Comparison between GDx VCC scanning laser polarimetry and Stratus OCT optical coherence tomography in the diagnosis of chronic glaucoma

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ABSTRACT.

Purpose: **To compare the abilities of scanning laser polarimetry with the variable corneal compensator (GDx VCC) with those of optical coherence tomography (Stratus OCT) in discriminating between healthy and early-to-moderate perimetric glaucomatous eyes.**

Methods: **A total of 95 glaucomatous patients (mean deviation −3.7 ± 3.0 dB, pattern standard deviation 4.5 ± 2.7 dB) and 62 control subjects underwent imaging by the GDx VCC and Stratus OCT using both optic nerve head (ONH) and retinal nerve fibre layer (RNFL) scan protocols. One eye per patient was considered. Sensitivity at ≥90% specificity and area under the receiver operating characteristic curve (AROC) were calculated for each GDx VCC and Stratus OCT index.**

Results: **The largest AROCs with Stratus OCT were associated with cup : disc area ratio (0.88) for ONH scan indices, and with average thickness (0.84) for RNFL scan indices. The nerve fibre indicator provided the greatest AROC for the GDx VCC indices (0.85).**

Conclusions: **Both the GDx VCC and Stratus OCT instruments were shown to be useful in the detection of glaucomatous damage. The best performing indices for the GDx VCC and Stratus OCT with both ONH and RNFL scans gave similar AROCs, showing a moderate sensitivity in early-to-moderate glaucoma patients.**

Key words: scanning laser polarimetry – optical coherence tomography – ocular hypertension – primary open-angle glaucoma – sensitivity – specificity

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Introduction

Glaucoma is a chronic optic neuropathy in which morphological changes occur at the optic nerve head (ONH) and the retinal nerve fibre layer (RNFL), which may be associated with functional deficits (visual field defects). Although standard automated perimetry (SAP) is still considered to be the gold standard for the diagnosis of visual field (VF) defects, several studies have demonstrated that it can only detect VF loss after a significant percentage (30–40%) of nerve fibre loss (Quigley et al. 1982).

There is increasing evidence in the literature that ONH and peripapillary RNFL structural damage may precede SAP VF loss (Quigley et al. 1982, 1989; Sommer et al. 1991; Harwerth et al. 1999; Johnson et al. 2000). An accurate evaluation of RNFL and ONH damage thus seems to be crucial for an early diagnosis of glaucoma.

New, computerized, non-contact glaucoma imaging techniques, such as scanning laser polarimetry (SLP) and optical coherence tomography (OCT), appear to facilitate accurate quantitative analysis of the ONH and RNFL.

Scanning laser polarimetry assesses peripapillary RNFL thickness. The measurement is based on the birefringence properties of ganglion cell axon neurotubules that alter the laser scanning beam polarization according to thickness (Weinreb et al. 1995). The new SLP version, the glaucoma diagnosis system with variable corneal compensator (GDx VCC) (Zhou & Weinreb 2002), has been shown to improve the diagnostic ability of the SLP system in discriminating between healthy and glaucomatous eyes (Greenfield et al. 2002).

Optical coherence tomography (Huang et al. 1991) uses a scanning interferometer to obtain a cross-section of the retina. The topographic representation is based on the reflectivity of the different retinal layers (Schuman et al. 1995). Optical coherence tomography was originally designed for assessing various layers of the retina, but recent improvements in third-generation machine software, Stratus OCT, have enabled the analysis of both RNFL thickness and the ONH (Medeiros et al. 2005).

Both SLP and OCT are able to provide reproducible measurements of RNFL thickness (Weinreb et al. 1995; Schuman et al. 1996) and to differentiate glaucomatous from normal eyes (Hoh et al. 2000; Bowd et al. 2001; Zangwill et al. 2001; Greaney et al. 2002; Medeiros et al. 2004a). There is considerable interindividual variability in RNFL thickness measurements in the healthy population (Quigley et al. 1990; Poinoosawmy et al. 1997), and thus the accurate diagnosis of glaucoma using computerized imaging techniques remains difficult.

The purpose of this study was to compare the abilities of the current commercially available versions of SLP and OCT, the GDx VCC and Stratus OCT, respectively, in discriminating between healthy eyes and those with early-to-moderate glaucomatous VF loss.

Materials and Methods

A total of 62 normal subjects and 95 patients with primary open-angle glaucoma (POAG) were enrolled in this observational cross-sectional study. Glaucoma patients were recruited from patients under the care of the Glaucoma Service of the Department of Ophthalmology at the Santa Maria della Misericordia Hospital, Udine, Italy. Normal subjects were recruited from staff members and volunteers. The research was conducted according to the tenets of the Declaration of Helsinki. Institutional Review Board approval was obtained for the study.

After giving informed consent, all subjects underwent a complete ophthalmological examination including best corrected visual acuity (BCVA) evaluation, slit-lamp examination, Goldmann applanation tonometry, gonioscopy and fundus biomicroscopy, followed by standard automated perimetry (SAP) testing, GDx VCC imaging of the peripapillary RNFL, and Stratus OCT imaging of both the ONH and the RNFL. All examinations were conducted within a period of 3 months. One eye per patient was randomly selected for inclusion, with the exception of cases in which only one eye met our inclusion criteria.

Inclusion criteria included: BCVA ≥ 0.7; open anterior chamber angle; absence of ocular pathologies other than glaucoma; reliable SAP testing results, and good SLP and OCT image quality.

Exclusion criteria included: refractive error higher than $\pm$ 5 dioptres; pupils < 3 mm in diameter; anterior angle alterations; presence of secondary causes of glaucoma; advanced glaucomatous VF defects; papillary anomalies; large peripapillary atrophy, and a history of previous intraocular surgery, diabetes mellitus, neurological disorders or medication that might alter SAP results. Mild nuclear sclerosis or rare drusen were not considered as exclusion criteria.

Controls were screened to ensure that they had normal intraocular pressure (IOP), normal ONH and RNFL appearance (no diffuse or focal rim thinning, cupping, optic disc haemorrhage or RNFL defects), and normal SAP results, and to exclude subjects with a family history of glaucoma or any ocular pathology. A normal visual field was defined as a mean deviation (MD) and pattern standard deviation (PSD) within 95% confidence limits and a glaucoma hemifield test result 'within normal limits'.

Patients who had both IOP $>$ 21 mmHg before treatment and reproducible SAP glaucomatous VF defects in two consecutive tests were diagnosed as having glaucoma, regardless of the appearance of the optic disc.

Standard automated perimetry testing was performed using the Humphrey field analyser (HFA) II 750 (Carl Zeiss Meditec Inc., Dublin, CA, USA) 30–2 test with the standard Swedish interactive threshold algorithm (SITA) strategy.

The results of SAP tests were classified as glaucomatous according to Anderson's criteria (Anderson & Patella 1999), in which at least one of the following was present:

(1) a cluster of at least three points in the pattern deviation probability plot, located in areas typical of glaucoma, having a probability level of $p \leq 5\%$, with at least one point having a probability level of $p \leq 1\%$; none of the points could be edge-points unless they were located immediately above or below the nasal horizontal meridian;
(2) a PSD with a probability level of $p < 5\%$, and
(3) glaucoma hemifield test results outside normal limits.

Reliable criteria for HFA tests included false-positive and false-negative responses of $< 33\%$ and fixation losses of $< 20\%$.

Glaucomatous VF defects were classified using the Glaucoma Staging System (Brusini 1996), which classifies severity in five stages. Fifty-four of the 95 glaucomatous eyes were classified as stage 1 (MD better than -5.0 dB, PSD < 5.0 dB) and 41 eyes as stage 2 (MD -5.0 dB to -9.0 dB, PSD 5.0–8.0 dB).

Scanning laser polarimetry imaging was performed using the GDx VCC (Carl Zeiss, Meditec Inc., Dublin, CA, USA) Version 5.1.0. General details regarding the GDx setting have been described elsewhere (Weinreb et al. 1995; Zhou & Weinreb 2002). The SLP imaging was performed using a scan circle of 3.2-mm diameter centred on the optic disc, and the mean of three measurements was used. All images with quality score gradings < 8 were excluded.

Optical coherence tomography imaging was performed using the Stratus OCT (Carl Zeiss Meditec Inc., Dublin, CA, USA) Version 2.0. Detailed descriptions of OCT principles have

been published previously (Huang et al. 1991; Hee et al. 1995). The OCT scans of the ONH and the RNFL were obtained with the fast-scanning mode, using the Fast Optic Disc Scan and the Fast RNFL Thickness 3.46 Scan protocols, respectively, in which all scans are aligned and acquired automatically after initial positioning by the operator. Measurements of the ONH by OCT were generated from six 6-mm radial linear scans, with each line 30 degrees apart, including 128 A-scans of the ONH. The automatic determination of the ONH margin as defined by the OCT software was used. The circumpapillary OCT scan was created from the mean of three 360-degree circular 3.46-mm diameter circumpapillary scans centred at the ONH. Each scan consisted of 256 individual A-scan samples distributed along the circle circumference. Good quality scans were defined as those with signal : noise ratios > 40 dB without an overt misalignment of the surface detection algorithm > 15% consecutive or 20% cumulative sampling points (A-scans). All images with uneven image reflectance and poor centration of the ONH were excluded.

The following parameters were considered:

- for the GDx VCC the 16 parameters listed in the extended parameter table printout, except inter-eye symmetry, were used. The GDx VCC software calculates summary parameters based on temporal (335–24 degrees), superior (25–144 degrees), nasal (145–214 degrees) and inferior (215–334 degrees) quadrants, and
- for the Stratus OCT the parameters listed in the ONH analysis results printout and the parameters listed in the RNFL thickness average analysis report printout were used. The software calculates average thickness (360-degree measurements), temporal quadrant thickness (316–45 degrees), superior quadrant thickness (46–135 degrees), nasal quadrant thickness (136–225 degrees), inferior quadrant thickness (226–315 degrees).

The differences between healthy and glaucomatous eyes were evaluated using the Mann–Whitney test. The best cut-off point for each GDx VCC and Stratus OCT index, defined as the numerical value dividing healthy from glaucomatous eyes with the highest probability, was determined. Sensitivity at ≥90% specificity and areas under the receiver operating characteristic curve (AROCs) for discriminating between healthy and glaucomatous eyes were calculated for the GDx VCC and Stratus OCT indices; an IOP > 21 mmHg and a repeatable abnormal SAP test were considered as gold standards. Differences between the AROCs were evaluated using the Hanley–McNeil method (Hanley & McNeil 1983). Statistical analysis was performed using SPSS 11.0 for Windows (SPSS Inc, Chigaco, IL, USA). A p-value of < 0.05 was considered statistically significant.

Results

The control subjects were significantly younger than the glaucomatous patients (Mann–Whitney test, $p < 0.02$; Table 1). Significant differences were found between control and POAG eyes for both SAP MD and PSD values (Mann–Whitney test, $p < 0.001$; Table 1).

As Tables 2 and 3 show, statistically significant differences were found between normal and POAG eyes for all indices, except: symmetry by GDx VCC, and disc area (ONH scan), Imax/Smax, Smax/Imax, Smax/Tavg, Imax/Tavg, Smax/Navg (RNFL scan) by Stratus OCT.

The sensitivities at ≥90% specificity of the GDx VCC indices ranged from 30.5% of the inferior maximum index to 67.4% of the nerve fibre indicator (NFI) index. For Stratus OCT ONH scan indices, sensitivities at ≥90% specificity ranged from 51.6% of the rim area index to 71.6% of the cup : disc area ratio index. For OCT RNFL scan indices, the values ranged from 27.4% of the nasal thickness average index to 65.3% of the average thickness index (Tables 2 and 3).

The single indices associated with the greatest AROC (Tables 2 and 3) were:

- GDx VCC: the NFI (AROC = 0.85), and
- Stratus OCT: the cup : disc area ratio (AROC = 0.88) for the ONH scan, and the average thickness (AROC = 0.84) for the RNFL scan.

No statistically significant differences were found between the AROCs for the best parameters of the GDx VCC (NFI, AROC 0.85) and Stratus OCT (cup : disc area ratio, AROC 0.88) (Henley–McNeil method, $z = 0.81$, $p = 0.43$). The same was observed for the AROCs for the best parameters of the Stratus OCT ONH scan (cup : disc area ratio, AROC 0.88) and of the Stratus OCT RNFL scan (average thickness, AROC 0.84) (Henley–McNeil method, $z = 1.17$, $p = 0.28$).

The best cut-off points for each GDx VCC and Stratus OCT index are listed in Tables 2 and 3, respectively. Cut-off points were not determinable for the indices for symmetry (GDx VCC), disc area (Stratus OCT ONH scan) or Imax/Smax, Smax/Imax, Smax/Tavg, Imax/Tavg, Smax/Navg (Stratus OCT RNFL scan) (Tables 2 and 3).

Discussion

There is increasing evidence of a redundancy in retinal ganglion cells and that structural damage of the ONH and peripapillary RNFL precedes detectable VF loss using SAP in early glaucomatous optic neuropathy (Sommer et al. 1991; Harwerth et al. 1999). Quigley et al. (1982, 1989) demonstrated that 40% axonal loss may occur before any detectable change in visual function with SAP. Sommer

Table 1. Patient demographics and Humphrey field analyser 30-2 test results.

	Controls (eyes = 62)		POAG (eyes = 95)		Comparison between groups p*
	Mean ± SD	Range	Mean ± SD	Range	
Age (years)	66 ± 9.9	(38–79)	71 ± 10	(39–83)	< 0.02
MD (dB)	− 0.5 ± 0.6	(0.54 to − 1.5)	− 3.7 ± 3.0	(1.1 to − 7.6)	< 0.001
PSD (dB)	1.5 ± 0.3	(1.0–2.2)	4.5 ± 2.7	(1.8–8.2)	< 0.001

POAG = primary open-angle glaucoma; SD = standard deviation; PSD = pattern standard deviation.
* Mann–Whitney test.

Table 2. Sensitivity at ≥90% specificity, area under the AROC and best cut-off points of GDx VCC indices.

Parameters	Control group	POAG group	p*	Sensitivity at ≥90% specificity (%)	AROC	Best cut-off point
Nerve fibre indicator	19.0 ± 8.2	41.9 ± 21.6	< 0.01	67.4	0.85	> 25
TNSIT average	55.8 ± 5.1	49.6 ± 8.0	< 0.01	45.3	0.73	< 50.71
Superior average	68.3 ± 6.5	56.6 ± 10.9	< 0.01	55.8	0.82	< 58.62
Inferior average	62.3 ± 6.8	54.6 ± 10.2	< 0.01	42.1	0.75	< 53.53
TNSIT standard deviation	21.6 ± 4.1	16.6 ± 5.0	< 0.01	56.8	0.78	< 17.89
Symmetry	0.97 ± 1.1	0.96 ± 1.0	NS	–	–	NA
Superior ratio	2.90 ± 0.64	2.10 ± 0.75	< 0.01	57.9	0.78	< 2.18
Inferior ratio	2.84 ± 0.73	2.17 ± 0.69	< 0.01	53.7	0.74	< 2.32
Superior/nasal	2.32 ± 0.56	1.88 ± 0.63	< 0.01	48.4	0.71	< 1.95
Maximal modulation	2.10 ± 0.70	1.44 ± 0.68	< 0.01	35.8	0.75	< 1.76
Superior maximum	79.8 ± 8.5	66.8 ± 15.3	< 0.01	46.3	0.74	< 70.53
Inferior maximum	77.7 ± 11.7	70.1 ± 13.8	< 0.05	30.5	0.67	< 71.95
Ellipse modulation	3.47 ± 1.11	2.40 ± 1.0	< 0.01	46.3	0.77	< 2.36
Normalized superior area	0.139 ± 0.02	0.100 ± 0.03	< 0.01	64.2	0.84	< 0.1179
Normalized inferior area	0.137 ± 0.03	0.111 ± 0.03	< 0.01	42.1	0.73	< 0.1165

POAG = primary open-angle glaucoma; AROC = receiver operating characteristic curve; TNSIT = temporal-nasal-superior-inferior-temporal; NS = not significant; NA = not applicable.
* Mann-Whitney test.

Table 3. Sensitivity at ≥90% specificity, area under the AROC and best cut-off points of Stratus OCT indices.

Parameters	Control group	POAG group	p	Sensitivity at ≥90% specificity(%)	AROC	Best cut-off point
Optic nerve head scan						
Vertical integrated rim area (vol)	0.60 ± 0.34	0.24 ± 0.22	< 0.01	68.4	0.86	< 0.278
Horizontal integrated rim width (area)	1.87 ± 0.34	1.37 ± 0.31	< 0.01	67.4	0.87	< 1.491
Disc area	2.38 ± 0.51	2.39 ± 0.51	NS	–	–	NA
Cup area	0.55 ± 0.51	1.17 ± 0.65	< 0.01	64.2	0.82	> 0.824
Rim area	1.83 ± 0.61	1.22 ± 0.51	< 0.01	51.6	0.81	< 1.337
Cup : disc area ratio	0.23 ± 0.19	0.48 ± 0.22	< 0.01	71.6	0.88	> 0.337
Cup : disc horizontal ratio	0.48 ± 0.18	0.69 ± 0.19	< 0.01	60.0	0.81	> 0.631
Cup : disc vertical ratio	0.43 ± 0.16	0.65 ± 0.18	< 0.01	63.1	0.84	> 0.564
Retinal nerve fibre layer scan						
Superior thickness average	127.9 ± 18.4	98.0 ± 24.4	< 0.01	63.1	0.83	< 105
Inferior thickness average	128.3 ± 20.8	100.9 ± 28.1	< 0.01	53.7	0.78	< 103
Nasal thickness average	79.5 ± 17.7	65.9 ± 19.5	< 0.01	27.4	0.71	< 63
Temporal thickness average	71.7 ± 12.7	59.2 ± 15.0	< 0.01	42.1	0.74	< 59
Superior maximum	157.6 ± 20.6	123.8 ± 26.7	< 0.01	61.0	0.83	< 132
Inferior maximum	161.8 ± 28.8	129.7 ± 35.6	< 0.01	40.0	0.74	< 133
Imax/Smax	1.0 ± 0.16	1.1 ± 0.2	NS	–	–	NA
Smax/Imax	1.0 ± 0.15	1.0 ± 0.2	NS	–	–	NA
Smax/Tavg	2.2 ± 0.4	2.2 ± 0.5	NS	–	–	NA
Imax/Tavg	2.3 ± 0.5	2.2 ± 0.6	NS	–	–	NA
Smax/Navg	2.1 ± 0.5	2.0 ± 0.6	NS	–	–	NA
Maximum–minimum	125.3 ± 24.8	101.5 ± 23.6	< 0.01	46.3	0.74	< 105
Average thickness	101.8 ± 11.8	80.9 ± 18.0	< 0.01	65.3	0.84	< 88.79

POAG = primary open-angle glaucoma; AROC = receiver operating characteristic curve; TNSIT = temporal-nasal-superior-inferior-temporal; NS = not significant; NA = not applicable.
* Mann-Whitney test.

et al. (1991) reported that 60% of patients with ocular hypertension had evidence of RNFL loss that occurred up to 6 years before a detectable change in SAP. Harwerth et al. (1999) found a non-linear relationship between ganglion cell loss and visual sensitivity in rhesus monkeys with unilateral experimental glaucoma for ganglion cell losses of 30–50%. The Ocular Hypertension Treatment Study (Kass et al. 2002) demonstrated that 55% of eyes that converted to glaucoma had isolated progressive optic disc structural damage without co-existing changes in visual function using SAP. Sampaolesi et al. (2003) found significant defects using frequency doubling technology in 40% of patients with ocular hypertension having an optic nerve damage shown by the Heidelberg Retina Tomograph.

Significant advances in imaging technologies, such as SPL and OCT, allow quantitative and reproducible measurements of the ONH and the peripapillary RNFL (Weinreb et al. 1995; Schuman et al. 1996). Previous studies using former versions of the SLP and OCT systems have demonstrated similar ability in the diagnosis of early-to-moderate glaucoma (Sanchez-Galeana et al. 2001; Greaney et al. 2002). Some

authors have even suggested that OCT may be better than GDx at detecting glaucomatous RNFL loss (Bowd et al. 2001; Zangwill et al. 2001).

The software has recently been updated in both devices. For the SLP, a variable corneal compensator has replaced the former fixed compensator, which in essence, has improved GDx diagnostic accuracy (Greenfield et al. 2002; Zhou & Weinreb 2002; Weinreb et al. 2003). The new Stratus OCT provides better resolution (8–10 μm compared with 10–15 μm in the former versions) and easier image acquisition, thus reducing the need for pupil dilatation. It also provides data on the probability of abnormality of patient examination results by comparison with an internal normative database (Jaffe & Caprioli 2004). The ONH can also be studied with the new Stratus OCT, although a normative database for ONH scan parameters is not yet available. A recent study comparing the GDx VCC with Stratus OCT found them to give similar diagnostic performances in discriminating between healthy and glaucomatous eyes; however, the Stratus OCT ONH scan indices were not considered (Medeiros et al. 2004b).

To the best of our knowledge, this is the first study to provide a comparison of the diagnostic abilities of the current GDx VCC and Stratus OCT in which Stratus OCT ONH scan indices were considered.

To avoid introducing a subjective component to our analysis, the OCT automatic algorithm for detecting the disc margin was used in this study, although a manual algorithm is also available. In any case, the manual and automatic algorithms have been demonstrated to have comparable performances (Schuman et al. 2003).

The measurements obtained in the present study for healthy control eyes (Tables 2 and 3) were comparable with those reported by other authors for both the GDx VCC (Medeiros et al. 2004a, 2004b) and Stratus OCT (Medeiros et al. 2004b, 2005; Wollstein et al. 2005).

As other authors (Reus & Lemij 2004) have found, the single index of the GDx VCC with the best diagnostic performance was the NFI, with an AROC of 0.85. The Stratus OCT indices with the largest AROC were cup : disc area ratio (AROC 0.88) for ONH scan indices, and average thickness (AROC 0.84) for RNFL scan indices. No statistically significant differences were found between the AROCs of the best performing indices of the GDx VCC (NFI, AROC 0.85) and Stratus OCT (cup : disc area ratio, AROC 0.88).

With regards to the Stratus OCT indices, the ONH scan indices generally performed better than those for the RNFL (Tables 2 and 3). The AROCs of the best discriminating indices for the ONH and RNFL scans (cup : disc area ratio and average thickness, respectively) did not, however, show any statistically significant difference (0.88 versus 0.84), in agreement with previous reports (Medeiros et al. 2005; Wollstein et al. 2005).

As is already known, glaucomatous optic nerve damage seems to begin in the inferotemporal and superotemporal areas (Mabuchi et al. 2004). According to this clinical observation, assessing RNFL thickness in the superior (Nouri-Mahdavi et al. 2004) and inferior regions (Bowd et al. 2001; Zangwill et al. 2001; Medeiros et al. 2004b) is often the best way of discriminating healthy eyes from eyes with early-to-moderate glaucoma, using OCT. In our experience, superior thickness average performed better than that for the inferior quadrant (Table 3). However, the values refer to the entire quadrant and may underestimate a reduction in thickness in a single clock-hour sector.

Further, the ratio indices of the GDx VCC performed significantly better than those provided by the Stratus OCT (Tables 2 and 3). This difference may be related to the different extension of the peripapillary RNFL quadrants provided by the two instruments.

The AROCs of all indices analysed in this study were slightly lower than those reported in previous studies, both for the GDx VCC (Medeiros et al. 2004a, 2004b) and the Stratus OCT (Medeiros et al. 2004b, 2005; Wollstein et al. 2005). This discrepancy may be due to differences in glaucoma severity in the sample studied, with our patients having a level of damage lower than that of patients in the studies cited above.

Our results accord with those of other studies (Medeiros et al. 2004b; Reus & Lemij 2004; Budenz et al. 2005) that show that both GDx VCC and Stratus OCT fail to identify a moderate number of glaucomatous patients with VF defects when SAP is taken as the gold standard. This could be due to the wide variability in RNFL measurements in healthy subjects. Another important point to note is that software parameters are based on data from a large region of the ONH and/or the RNFL, thus limiting the detection of certain localized nerve fibre layer defects. Moreover, both imaging devices give morphological quantitative information but no information is available as to whether this tissue is fully functional, which is still a matter of great debate. Clinical decisions based solely on the interpretation of data obtained from any new glaucoma imaging technology should thus be made with caution.

Our study presents some limitations. Firstly, because ageing affects RNFL thickness and ONH topography, the difference in age between the normal and glaucomatous groups might have artificially improved the AROCs reported in this study. Secondly, another bias of our study was that the inclusion criteria for normal subjects required a normal optic nerve appearance at the clinical examination. This was required to avoid the inclusion of subjects with glaucomatous optic neuropathy but normal visual fields in the control group. This inclusion criterion may have overestimated the diagnostic accuracy of the OCT parameters, especially of ONH parameters. However, this is a limitation common to case-control studies of this type and no practical solution to the problem is currently available.

In conclusion, both the GDx VCC and Stratus OCT instruments were shown to provide clinically relevant information in the detection of glaucomatous damage. The best performing indices for the GDx VCC and Stratus OCT gave similar AROCs, showing a moderate sensitivity in early-to-moderate glaucoma patients. The ONH indices of the Stratus OCT seem to provide additional useful information in glaucoma patients, although an internal normative database for ONH scan indices would be advantageous in the clinical practice. Further studies are needed to better understand the relationship between structure and

function in glaucoma, especially when interpreting imaging data.

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