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Clinical Validation of a Smartphone-based Handheld Fundus Camera for Evaluation of Optic Nerve Head

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Abstract

Purpose: The objectives of this study were to compare the quality of retinal images taken with a smartphone-based hand-held fundus camera (SHFC) with those from a commercial fundus camera (CFC), and to analyze their agreement in determining the cup-to-disc ratio in a cohort of ophthalmological patients.

Methods: Fifty patients from a secondary ophthalmic outpatient service underwent a bilateral fundus examination under mydriasis using the SHFC and CFC (four images per patient). A multivariate regression analysis was performed to evaluate factors associated with the image quality. Two masked ophthalmologists determined the vertical cup-to-disc ratio of each fundus image, and both the intraobserver (between devices) and interobserver agreement between them was calculated.

Results: Ninety-eight images from 49 patients presented sufficient quality and were used in this study. The medians [interquartile interval] of image quality were not significantly different between the SHFC and CFC 4 [4-5] versus 4 [3-4] respectively, p=0.06); however imagens taken with the CFC, as well as the presence of media opacity presented a significant negative correlation with image quality. Both the intraobserver and interobserver agreements were excellent and statistically significant (p<0,01).

Conclusions: Our results indicate that the SHFC presents image quality similar to CFC, with significant agreement in the analysis of the cup-to-disc ratios. Besides the good results observed, the SHFC may be considered as a portable, low cost alternative for fundus documentation in further telemedicine settings.

Key words: Fundus camera, portable, smartphone-based, optic nerve head, telemedicine.

Introduction

The impact of senile chronic diseases in Brazil have become more important considering the current aging pattern observed in the Brazilian population.[1] Ocular diseases such as glaucoma, macular degeneration, and diabetic retinopathy, besides cataract, are the leading causes of blindness in individuals older than 50 years.[2] The increasing prevalence of those diseases reinforces the need for a diagnosis based on fundus examination in national health programs.

Unfortunately, eye health programs are often not well integrated with the health system.[3] Barriers to access healthcare derive from limitations associated with technologies, providers, geographical distances, as well as cultural, cognitive and behavioral differences of health service users.[4]

Previous studies in India[5] and Kenya[6] have shown that handheld devices for the detection of retinal diseases could be used for fundus documentation by non-ophthalmologists in areas lacking assistance. Nevertheless, non-ophthalmologist healthcare workers were able to capture high quality images in children screened for retinopathy of prematurity with a portable fundus camera. Their photographs were uploaded and remotely graded for retinopathy of prematurity by a retina specialist with good sensitivity and specificity levels.[7] All the recent advances in mobile devices that may facilitate telemedicine strategies would improve the integration of eye healthcare system in countries with low resources. In this scenario, the purpose of the present study was to validate a new smartphone hand-held fundus camera (SHFC) by evaluating both the images quality, and the agreement with a commercial fundus camera (CFC) in determining the cup-to-disc ratio in a cohort of ophthalmological patients.

Materials and Methods

Ethics Approval

This cross-sectional study was approved by the Research Ethics Committee of the PIO XII Foundation, Barretos - SP and by the Research Ethics Committee of Hospital das Clínicas da Faculdade de Medicina de RibeirãoPreto - SP. The norms of the Declaration of Helsinki and the International Conference on Standardization Note for Guidance on Good Clinical Practice (ICH, Topic E6, 1995) were followed. All selected subjects received extensive and detailed oral and written explanations of all project-related events and signed an informed consent form.

Participants

Fifty patients, previously scheduled for eye examination by independent ophthalmologists from the ophthalmologic service of the AME –Barretos (São Paulo, Brazil), were considered for participating in this study.

Patients were selected for the study according to the following inclusion criteria: 18 years or older, no cognitive disability, ability to perform all necessary exams, and no previous eye surgeries performed over the last two months.

Device development

The SHFC was developed using an optical system capable of generating high resolution images within the 45 degree of the fundus view. It was attached to a smartphone (Samsung Galaxy S7, Samsung Electronics Co., Suwon, Korea) and uses its processor, display, global positioning system and internet access for handling patient, exams and reports data. Safety of light exposure was previously evaluated by the comparison of the energy levels necessary for performing colored

fundus imaging between SHFC and other commercial available fundus camera (CFC - Topcon retinal camera, Topcon Healthcare Solutions, Oakland, USA). All measurements were performed using a handheld power/energy meter (Vega, Ophir Photonics, Newport Co., Jerusalem, Israel) and a thermopile based laser energy sensor (Model 3A Ophir Photonics, Newport Co., Jerusalem, Israel).

Procedures

All patients scheduled for fundus imaging received at least one comprehensive ophthalmologic evaluation. On the scheduled day, patients received one drop of 1% tropicamide and 10% phenylephrine for pupil dilation. After 25 minutes, a series of three photographs, followed by a series of four photographs of each eye, were taken by two trained nurses using the CFC and the SHFC, respectively. They underwent three separate one-hour period of training previously. A masked examiner was responsible for selecting the best fundus picture of each eye from all patients, taken with both devices.

Photographs of the anterior segment of both eyes were also taken, serving for the measurement of the horizontal pupil diameter. Individual spherical equivalent, diagnosis (glaucoma and suspects, retinal diseases, refraction errors, and cataract), and age (years) were recorded on the same day and subsequently analyzed.

Two experienced masked ophthalmologists evaluated all the fundus images on the same 19-inch LCD computer monitor. Each examiner graded each image according to a quality score, using a Likert 1-5 scale: 1. Poor, unsatisfactory or impossible to catch; 2. Regular or partially satisfactory; 3. Good or satisfactory; 4. Very good or quite satisfactory; 5. Excellent or totally satisfactory.

The examiners also evaluated the randomly assorted individual pictures, and attributed values to the vertical cup/disc ratio, using a double-masked database of images (for both the patient identification and the device used).

Statistical analysis

Variables were described using the mean, median, standard error, 95% confidence interval (95% IC) and frequencies as needed. A linear mixed effects multivariate regression was used to identify factors associated with the image quality, as follows: device type, ocular diagnosis, pupil diameter (after mydriasis), spherical equivalent and age.

In addition, an Intraclass Correlation Coefficient (ICC) was used to assess interobserver agreement (for each device) and agreement between devices (for each observer), combined with a Bland-Altmann plot analysis. All analyzes were performed using Stata software (Stata 14.2, StataCorp LLC, Texas, USA). Statistical significance was determined at $p < 0.05$.

Results

The results of ocular safety when exposed to the SFHC are shown in Table 1. SHFC's optical power in preview mode is at least 10 times lower than the direct and indirect reference commercial binocular ophthalmoscope. With its presented lighting levels, the SHFC device is classified as Group 1 (safe) according to both ISO 10940 and 15004-2. Ninety-eight eyes of 49 patients were included in this study, 33 women (67.3%), with a mean age of 62.1 ± 10.2 years. Table 2 shows demographic data and diagnoses.

One patient was excluded from all data analyzes due to loss of his images captured using the CFC. Another five patients were not included in the agreement analyzes (for the cup-to-disc ratios; 44 patients, 88 eyes) due to the poor quality of the acquired images (grade 1 or 2), but were considered in the quality analyzes. Of these five unclassifiable patients, four were acquired by the CFC device and one by the SHFC device.

Figure 2 shows examples of retinal images taken on the same patient with both devices. The median [interquartile interval] score for image quality was 4 [4-5] for the SHFC and did not differ from CFC's (4 [3-4]; p=0,06). We observed that the use of the CFC device and the diagnosis of “cataract” showed a significant negative correlation with image quality (Table 3).

The interobserver agreement for the evaluation of the cup-to-disc ratio was considered good with the SHFC images (ICC = 0.70) and very good with the CFC images (ICC = 0.81; p=0.001). The agreement coefficients between the devices were very good (examiner 1: ICC = 0.82 and examiner 2: ICC = 0.83; p<0.001) (Table 4), which is in accordance with the Bland-Altmann plot analyzes (Figure 3).

Discussion

Recent data estimates that at least 2.2 billion people present visual impairment, and age-related macular degeneration, glaucoma, and diabetic retinopathy are the most common causes, besides cataract and refractive error. [8-12] Latin America and Caribbean countries could have saved $ 6,281 million by 2020 if blindness prevention programs had been implemented in the past 13 years. [13] These data reinforce the need for an integrated health system, capable of early detection of these conditions and prevention of blindness at lower costs. Portable equipment consistent with Telemedicine could provide a low-cost integration of the health system for the burden ocular diseases.[14]

Among a few others, the prototype used in this study may be considered as a safe alternative for developing a telemedicine-based system for the detection of ocular diseases integrated with the health system. Besides safety, its cost (estimated in US$ 5,000) seems suitable, since it is about six times less than most available table retinal cameras.

Regarding the quality of images, there was a slight superiority of the SHFC compared to CFC scores (Table 3). However, the multivariate analysis pointed to a significant correlation with the device type (SHFC), besides the presence of cataract. The other parameters analyzed (age, pupil diameter, retinal diseases, and refractive errors) presented no significant association with image quality.

The clinical validation of the SHFC was verified using the determination of cup-to-disc ratios in fundus images, compared to the CFC, across two masked examiners. Our results showed good, significant agreement between the observers for both

devices, being slightly better in the CFC device (ICC 0.81) than in the SHFC (ICC 0.70; p=0.001). We speculate that such minor differences may be related to the different examiner's background, rather than characteristics of each device. One is a glaucoma specialist, and the other is a general practice ophthalmologist, both with years of clinical experience. Interobserver agreement in the clinical evaluation of the optic nerve may vary but has been shown higher if the analysis is based on retinal images of the fundus. [14,15] Thus, the good correlation observed herein accounts for the higher credibility of both examiners.

The intraobserver agreement in determining the cup-to-disc ratio was also good and significant for each examiner (ICC: 0.81 versus 0.83, p<0.001). These consistent results of comparable performance between devices, in produce reliable fundus image (at least for good determination of the optic nerve excavation boundaries), account for the clinical validation of SHFC, despite all technical differences between them.

The study presents some limitations. There was no healthy control group, so our sample was used for the evaluation of a sort of all cup-to-disc ratios, because patients with glaucoma and suspects were included in the regression analyses. Also, despite patients and examiners reported great comfort with the SHFC device at the very first tests, comfort and ease of handling were not objectively analyzed. Besides, a new non-mydriatic version of the SHFC (Figure 1) is now commercially available but has not been tested in this study.

Several portable retinal imaging devices have arisen in the past few years as alternatives aiming a better-integrated eye health care. We believe that an ideal portable device for fundus image should be light-weighted, easy to handle, of low

cost, non-mydriatic, and include data transfer features. Many new available portable devices meet some of those features, and the new version of the prototype presented in this study represents an option that fulfills all of them. Further research is required to determine its capability to generate good quality images without mydriasis and to evaluate its sensitivity and specificity levels for the diagnosis of glaucoma and the most prevalent retinal diseases, being a new alternative in the telemedicine approach.

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References

1. Bourne RRA, Flaxman SR, Braithwaite T, Cicinelli MV, Das A, Jonas JB, et al. Vision Loss Expert Group. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis. Lancet Glob Health. 2017;5(9):e888–97.

2. Schellini SA1,2, Meneghim RLFS1, Satto L1, Cavinatto P1, Galindo-Ferreiro A2, Khandekar R2. Magnitude of visual impairment, blindness and causes in the southwest region of São Paulo state, Brazil. Arq Bras Oftalmol. 2018 Sep-Oct;81(5):414-420.

3. Access Economics. The global economic cost of visual impairment. International Council of Ophthalmology. 2010 [cited 2010 Jun 14]. Available at: http://www.icoph.org/resources/146/The-Global-Economic-Cost-of-Visual-Impairment.html

4. O'Donnell, Owen. (2007). Access to health care in developing countries: breaking down demand side barriers. *Cadernos de Saúde Pública*, *23*(12), 2820-2834

5. Sengupta S, Sindal MD, Besirli CG, Upadhyaya S, Venkatesh R, Niziol LM, et al. Screening for vision-threatening diabetic retinopathy in South India: comparing portable non-mydriatic and standard fundus cameras and clinical exam. Eye (Lond). 2018 Feb;32(2):375-383.

6. Bastawrous A, Giardini ME, Bolster NM, Peto T, Shah N, Livingstone IA, et al. Clinical Validation of a Smartphone-Based Adapter for Optic Disc Imaging in Kenya. JAMA Ophthalmol. 2016;134(2):151-158.

7. Prakalapakorn SG, Freedman SF, Hutchinson AK, Wallace DK, Stinnett SS, Riggins JW, et al. Evaluating a Portable, Noncontact Fundus Camera for Retinopathy of Prematurity Screening by Nonophthalmogist Health Care Workers. Ophthalmology Retina 2017 Aug;2(8):864-871

8. WHO World Report on Vision. World Health Organization (cited 2019 out 8); p. 22-26. Available at: https://www.who.int/publications-detail/world-report-on-vision

9. Wong WL, Su X, Li X, Cheung CM, Klein R, Cheng CY, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. The Lancet Global Health. 2014 Feb;2(2):e106–16.

10. Flaxman SR, Bourne RRA, Resnikoff S, Ackland P, Braithwaite T, Cicinelli MV, et al. Global causes of blindness and distance vision impairment 1990-2020: a systematic review and meta-analysis. The Lancet Global Health. 2017 Dec;5(12):e1221–e1234.

11. WHO. Global report on diabetes: World Health Organization. 2016. Available at: http://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf;sessionid=4AE02F296163C562F2C152DE8FEDCE23?sequence=1

12. Yau J, Rogers S, Kawasaki R, Lamoureux E, Kowalski J, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012 Mar;35(3):556-64.

13. Ottaiano JA, Ávila MP, Umbelino CC, Taleb AC. As Condições de Saúde Ocular no Brasil 2019. Conselho Brasileiro de Oftalmologia (cited 2019 Mai 5); 84p.

Available at http://www.cbo.com.br/novo/publicacoes/condicoes_saude_ocular_brasil2019.pdf

14. Tielsch JM; Katz J, Quigley HA, Miller NR, Sommer A. Intraobserver and Interobserver Agreement in Measurement of Optic Disc Characteristics. Ophthalmology, 1988 Mar; 95(3):350-6.

15. Kumar S, Giubilato A, Morgan W, Jitskaia L, Barry C, Bulsara M, et al. Glaucoma screening: analysis of conventional and telemedicine-friendly devices. Clin Exp Ophthalmol. 2017 Apr;35(3):237-43.

Figure Legends

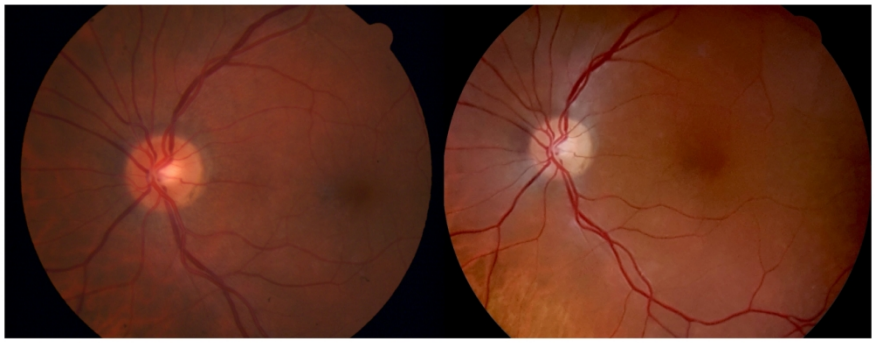
Figure 1. Photographs displaying prototype used in this study (SHFC, on the left) and the new available commercial version (*Eyer*, on the right).

Figure 2. Examples of fundus images taken on the same patient using both devices. On the left, an image from participant #27 acquired with the CFC. On the right, an image from the same participant using the SHFC.

Figure 3. Bland-Altmann plots showing the agreement analyses in the assessment of the vertical cup-to-disc ratios between the two devices for examiner 1 (on the left) and examiner 2 (on the right).

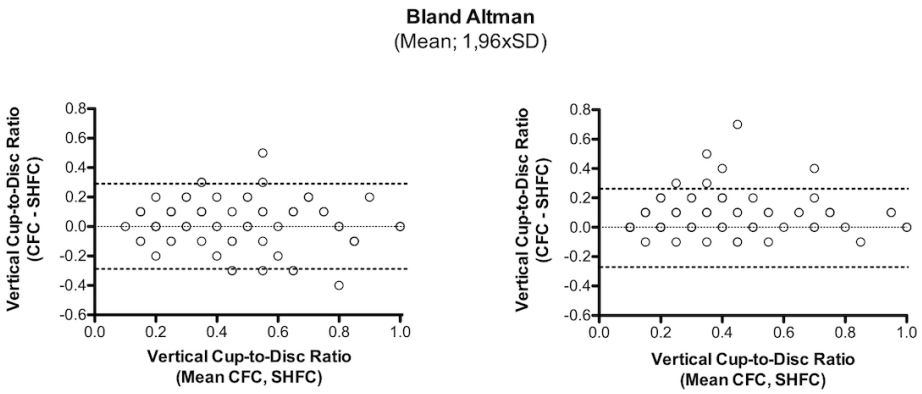
Photographs displaying prototype used in this study (SHFC, on the left) and the new available commercial version (Eyer, on the right).

232x198mm (72 x 72 DPI)



Examples of fundus images taken on the same patient using both devices. On the left, an image from participant #27 acquired with the CFC. On the right, an image from the same participant using the SHFC.

529x246mm (72 x 72 DPI)



Bland-Altmann plots showing the agreement analyses in the assessment of the vertical cup-to-disc ratios between the two devices for examiner 1 (on the left) and examiner 2 (on the right).

99x43mm (300 x 300 DPI)

Table 1. Illumination levels for color fundus imaging obtained with SHFC and CFC for retinal documentation.

Device	Optical Power (Preview Mode)		Radiant Flash Energy (Capturing Mode)	
	Typical Value	Maximum Value	Typical Value	Maximum Value
SHFC	0.14 mW	0.28 mW	0.29 mJ	0.29 mJ
CFC	0.50 mW	14.50 mW	6.40 mJ	46.00 mJ

Table 2. Demographics of the participants included in the study.

Diagnosis	Age (years)	*Gender*		Total
		Female	*Male*	
Glaucoma/ Suspects	63.0±8.0	14 (28.5%)	9 (18.3%)	23 (46.9%)
Retinal diseases	64.2±11.3	14 (28.5%)	5 (10.2%)	19 (38.7%)
Refractive errors	52.8±12.0	4 (8.2%)	2 (4.1%)	6 (12.2%)
Cataract	59.0	1 (2.0%)	0	1 (2.0%)
Total	62,1±10.2	33 (67.3%)	16 (32.6%)	49 (100%)

Table 3. Analysis of correlation of device, pupil diameter, spherical equivalent, age and diagnosis with image quality.

	ICC	95% CI	p value
*A. CFC**	-0.33	-0.51:-0.15	0.001
B. Pupil Diameter	-0.02	-0.18:0.13	0.74
C. Spherical equivalent	0.10	-0.03:0.24	0.13
D. Age	-0.01	-0.03:0.01	0.31
*E. Diagnosis***			
1. Retinal diseases	-0.21	-0.74:0.30	0.41
2. Cataract	-1.17	-2.30:-0.02	0.04
3. Refractive errors	0.16	-0.47:0.80	0.61

*Comparing to the SHFC device; ** Comparing to the diagnosis of glaucoma and suspects. ICC: intraclass correlation coefficient; 95% CI: 95% confidence interval.

Table 4. Intraclass correlation analysis of the agreement between devices for each examiner, regarding the cup-to-disc ratio results.

Examiner	ICC	95% CI	pvalue
1	0.82	0.73:0.87	<0.001
2	0.83	0.75:0.88	<0.001