

ASSESSMENT OF CLINICAL AND IMAGISTIC STRUCTURAL PROGRESSION IN GLAUCOMA

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Abstract

Glaucoma is a progressive optic neuropathy, characterized by loss of retinal ganglion cells and retinal nerve fiber layer as well as visual field loss. Therefore, in glaucoma, the correlation between structure and function is important, since it can be useful for tracking glaucomatous changes and for following the progression of the disease.

Keywords: glaucoma progression, structural progression, optic nerve damages, optical coherence tomography

Glaucoma is a progressive optic neuropathy, characterized by loss of retinal ganglion cells and retinal nerve fiber layer (RNFL) as well as visual field loss [1,2]. Therefore, in glaucoma, the correlation between structure and function is important, since it can be useful for tracking glaucomatous changes and for following the progression of the disease [3].

In everyday practice, spectral domain ocular coherence tomography (SD-OCT) became rapidly one of the most outspread technologies, due to the high resolution of the images and to the accuracy of measurements. It is assumed that thickness changes in RNFL usually precede visual field defects [4].

Histological findings show that visual field defects occur only after the loss of an important number of retinal ganglion cells [5,6]. Furthermore, it has been proved that in the initial stages of glaucoma, modifications of the optic nerve are more obvious than those in the visual field, while in more advanced stages, visual field changes are more pronounced comparing to the morphological changes [7].

Assessment of the optic disc and RNFL is an essential step in detecting glaucoma progression and consists of: slit lamp examination using proper lenses (60D, 78D, 90D) or by stereo photography, when is possible. If stereo photography is not available, describing cup/disc ratio and drawing the optic disc appearance can be useful for quantifying its aspect at a certain moment. However, the high interobserver variability makes this method a limited one, whenever assessment of progression is necessary. Although stereo photography of the optic disc offers an objective documentation, it can be interpreted in a very subjective way.

While examining serial photographs of the optic disc, made during time, for spotting the progression, clinician must look for the following elements (**Fig. 1**):

- Diffuse or focal enlargement of optic nerve cup, with the corresponding shrinking of the neuroretinal rim. Usually, the enlargement of the optic nerve cup is vertical, first changes being

spotted at the inferior or superior sectors of the excavation;

- Displacement of retinal vessels concomitant with the enlargement of the excavation, due to the disappearance of the tissular support. The displacement is mostly nasal, the typical aspect being "bayonet"-like;

- Peripapillary hemorrhages –with a "flame"like aspect, usually located in the inferior sector of the optic disc. Approximately 60% of the glaucoma patients that have a peripapillary hemorrhage develop progression of the visual field defects, corresponding to the location of the haemorrhage, in the next 16 months.

- Development and widening of the retinal nerve fiber layer defects.

- Widening of the peripapillary atrophy. A loss of neuroretinal rim and a correspondent visual field defect can occur correspondent with the atrophic area.

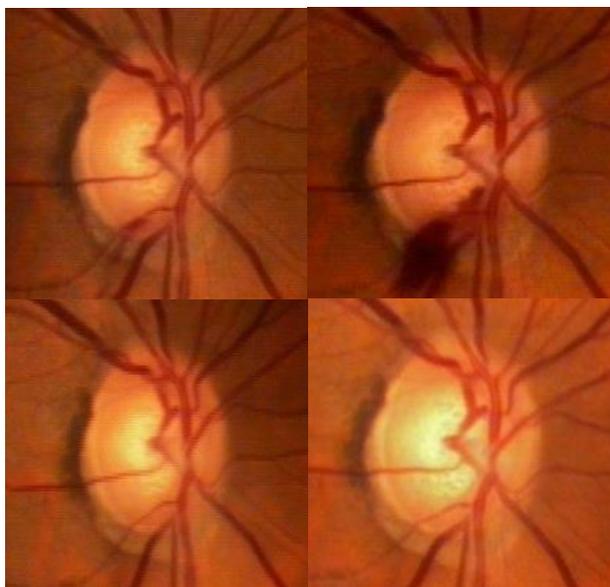


Fig.1 Evolution of structural defects after 3years: diffuse thinning of the temporal and inferotemporal rim, evolving localized defect ("notch") after resolution of papillary hemorrhage; C/D ratio has increased from 0.5 (initial) to 0.7 (final).

One has to remember that poor quality images and the differences of exposure, focus, magnification and angle of acquiring the image

scan give a false impression of evidence of progression.

Optical coherence tomography (OCT)

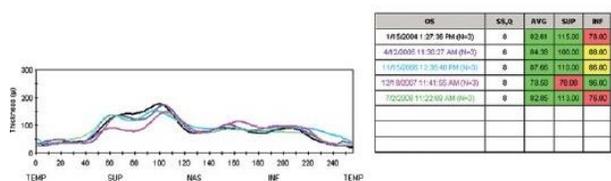
Time Domain OCT (TD OCT)

Stratus OCT provides images with an axial resolution of 8-10 μ and a transverse resolution of about 20 μ . The device can acquire several sections, linear or circular, but the most used to assess glaucoma is "Fast RNFL Scan". This makes a circular scan centered on the optic nerve, with a diameter of 3.4 mm, automatically determining the thickness of the RNFL, which is reported as the average thickness in the 4 quadrants of the 12 hours, a thinning of RNFL being an early sign of glaucoma. Quantitative information about the optic nerve and macular thickness are also provided.

It is shown that OCT has a high reproducibility intra- and interest in detecting diffuse or focal glaucomatous defects. Therefore, little variability in the measurements of RNFL makes OCT to be a useful tool for longitudinal follow-up of patients and to detect progression. In terms of repeatability of data, it is accepted that, in 95% of measurements made in 2 consecutive days in the same eye, to obtain a mean RNFL changed by no more than 8 to 9.5 μ . Values outside this range can suggest progression. Also, the variability is higher in quadrants and sectors compared to those recorded in the average RNFL thickness.

Stratus OCT latest model shave the following three ways of determining the change occurring over time (**Fig. 2**):

- A summary of the average RNFL thickness, including upper and lower quadrants at all visits.
- A graphical representation of RNFL thickness at all visits.
- A linear regression analysis to determine the thickness of the RNFL change over time.



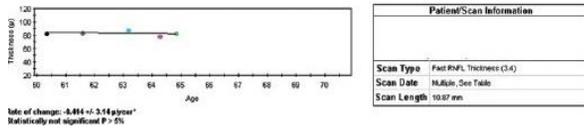


Fig. 2 Change of average RNFL thickness, statistically insignificant

The first two methods allow the identification of changes occurring over time, but do not indicate the significance of this change. Linear regression analysis indicates whether the change is significant only to "zero slope" (no change). In most cases this change may be due to RNFL loss caused by ageing process, which according to studies can vary between 0.16 to 0.31 µm/year. Therefore, this type of analysis can indicate the change because of the physiological loss due to aging and not always due to progression of glaucoma.

Clinical studies that have evaluated the utility of TD-OCT in assessing the progression revealed a higher rate of progression detected with OCT compared with standard automated perimetry, suggesting that OCT might be more sensitive to change. This conclusion can be explained by the fact that structural changes precedes functional loss in glaucoma or it may represent a high false positive rate. Therefore, further longitudinal studies are needed to better understand how to discriminate between the real progression of the disease and the false positive results.

Spectral Domain OCT (SD-OCT)

SD-OCT represents a newer generation of OCT, with a shorter scanning time and increased resolution comparing to TD-OCT (axial resolution of 5-6 µ meters and transverse resolution of 20 µ meters). It also offers 3D images of the scanned areas. Due to these improvements and the very good intra-test and inter-test reproducibility, SD-OCT is a very efficient tool in detection of glaucoma progression. A decrease of 4 µ meters or more of the RNFL thickness may represent a real structural change suggestive for progression. The most important devices that use this technology are: Spectralis OCT (Heidelberg Engineering Carlsbad, California), Cirrus HD-OCT (Carl Zeiss Meditec), RTVue-100 (Optovue,

Fremont, California) and Topcon 3D-OCT 2000 (Topcon, Oakland, New Jersey). Each of these has a different scanning model and different software for glaucoma progression analysis.

Cirrus HD-OCT Guided Progression Analysis (GPA) offers a comparison between the first visit (set as baseline) and the following exams in terms of RNFL thickness measured circumpapillary in a circle of 3.4 mm diameter centered on the optic disk. It also provides a linear regression analysis of the mean RNFL thickness, for the superior and the inferior quadrants and for C/D ratio. The software also reports the change from baseline for every scanned pixel, which also makes possible the analysis of change outside the circumpapillary area, when we suspect the extension of the defects outside the limits of the scan circle (**Fig. 3**).

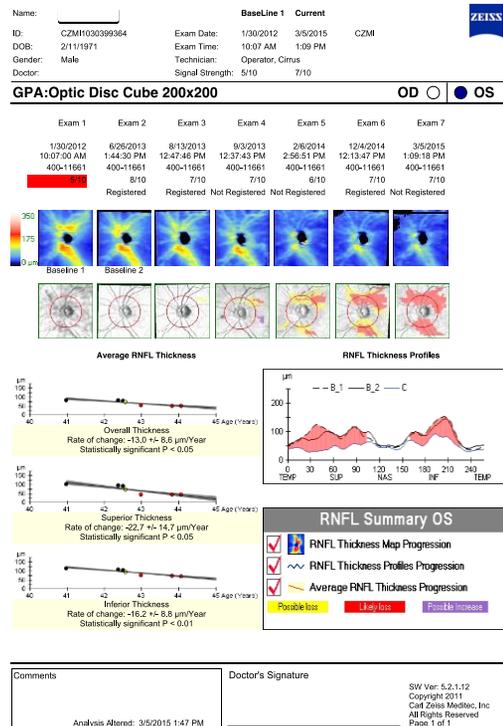


Fig. 3 GPA showing progression

In progression analysis using SD-OCT, artifacts should be carefully detected and corrected. Except for the Spectralis OCT with its eye-tracking technology, motion artifacts can

occur and interfere with accurate progression analysis.

Media opacity or irregular corneal surface can cause suboptimal OCT image quality that also affects the RNFL or macular thickness measurements. Coexisting posterior segment pathologies including epiretinal membrane and retinoschisis may cause overestimation of RNFL or macular thickness, leading to false-negative results. Additionally, clinicians should also consider age-related decline of RNFL and macular thickness when assessing glaucoma progression [8].

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