predictive of future functional loss[17] and therefore carry clinically relevant prognostic information. The current gold standard method of structural progression detection in glaucoma is serial stereo-disc photography which is inherently difficult due to the qualitative and subjective nature of the assessment. By utilising the resolution and reproducibility capability of OCT, significant potential lies in monitoring structural parameters over time to identify glaucomatous progression. Indeed, several studies have been able to use OCT to reliably detect changes in RNFL thickness,[12,14,18–20] macular thickness[12,14,16] and ONH parameters[9,17] over time in both healthy individuals and those with glaucoma. OCT software typically utilises event-analysis to compare measurements to a specific baseline and look for statistical differences, or trend-analysis to assess gradual change over time, or indeed both as shown in Figure 11.

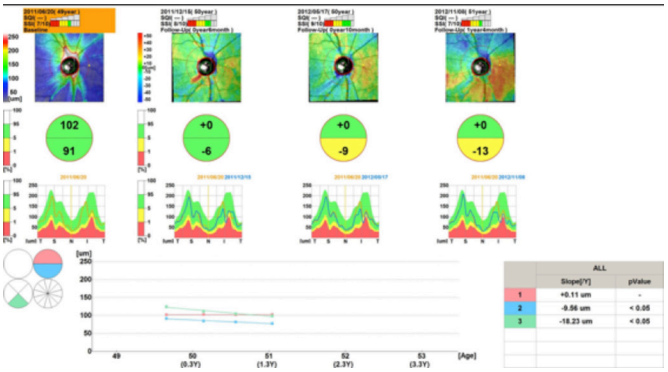

Figure 11: RNFL progression by Scan Duo depicts both event-analysis comparing sequential imaging to a baseline (top left image) including inferior/superior thickness change, together with trend-analysis shown in the lower graph.

However, the analysis of glaucoma progression using OCT has been hampered by several factors, particularly the uncertainty surrounding the precise definition of what constitutes progression. Lack of compatibility between current devices and prior models, relatively infrequent testing frequency,[21] and a wide variation of change between both healthy individuals[17] and those with glaucoma[19] can muddy the waters. Progression detection can also be variable at best, or poor at worst, depending on the detection strategy used.[12] Furthermore, myopia confounds the evaluation of glaucoma progression as it is difficult to discern the difference between progression due primarily to myopia or glaucoma.[8]

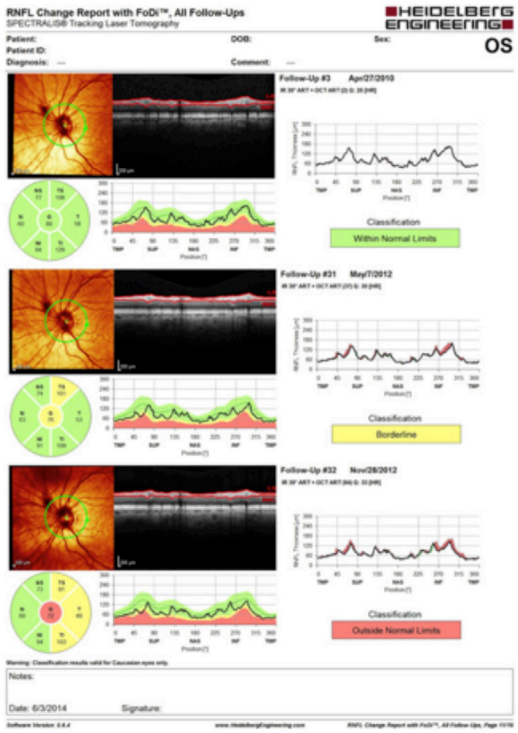

Figure 12: Spectralis RNFL change report indicating event-analysis change both by sector (on the left) and thickness graph (to the right) over successive scans.

Currently, RNFL measures have been found to be the dominant parameter in the detection of glaucoma progression;[8,19] however, the newer BMO-MRW measures are promising.[7] Despite the drawbacks outlined above, glaucomatous progression is now being indicated by OCT with an annual reduction in RFNL thickness of just over 2µm per year;[14,20] it remains to be seen if this will become the accepted standard.

Summary

Although OCT parameters have been shown to exhibit diagnostic capabilities for glaucoma, they do not yet have sufficient capability to be used as a screening tool.[22] The best diagnostic detection comes from combining RNFL, ONH and GCC analysis with the traditional assessment of ocular examination, IOP measurement and visual field testing. With ever-improving scan and software technology, reliable detection of glaucomatous progression is now on our doorstep.

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