Eye Diseases Monitoring Using Statistical Analysis of Disc Topography and RNFL Circular Tomogram Parameters

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Abstract. In this paper, Statistics method for data taken from ophthalmology institute of Cairo, Egypt used to pinpoint the absolute measurement precision of high resolution technique of Topcon three dimensional optical coherence topography FA plus (Topcon 3D OCT FA plus) parameters by expressing them as limit of agreement percentage (LA95%) then, suggest a method for mathematically evaluating the ability of parameter to monitor ailment progression expressed as Discriminate Capacity Index (DCI) then, select parameters suitable for both conversion to glaucoma and modify to outright glaucoma. The used Parameters were area of disc, cup, rim and cup to disc ratio, linear and veridical cup to disc ratio, volume of cup, rim volume, horizontal and vertical diameter, total thickness of retinal nerve fiber layer (RNFL), average superior thickness of RNFL and average inferior thickness of RNFL parameters have been arranged with a DCI ≥ 0.4 for glaucoma detection and with a DCI≥ 2.3 for continue of glaucoma. The most adequate parameters for both detection and follow-up of glaucoma are Inferior thickness of RNFL (DCI=4.1976), total thickness of RNFL (DCI=16.56) and vertical cup- to- disc ratio (CDR) (DCI=22.1875).

Keywords: Discriminate Capacity Index; limit of agreement percentage; retinal nerve fiber layer; scan laser ophthalmoscope; Heidelberg retina topography; 3D OCT; glaucoma.

1. Introduction
Glaucoma is a collection of eye ailments, which causes destroying of optic disc and vision loss [1-4]. Presently, the mainstays of diagnosis include ophthalmoscope are the evaluation of optic disc and RNFL and testing of the vision field [5-8]. Several mechanisms are evolving to simulate the anatomy of optic disc parameters is shown in Table 1 morphology and ameliorate the precision of making detection and diagnosing of glaucoma advancement [9]. One of mechanisms is color fundus FA plus is assimilate for monitoring RNFL thickness of patients retinal physiology using low coherence interferometer to disunite tissue in eye [10], which supplies images of disc topography and calculates parameters of image to define a three-dimensional structure. Color fundus FA plus is method of imaging in Topcon 3D OCT FA plus which has better scanning depth and scanning speed than method of scan laser ophthalmoscope (SLO) in Heidelberg Retina topography (HRT) device [11-12]. All features of spectral domain -optical coherence topography (SD-OCT) of devices similar in improved
resolution, more accurate retinal maps, improved information of registration, cube scans and 3D views but they have dissimilar features of wavelength, scanning depth, axial resolution, speed of scanning and method of imaging [13]. Limit of agreement midset the two trials is defined by a 95% prediction interval of a particular value of the difference which provides the utter difference between measures that must be overridden to disclose statistically significant changes over time due to development or progression of disease. DCI is defined by dividing the measurement range of each parameter by its LA95% for reproducibility. The diagnostic range was arbitrarily defined as the utter difference between the mean values of a parameter in healthy patients and mild glaucoma patients. The follow-up range was defined as the utter difference between the mean values of a parameter in mild and severe glaucoma patients to analyse progression of ailment measurement factor. It requires the utter difference follow up measurements to disclose significant change across time [14-17]. The target of this paper, firstly determine all optic disc parameters to calculate LA95% for each parameter that defined as absolute measure of change that used as clinical diagnostic tool, secondly estimate which parameters proper for clinical ailment detection and follow-up by using DCI based on LA95%. Dimensionless DCI allows comparison among various parameters and technologies.

| Table 1: parameters from Topcon 3D OCT FA plus device |
|------------------------------------------------------|
| Disc topography parameters                          | Average thickness RNFL parameters |
| Disc Area | Cup Area | Rim Area | C/D Area | Linear CDR | Vertical CDR | CUP Volume | Rim Volume | Horizontal D.D | Vertical D.D | Total Thickness | Superior | Inferior |

2. Materials and procedures

2.1 Overview

Color fundus FA plus is a method in Topcon 3D OCT FA plus provides images of disc topography and calculates parameters of image to define a three-dimensional structure in Figure 1, which provide better scanning depth and scanning speed than process of scan laser ophthalmoscope (SLO). SLO is process of imaging in Heidelberg Retina topography (HRT) device [11-12]. All features of spectral domain -optical coherence topography (SD-OCT) of devices similar in improved resolution, more accurate, retinal maps, improved information of registration, cube scans and 3D views but they have dissimilar features of wavelength, scanning depth, axial resolution, speed of scanning and process of imaging [13].

![Figure 1. Parameters for (a) normal and (b) glaucoma case](image-url)
2.2 Statuses of patients
The work was done on statuses of patients from the Institute of Ophthalmology of Cairo, Egypt and collected a medical reports that determine the type of case normal or glaucoma and during the preparation of the patient if the internal pressure of the patient eye is not measured, the doctor pressed the eyelid eye for diagnosis before using Topcon 3D OCT FA plus device. These measures made in a number of cases. The measurements on 4 Normal patients and 4 glaucoma patients in details 2 Normal cases, 2 Normal cases Caucasian, one mild glaucoma case, and 3 severe glaucoma cases.

2.3 Retinal nerve Fiber Analysis test
The details of Topcon 3D OCT FA plus device have been explained in another place [1]. In brief the device with high resolution mechanism to collect between OCT & fundus camera properties using IR images of disc topography and RNFL tomography. Disc parameters are determined at reference plane height of 120 μm from the Retina Pigment Epithelium (RPE) in this version. The instrument software then, automatically calculated optic disc parameters arranged as normal, mild glaucoma and severe glaucoma as appeared in Figure 2.

| image | parameter | abbreviation | Measure | Type of case |
|-------|-----------|--------------|---------|--------------|
|       | Disc area | Ca+Ra        | 3.76 mm² | normal patient |
|       | Cup area  | Ca           | 1.18 mm² |              |
|       | Rim area  | Ra           | 2.58 mm² |              |
|       | Rim volume| Rv           | 0.73 mm² |              |
|       | Cup volume| Cv           | 0.23 mm² |              |
|       | Total thickness RNFL | T     | 100 μm   |              |
|       | Average superior thickness RNFL | S    | 114 μm   |              |
|       | Average inferior thickness RNFL | I    | 123 μm   |              |
|       | Cup to disc area ratio | Ca/(Ca+Ra) | 0.31 | Mild glaucoma patient |
|       | Horizontal CDR | H1/H2 | 0.56 |              |
|       | Vertical CDR | V1/V2 | 0.54 |              |
|       | Disc area | Ca+Ra        | 2.45 mm² | severe glaucoma patient |
|       | Cup area  | Ca           | 0.96 mm² |              |
|       | Rim area  | Ra           | 1.49 mm² |              |
|       | Rim volume| Rv           | 0.33 mm² |              |
|       | Cup volume| Cv           | 0.19 mm² |              |
|       | Total thickness RNFL | T     | 78 μm    |              |
|       | Average superior thickness RNFL | S    | 95 μm    |              |
|       | Average inferior thickness RNFL | Ca/(Ca+Ra) | 0.39 |              |
|       | Cup to disc area ratio | H1/H2 | 0.63 |              |
|       | Horizontal CDR | V1/V2 | 0.65 |              |
|       | Vertical CDR |       |       |              |

*Figure 2.* Schematic of OCT parameters of disc topography at RPE of 120μm from reference plane of normal, mild glaucoma, severe glaucoma patient
2.4 Measure the limit of agreement percentage

Factor as vector of the limit of agreement percentage from the 13 Color fundus FA plus parameters of optic disc and Average thickness RNFL parameters can be calculated [19-20]. LA95% values were calculated as follows in equation (1, 2):

\[ LA_{95\%} = 1.96 \sqrt{2 \sigma_{within\text{-}patient}^2} \]  

(1)

Where \( \sigma_{within\text{-}patient} \) is the standard deviation (SD) which calculated for every parameter as follow?

\[ \sigma_{within\text{-}patient} = \sqrt{\frac{\sum_{i=1}^{n} (x_i - \overline{x})^2}{n-1}} \]  

(2)

The LA95% detects the development or progression of disease.

2.5 Discriminate capacity index
DCI is a factor as vector used to detect the fitness of any parameter to monitor the development of ailment[20].

2.5.1 DCI detection of glaucoma
For each parameter of Color fundus FA plus the DCI can be calculated by dividing the utter difference between the mean values of normal and mild glaucoma patients on its LA95% as follows in equation (3):

\[ DCI_{glaucoma\ detection} = \frac{|mean_{normal\ patients} - mean_{mild\ glaucoma\ patients}|}{LA_{95\%_{normal\ patients}}} \]  

(3)

2.5.2 DCI follow-up of progressive glaucoma
For each parameter of Color fundus FA plus the DCI can be calculated by dividing the utter difference between the mean values of mild and severe glaucoma patients on its LA95% as follows in equation (4):

\[ DCI_{glaucoma\ follow-up} = \frac{|mean_{mild\ glaucoma\ patients} - mean_{severe\ glaucoma\ patients}|}{LA_{95\%_{glaucoma\ patients}}} \]  

(4)

Mean and SD values of the 13 disc topography and RNFL circular tomogram parameters obtained in normal and glaucoma ailments calculated by Color fundus FA plus from table is shown in Table 2 used to calculate the detection and follow up of glaucoma patients, the steps of methodology of monitoring the glaucoma diagnose representing in the following block diagram in Figure 3.
3. Results

3.1 Limit of agreement percentage
Table 3 shows factor as vector of LA95% from all 13 disc topography and RNFL circular tomogram parameters for both Normal and glaucoma patients. From this table the LA95% is smaller in glaucoma patients than in normal patient. So the absolute difference of value can be detected to differentiate between normal or glaucoma ailments in Figure 4.

3.2 The Discriminate Capacity Index
Table 4 illustrate that the DCIs in glaucoma patients were greater value than those in normal patients from this table it be notice that DCI able to detect the conversion of case to glaucoma and change the case to absolute glaucoma in Figure 5, in Table 5, 6 parameters have been arranged with a DCI ≥ 0.4
for detection of glaucoma and with a DCI ≥ 2.3 for continue of glaucoma. Where the highest DCI in detection of glaucoma appeared in parameter such as Inferior thickness of RNFL (DCI=4.1976) and the highest DCI in follow up of glaucoma appeared in parameters as vertical CDR (DCI=22.1875) and total thickness of RNFL (DCI=16.56) so the best coefficient for detection and Continue of glaucoma are Inferior thickness of RNFL, total thickness of RNFL and vertical CDR.

Table 3. Display LA95% of all disc topography and RNFL circular tomogram parameters for both normal and glaucoma patients

| parameters       | unit | mean (Normal-Mild glaucoma) | SD (Normal-Mild glaucoma) | LA95% Normal | mean (Mild glaucoma-Normal) | SD (Mild glaucoma-Normal) | LA95% glaucoma |
|------------------|------|-----------------------------|---------------------------|--------------|-----------------------------|--------------------------|----------------|
| Disc Area        | mm²  | 0.8625                      | 0.3406                    | 0.9442       | 0.065                       | 0.7399                   | 2.051          |
| Cup Area         | mm²  | 0.51                        | 0.3209                    | 0.8896       | -1.2575                     | 0.7667                   | 2.1251         |
| Rim Area         | mm²  | 0.3525                      | 0.6401                    | 1.7743       | 1.315                       | 0.0661                   | 0.1832         |
| C/D Area         |      | 0.0625                      | 0.14104                   | 0.391        | -0.53                       | 0.04                     | 0.13           |
| Linear CDR       |      | 0.0375                      | 0.1044                    | 0.2893       | -0.3275                     | 0.0206                   | 0.0571         |
| Vertical CDR     |      | 0.0125                      | 0.1072                    | 0.2971       | -0.355                      | 0.008774                 | 0.016          |
| CUP Volume       | mm³  | 0.3175                      | 0.277                     | 0.7676       | -0.565                      | 0.654                    | 1.8129         |
| Rim Volume       | mm³  | 0.0875                      | 0.247                     | 0.6847       | 0.32                        | 0.008165                 | 0.0226         |
| Horizontal D.D   | mm   | 0.2025                      | 0.1135                    | 0.3147       | 0.105                       | 0.3375                   | 0.9355         |
| Vertical D.D     | mm   | 0.325                       | 0.1801                    | 0.4992       | 0.0125                      | 0.1855                   | 0.5143         |
| Total Thickness  | mm   | 0.02375                     | 0.0041932                 | 0.0116231    | 0.0265                      | 0.0005774               | 0.0016         |
| Superior         | mm   | 0.0165                      | 0.0088882                 | 0.0256368    | 0.03975                     | 0.0061847               | 0.017143       |
| Inferior         | mm   | 0.057                       | 0.00489898                | 0.0135793    | 0.014                       | 0.0080416               | 0.02229        |

Table 4. The Discriminate Capacity Index

| parameters       | Glaucoma detection DCI | Glaucoma Follow up DCI |
|------------------|-------------------------|------------------------|
| Disc Area        | 0.9135                  | 0.0317                 |
| Cup Area         | 0.5733                  | 0.5917                 |
| Rim Area         | 0.1987                  | 7.178                  |
| C/D Area         | 0.1598                  | 4.0769                 |
| Linear CDR       | 0.1296                  | 5.7356                 |
| Vertical CDR     | 0.0421                  | 22.1875                |
| CUP Volume       | 0.4136                  | 0.3117                 |
| Rim Volume       | 0.1278                  | 14.1593                |
| Horizontal D.D   | 0.6435                  | 0.1122                 |
| Vertical D.D     | 0.651                   | 0.0243                 |
| Total Thickness  | 2.0433                  | 16.56                  |
| Superior         | 0.6697                  | 2.3187                 |
| Inferior         | 4.1976                  | 0.6281                 |
Table 5: parameters that may suitable for detection of glaucoma

| parameters          | Glaucoma detection DCI | LA95% healthy | unit |
|---------------------|-------------------------|---------------|------|
| Inferior            | 4.1976                  | 0.0135793     | mm   |
| Disc Area           | 0.9135                  | 0.9442        | mm²  |
| Vertical D.D        | 0.651                   | 0.4992        | mm   |
| Horizontal D.D      | 0.6435                  | 0.3147        | mm   |
| CUP Volume          | 0.4136                  | 0.7676        | mm³  |

Table 6: parameters that may be suitable for follow-up of glaucoma

| parameters          | Glaucoma Follow up DCI | LA95% glaucoma | unit |
|---------------------|-------------------------|----------------|------|
| Vertical CDR        | 22.1875                 | 0.016          | mm   |
| Total Thickness     | 16.56                   | 0.0016003      | mm²  |
| Rim Volume          | 14.1593                 | 0.0226         | mm³  |
| Rim Area            | 7.178                   | 0.1832         | mm²  |
| Linear CDR          | 5.7356                  | 0.0571         | mm²  |
| C/D Area            | 4.0769                  | 0.13           | mm²  |
| Superior            | 2.3187                  | 0.017143       | mm   |

Figure 4. Limit of agreement percentage of all disc topography and RNFL circular tomogram parameters for both normal and glaucoma patients
4. CONCLUSION AND DISCUSSION
The current study introduces the factor as vector LA95% for disc topography and RNFL circular tomogram parameters calculated with Color fundus FA plus in normal glaucoma patients for each parameter. This limit of agreement focus on absolute difference between measurements required to reveal noticeable change in addition the factor as vector of dimensionless DCI measured for each parameter. Color fundus FA plus has the greatest suitable parameters for glaucoma disclosing such as disc area [21-23], cup volume, horizontal-D, vertical-D and inferior RNFL [24], also has the most suitable parameters for glaucoma follow-up such vertical CDR, linear CDR, rim area, rim volume, Cup/Disc area ratio, total thickness of RNFL and superior RNFL [25-26], finally the most suitable Topcon parameters both for glaucoma disclosing and follow-up glaucoma are inferior thickness of RNFL, total thickness of RNFL and vertical CDR. While the previous study of SLO suitable parameters are rim area, cup volume and total thickness of RNFL.[20].

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