

# Quantitative assessment of optic disc photographs in normal and open-angle glaucoma patients

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## ABSTRACT

**BACKGROUND:** The purpose of the study was to quantitatively assess the optic nerve head (ONH) parameters from fundus photographs in normal and open-angle glaucoma patients and to compare them with those provided by spectral-domain optical coherence tomography (SD-OCT).

**MATERIAL AND METHODS:** This study compares 30 glaucomatous eyes to 30 healthy control eyes. One eye from each subject was randomly enrolled. From color photographs, different parameters were measured using image processing software (Adobe Photoshop CS6) after delimiting the boundaries of the optic disc and the excavation. The correlation between these measurements and those obtained by SD-OCT was evaluated.

**RESULTS:** Glaucomatous and normal patients groups were comparable in terms of age ( $p = 0.94$ ), sex ( $p = 0.57$ ), presence of diabetes ( $p = 0.52$ ), hypertension ( $p = 0.40$ ), and smoking ( $p = 0.67$ ). The areas of the optic disc and the cup were significantly larger in glaucomatous patients ( $p = 0.004$  and  $p < 0.001$ , respectively). The area of the neuroretinal rim was smaller in glaucomatous patients ( $p < 0.001$ ). The vertical and horizontal cup-to-disc ratios were larger in glaucomatous patients ( $p < 0.001$ ). The thicknesses of the rim in the four meridians were significantly reduced in the glaucoma group. The "ISNT" rule was fully respected in 87% of normal eyes and in only 2 cases (7%) of the glaucoma group ( $p < 0.001$ ). There was an excellent correlation between different measurements obtained on photography and those provided by the SD-OCT. Pearson's correlation coefficient was  $R = 0.95$  ( $p < 0.0001$ ) for the optic disc area,  $R = 0.94$  ( $p < 0.0001$ ) for the rim area, and  $R = 0.98$  ( $p < 0.0001$ ) for the vertical cup-to-disc ratio.

**CONCLUSION:** Color photography is very useful in the diagnosis and monitoring of glaucoma. The determination of normative values can further corroborate its interest in this indication. Despite the relatively high interobserver variability, ONH parameters obtained on photography showed excellent correlation with those measured by OCT

**KEY WORDS:** photography; SD-OCT; quantitative assessment; glaucoma; optic disc

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## INTRODUCTION

Open-angle glaucoma is a progressive optic neuropathy characterized by retinal ganglion cell loss

and structural changes in the retinal nerve fiber layer (RNFL) and optic nerve head (ONH) that may lead to visual field loss [1]. Diagnosis of glaucomatous

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damage is based on the ability of the clinician to detect signs of the disease through clinical evaluation of intraocular pressure (IOP), the appearance of the ONH and RNFL, and VF testing. The changes in the ONH can be described by many variables such as the size and shape of the optic disk; size, shape, and pallor of the neuroretinal rim; the size of the optic cup in relation to the area of the disc, ratio of cup-to-disc diameter and cup-to-disc area. The evaluation of the optic disc is an essential step in the diagnosis and monitoring of glaucoma. This assessment is based on quantitative and qualitative parameters. Initially, the optical disc was evaluated ophthalmoscopically by approximate measurements of its structure using a lens and a slit lamp with an adjustable slit height. These values are then multiplied by a corrective factor depending on the lens used. The main limitations of this technique are its high intra- and intergrader variability in interpreting the features of glaucomatous optic neuropathy, even among specialists [2]. Compared to ophthalmoscopic examination, photography offers the advantage of providing a permanent recording, which is very useful for documentation of the nerve's appearance at a given time, allowing more detailed scrutiny then and later comparison for changes.

Since it was introduced in 1991, optical coherence tomography (OCT) has risen to the forefront of ocular imaging because of its ability to deliver high resolution, reproducible, quantitative assessment of the optic nerve head parameters with advanced segmentation algorithms and rapid data acquisition [3]. It is important to note that OCT does not replace fundus photography in glaucoma screening and diagnosis. The two imaging modalities complement one another. Used in conjunction with OCT and visual field, optic disc photography improved glaucoma diagnosis accuracy and reduced variability [3, 4].

In this study, we evaluate the morphological profile of the optic disc in glaucomatous eyes compared to healthy eyes by performing quantitative measurements of different parameters from color photographs: the area of the optic disc, the cup and the neuroretinal rim, the vertical and horizontal cup-to-disc ratio, the width of the neuroretinal rim in its lower, upper, nasal and temporal regions. We also assess the agreement and correlation between these measurements and those obtained automatically by SD-OCT.

## MATERIALS AND METHODS

This is a prospective study including 30 glaucomatous patients. They were compared with

30 control patients matched for age, gender, and vascular risk factors. It was conducted in the ophthalmology department of the Military Hospital Med-V of Rabat in Morocco between January and March 2018. The study was approved by the review board and adhered to the tenets in the Declaration of Helsinki.

All subjects underwent a full ophthalmological examination with intraocular pressure (IOP) measurement using Goldmann's applanation tonometer, a gonioscopic examination, fundus examination after pupillary dilation, OCT of the optic disc, and automated perimetry (24-2 standard automated perimetry visual field obtained with the SITA-Standard Automated Perimetry strategy (Humphrey VF Analyzer; Carl Zeiss Meditec).

For the "glaucoma" group, we included patients followed up for primary open-angle glaucoma with:

- age over 45 years old;
- IOP (before treatment) > 21 mm Hg with or without glaucomatous abnormality of the optic disc in the biomicroscopic examination, with or without detectable deficit with OCT;
- visual field defects confirmed on at least two tests;
- open iridocorneal angle.

For the "control" group, the controls were selected from patients presenting for a reason other than glaucoma (prescription of glasses, ocular surface disorders) during the same period with:

- age over 45 years-old;
- IOP  $\leq$  21 mm Hg;
- normal visual field;
- open iridocorneal angle.

From the two groups, we excluded patients with:

- history of non-glaucomatous optic neuropathy;
- eyes with severe myopic degeneration, severe peripapillary atrophy, optic disc anomalies such as optic disc coloboma, optic disc drusen, optic disc edema, or optic nerve hypoplasia or atrophy;
- spherical refractive error over six diopters or astigmatism over three diopters;
- unilateral glaucoma (impossibility of randomization);
- poor-quality OCT scans (signal strength < 7/10).

All color photographs were taken on the same camera (Topcon TRC-50IX) at the same angle of coverage of 50°. The SD-OCT images of the optic nerve head were obtained with the commercial version of the Zeiss Cirrus 4000 HD-OCT instrument, Software version 6.0.2.81

The different measurements were carried out by the same blinded operator. The patient's iden-



**FIGURE 1.** **A.** Optic nerve head photography; **B.** The reader marks outlines of the optic disc and the cup; **C.** the reader marks the vertical diameter (VD) of the optic disc and the cup, the neuroretinal rim width at the inferior (I) and the superior (S) positions; **D.** the reader marks the Horizontal diameter (HD) of the optic disc and the cup, the neuroretinal rim width at the nasal (N) and the temporal (T) positions

tity, clinical information, SD-OCT images, and visual fields were not available to the reader of photographs. We used an image processing software: Adobe Photoshop CS6 extended. After delimiting the boundaries of the optic disc and the excavation by a senior reader, we measured: the areas of the optic disc, the excavation, and the neuroretinal rim; the vertical and horizontal diameter of the optic disc, and the width of the rim in its lower, upper, nasal and temporal regions (Fig. 1). The measurements in pixels were converted to an area (square millimeters) using a conversion factor. To find this conversion factor, representative photographs were obtained with the Topcon camera, and SD-OCT images were registered. From these, three pairs with excellent registration were chosen, and from identical portions of the two images, it was calculated that each pixel in the color photographs represented  $0.0000103 \text{ mm}^2$  or  $103 \text{ }\mu\text{m}^2$  in the SD-OCT image.

SPSS software version 20 was used for statistical analysis. The Kolmogorov-Smirnov test was used to assess the normal distribution of the variables. The significance of the differences in the findings was determined by Student's t-test, Mann-Whitney U test, Wilcoxon test, Chi-square test ( $\chi^2$ ). The Pearson correlation method was used to analyze the correlation of measurements with photography and OCT. A p-value less than 0.05 was considered statistically significant.

## RESULTS

The mean age was  $58 \pm 15$  years. Male/female ratio was 41/19. There were no significant differences between the two groups concerning age ( $p = 0.94$ ), sex ( $p = 0.57$ ), diabetes ( $p = 0.52$ ), hypertension ( $p = 0.40$ ), and smoking ( $p = 0.67$ ). The baseline characteristics of the patients are summarized in Table 1.

**Table 1. Baseline characteristics of subjects by groups**

Characteristics	Glaucoma group (n = 30)	Controls (n = 30)	p
Age*	58.8 ± 9	58.2 ± 17	0.94
Sex (Male/female)	22/8	20/10	0.57
Diabetes**	16.7	23.3	0.52
Hypertension**	26.7	36.7	0.40
Smoking**	6.7	13.3	0.67
Mean deviation [dB] <sup>†</sup> (visual field)	-7.29 ± 3.20	-1.12 ± 0.59	< 0.001

\*expressed as mean ± standard deviation; \*\*expressed as percentage

**Table 2. Optic disc parameters in the study groups measured by photography**

Parameter	Glaucoma group (n = 30)	Controls (n = 30)	p
<b>Area* [mm<sup>2</sup>]</b>			
Optic disc	2.52 ± 0.28	2.12 ± 0.35	0.004
Cup	1.58 ± 0.36	0.8 ± 0.12	< 0.001
Rim	0.87 ± 0.18	1.33 ± 0.27	< 0.001
<b>Disc diameter* [mm]</b>			
Vertical	1.84 ± 0.12	1.71 ± 0.13	0.01
Horizontal	1.68 ± 0.11	1.48 ± 0.15	0.002
<b>Cup-to-disc ratio</b>			
Vertical	0.60 ± 0.14	0.34 ± 0.15	< 0.001
Horizontal	0.54 ± 0.13	0.28 ± 0.09	< 0.001
<b>Rim width* [μm]</b>			
Inferior	414 ± 111	613 ± 81	< 0.001
Superior	394 ± 121	560 ± 81	< 0.001
Nasal	464 ± 121	532 ± 61	0.01
Temporal	353 ± 89	414 ± 70	0.02
ISNT rule intact**	2 (7)	26 (87)	< 0.001

\*expressed as mean ± standard deviation; \*\*expressed as number (percentage)

The dimensions of the optic disc were significantly larger in glaucomatous patients; the average optic disc area was  $2.52 \pm 0.28 \text{ mm}^2$  in the glaucoma group versus  $2.12 \pm 0.35 \text{ mm}^2$  in the control group ( $p = 0.004$ ). The vertical and horizontal diameters of the disc were larger in the glaucoma group ( $p = 0.01$  and  $p = 0.002$ , respectively). The cup area was significantly larger in glaucomatous patients ( $p < 0.001$ ). The rim area was smaller in glaucomatous patients ( $p < 0.001$ ). The vertical and horizontal cup-to-disc ratios were higher in glaucomatous patients ( $p < 0.001$ ). The width of the rim in glaucomatous patients was significantly smaller in its lower ( $p < 0.001$ ), upper ( $p < 0.001$ ), nasal ( $p = 0.01$ ) and temporal regions ( $p = 0.02$ ). The ISNT rule was fully respected in 87% of the control group and only in 7% of the glaucoma group

( $p < 0.001$ ). The measurements obtained from the photographs are presented in Table 2.

We compared the ONH parameter measurements obtained on photographs (optic disc area, rim area, vertical cup-to-disc ratio) with those automatically provided by SD-OCT. The mean areas of the optic discs and the neuroretinal rim determined by photography were larger by approximately 8% and 10%, respectively ( $p < 0.001$ ). On the contrary, the mean cup-to-disc area ratio was slightly smaller in photography by approximately 4,5% (Tab. 3). However, there was an excellent correlation between the different parameters measured on photographs and those provided by SD-OCT. Pearson's correlation coefficient was  $R = 0.95$  ( $p < 0.0001$ ) for the optic disc size,  $R = 0.94$  for the rim area ( $p < 0.0001$ ) and  $R = 0$ ,

**Table 3. Comparison between optic nerve head parameters obtained by photography and spectral-domain optical coherence tomography (SD-OCT)**

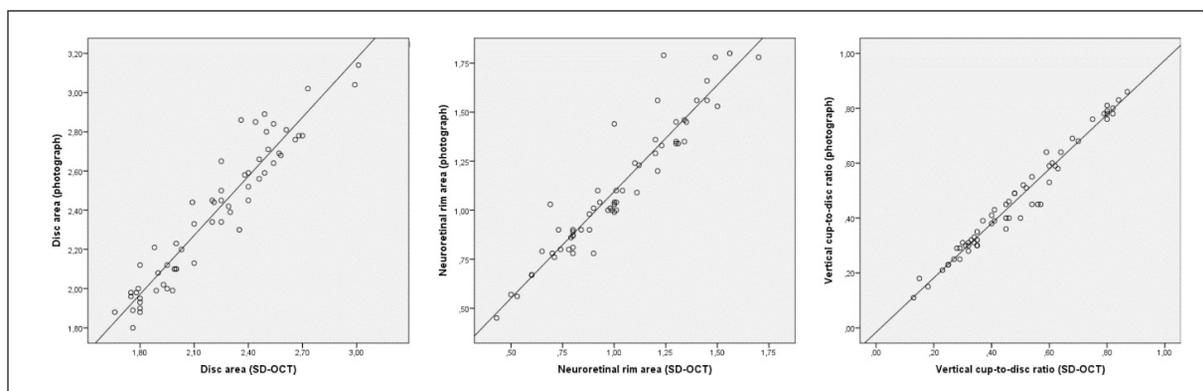
Parameter	Photography	SD-OCT	p
<b>Optic disc area [mm<sup>2</sup>]</b>			
Glaucoma group	2.52 ± 0.28	2.35 ± 0.23	< 0.001
Controls	2.12 ± 0.35	1.95 ± 0.29	< 0.001
<b>Rim area [mm<sup>2</sup>]</b>			
Glaucoma group	0.87 ± 0.18	0.80 ± 0.18	< 0.001
Controls	1.33 ± 0.26	1.22 ± 0.21	< 0.001
<b>Vertical cup-to-disc ratio</b>			
Glaucoma group	0.60 ± 0.14	0.62 ± 0.15	0.01
Controls	0.34 ± 0.15	0.37 ± 0.10	0.001

Data are presented as mean ± standard deviation

**Table 4. Correlation between optic nerve head parameters obtained by photography and spectral-domain optical coherence tomography (SD-OCT)**

Parameter	Photography	SD-OCT	Pearson's correlation coefficient ( <i>R</i> )	p
Disc area [mm <sup>2</sup> ]	2.38 ± 0.35	2.20 ± 0.33	0.95	< 0.001
Rim Area [mm]	1.11 ± 0.33	1.01 ± 0.28	0.94	< 0.001
Vertical cup-to-disc ratio	0.46 ± 0.19	0.48 ± 0.19	0.98	< 0.01

Data are presented as mean (standard deviation)

**FIGURE 2.** Correlation between the photographic measurements and spectral-domain optical coherence tomography (SD-OCT)

98 ( $p < 0.0001$ ) for the vertical cup-to-disc ratio (Tab. 4, Fig. 2).

## DISCUSSION

Careful observation of ONH is of great importance in the diagnosis and follow-up of glaucoma. Various techniques are available for estimating optic disc size. Each has specific strengths and limitations when applied to certain types of clinical and research objectives. Some of the measurement techniques are more applicable to clinical

practice than others [5]. Many studies have shown that qualitative and quantitative assessment of optic nerve photography is very useful for the detection of glaucoma with high sensitivity and specificity [6–9]. Comparisons have been made between human estimation and machine imaging with analysis software [10], as well as between different machines [11]. In the current study, we investigated the performance of the clinical evaluation, as represented by color photographs of the optic disc and its agreement with measurements obtained with SD-OCT.

Several studies have found equal optic disc sizes in both normal and glaucomatous eyes [12] while others have demonstrated larger disc areas in glaucomatous eyes. [13, 14] The optic disc area in the present study was significantly larger in the glaucomatous eyes. It was suggested that the large optic disc was one among other factors predisposing to glaucomatous optic nerve fiber loss even in the presence of a statistically normal intraocular pressure [15] Tuulonen et al. reported that large discs could be damaged by low intraocular pressure because of the property of the extracellular matrix [16]. Uysal et al. compared 70 eyes with early or moderate glaucomatous damage and 70 healthy eyes: mean disc area was significantly larger in the glaucoma group [13]. Mehdizadeh et al. presented a theoretical explanation for this finding. He proposed that biomechanical factors such as tensile stress ( $\sigma$ ) in the optic nerve head are the primary insult that leads to retinal ganglion cell loss. Tensile stress ( $s$ ) of the wall of a sphere is calculated by the formula:  $\sigma = PR/2t$ , where P is pressure, R is the inner radius of the sphere, and t is the wall thickness; then tensile stress and radius are directly related [17]. Considering that as a part of a sphere, the larger optic disc has a larger inner radius of curvature than that of a smaller disc, in a given constant IOP and lamina cribrosa thickness, the larger disc will suffer more tensile stress than that of a smaller disc. Therefore, a large optic disc is more susceptible to IOP rise than a small optic disc [18].

It has been shown that abnormalities in the appearance of the optic disc may precede visual field defects. These abnormalities include a high cup-to-disc ratio, an unusually small area of the neuroretinal rim, and an abnormal shape of the rim [19]. The estimation of the cup-to-disc ratio is one of the most frequently performed clinical methods for a simple assessment of the optic disc in glaucoma diagnosis and follow-up [5]. The vertical ratio is preferred to the horizontal ratio as the thinning of the rim and the optic cup enlargement in glaucomatous eyes may not be really concentric but, in fact, more vertical [12]. The studies are unanimous that the vertical cup-to-disc ratio is statically larger in glaucomatous eyes, which makes it one of the most valuable optic disc variables for detection and follow-up of glaucomatous optic nerve damage. The estimation of cup-to-disc is more practical with photography than biomicroscopy since it provides a permanent recording of the nerve's appearance at a given time, allowing more detailed scrutiny and

later comparison for changes. The use of software to measure this ratio on photographs makes this estimation more precise.

The rim area is of particular interest because, like the retinal nerve fiber layer thickness, it reflects the number of axons passing out of the eye [20]. In advanced glaucomatous optic nerve damage, the area of the neuroretinal rim progressively diminishes, and its form continuously changes. Like the present study, several studies reported that the average rim area was significantly lower in glaucomatous eyes than in healthy eyes and that the neuroretinal rim area had good diagnostic abilities [21, 22].

The neuroretinal rim in normal eyes shows a characteristic configuration. It is usually broadest in the inferior rim, followed by the superior and nasal rims, and thinnest in the temporal disc region. This pattern of rim width is known as the ISNT rule (inferior > superior > nasal > temporal). Harizman et al. evaluated the ISNT rule on stereoscopic disc photography. The rule was intact in 79% of normal eyes and 28% of glaucomatous eyes ( $p < 0.001$ ). [23] In our study, this rule was intact in only 7% of glaucomatous eyes, while it was respected in 87% of controls ( $p < 0.001$ ).

The measurements obtained on photographs were different from those measured by SD-OCT. Compared to SD-OCT, photography overestimates the disc and rim areas. The cup-to-disc ratio is also slightly different between the two methods. The discrepancy between photograph determinations of optic disc size and the determination from SD-OCT may be due to a different outlining of the optic disc boundaries. this finding can be explained by the fact that the SD-OCT considers the optic disc margin to be the opening in Bruch's membrane, whereas, on photography, the edge of Bruch's membrane is not always evident, and the designation of the optic disc boundary can be influenced by the contrast of optic disc tissue with surrounding peripapillary tissues [20]. Thus, photography tends to enlarge the boundary of the optic disc. The boundary of the cup is also difficult to determine, and the central retinal vessel trunk along its inner surface also makes the margins ambiguous [10, 20].

Despite being different, we found a very good linear correlation between the measurements of the different parameters obtained by photography and SD-OCT. Sharma et al. found a good and statistically highly significant correlation between measurements obtained on stereoscopic photographs after manual tracing of the optic disc and cup mar-

gins and those obtained with automatic analysis by SD-OCT [20]. The presence of this linear correlation means that we can rely on measurements by photography. However, there are several limitations to the use of this technique of measurement, it is time-consuming, and it depends upon subjective judgment of the optic disc boundaries.

This study presents certain biases: a selection bias due to the fact that the control group was included from the hospital and then would not be representative of the general population, and an evaluation bias given that the delimitation of the optic disc and the excavation boundaries was carried out manually, and we did not test the reproducibility of the ONH parameter measurements, which can constitute a measurement bias due to the possibility of operator-dependent variation. However, this bias was reduced by the fact that this analysis was carried out by the same blinded operator. Despite being prospective, our study has certain limits, namely, the small size of the study population, not including all age ranges. Larger cohorts of patients would provide more precise values and establish a normative database for different age groups.

## CONCLUSION

Comparison of serial optic disc photographs has long been considered the gold standard for assessing glaucoma progression. The use of software to measure different parameters on photographs makes this comparison more precise. We believe that the conception of an image processing software integrated into portable ophthalmoscopes, able to detect the optic nerve head and its different components according to a colorimetric scale and to perform measurements of different parameters could be an interesting fast, and inexpensive technique, particularly for glaucoma mass screening.

## Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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