Comparison of Smartphone Ophthalmoscopy With Slit-Lamp Biomicroscopy for Grading Diabetic Retinopathy

ANDREA RUSSO, FRANCESCO MORESCALCHI, CIRO COSTAGLIOLA, LUISA DELCASSI, AND FRANCESCO SEMERARO

• PURPOSE: **To assess the accuracy and reliability of smartphone ophthalmoscopy, we compared the ability of a smartphone ophthalmoscope with that of a slit-lamp biomicroscope to grade diabetic retinopathy (DR) in patients with diabetes mellitus (DM).**

• DESIGN: **Clinical-based, prospective, comparative instrument study.**

• METHODS: **This comparative clinical study was performed in 120 outpatients (240 eyes) with type 1 or type 2 DM. After pupil dilation, the patients underwent smartphone ophthalmoscopy with the D-Eye device, followed by dilated retinal slit-lamp examination, to grade DR according to a 5-step scale.**

• RESULTS: **Overall exact agreement between the 2 methods was observed in 204 of 240 eyes (85%) (simple $\kappa = 0.78$; CI 0.71-0.84) and agreement within 1 step was observed in 232 eyes (96.7%). Compared to biomicroscopy, the sensitivity and specificity of smartphone ophthalmoscopy for the detection of clinically significant macular edema were 81% and 98%, respectively. Smartphone ophthalmoscopy and biomicroscopy could not be used to examine the fundus and grade DR in 9 eyes (3.75%) and 4 eyes (1.7%), respectively, because of cataract and/or small pupil diameter.**

• CONCLUSION: **Smartphone ophthalmoscopy showed considerable agreement with dilated retinal biomicroscopy for the grading of DR. The portability, affordability, and connectivity of a smartphone ophthalmoscope make smartphone ophthalmoscopy a promising technique for community screening programs. (Am J Ophthalmol 2015;■:■–■.**

IN OPHTHALMOLOGY, IMAGES ARE USED EXTENSIVELY for disease documentation, treatment monitoring, and educational purposes. Traditionally, fundus images have been obtained with expensive and bulky tabletop units operated by a trained technician in a hospital clinic setting. The pervasive adoption of smartphones by physicians and their ever-improving built-in camera technology has raised much interest in their use for medical and ophthalmic imaging. The portability and immediate connection capabilities of smartphones make them an attractive device for acquiring retinal pictures in remote nonhospital settings. Indeed, telemedicine has the potential to reach patients and communities that currently receive no or suboptimal eye care as a result of geographic and/or sociocultural barriers.[1]

In the past decade, retinal screening programs for common eye diseases, such as diabetic retinopathy (DR), glaucoma, and age-related macular degeneration, have experienced rapid growth.[2,3] The application of these screening programs in rural, nurse-operated, highly remote primary care facilities highlights the importance of having access to an inexpensive, portable, easy-to-operate, and high-image-quality fundus camera.

Particularly, diabetes mellitus (DM) is a complicated chronic disease that requires continual medical care and patient education to minimize acute and long-term complications.[4] Most clinical practice recommendations suggest that a comprehensive eye examination must be performed at least annually to assess the DR grade in all patients with DM.[4] However, a large percentage of patients with DM (35%-79%) do not receive the recommended level of ophthalmic care.[5,6]

To capitalize on the potential versatility of smartphones in the screening of DR and other ocular diseases, various prototypes have been created to optically match the smartphone's camera to a slit-lamp ophthalmoscope,[7–9] or to use it in conjunction with a condensing lens based on the principle of indirect ophthalmoscopy.[8,10,11]

Smartphone ophthalmoscopy can nowadays be performed with the help of the D-Eye system, which is a novel, inexpensive, and very portable optical device designed to be magnetically attached to a smartphone.

The purpose of this study was to validate the efficacy of the D-Eye device to screen for diabetic retinopathy in the community. We compared the ability of smartphone ophthalmoscopy with that of dilated retinal biomicroscopy to grade DR in patients with DM.

AJO.com Supplemental Material available at AJO.com.
Accepted for publication Nov 2, 2014.

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0002-9394/$36.00
http://dx.doi.org/10.1016/j.ajo.2014.11.008

MATERIALS AND METHODS

• **STUDY DESIGN:** This was a prospective clinic-based comparative study of eyes affected by DR. This study was conducted in the ophthalmic Diabetic Center of "Spedali Civili di Brescia," according to the ethical principles of the Declaration of Helsinki. The institutional review board of the Eye Clinic (University of Brescia, Italy) approved the study protocol (registered with clinicaltrials.gov, identifier NCT02177747). All study participants provided written informed consent.

Overall, 120 consecutive patients with diabetes, new to the Diabetes Center's outpatient clinic, underwent dilated retinal digital imaging with a smartphone ophthalmoscope as a part of their routine examination for diabetes. Subsequently, they were referred for a comprehensive dilated retinal biomicroscopy with a slit lamp by a retinal specialist.

Dilating eye drops (0.5% tropicamide and 10% phenylephrine) were administered to outpatients with diabetes who were scheduled for an examination at the Diabetes Center; after 20 minutes; smartphone ophthalmoscopy was performed in these patients by a retinal specialist (L.D.). Subsequently, retinal slit-lamp examination, according to normal clinical practice, was performed by another retinal specialist (A.R.) who was masked to the findings of smartphone ophthalmoscopy. Each ophthalmoscopy procedure was reported using a similar template, in which physicians were asked whether the pupil was dilated and the media clear enough to visualize abnormalities in the fundus. Next, they were asked a series of questions regarding the presence or absence of microaneurysms, dot/blot hemorrhages, hard exudates, soft exudates, intraretinal microvascular abnormalities, venous beading, new vessel formation, fibrous proliferation, vitreous hemorrhage, scars of any previous laser photocoagulation, and clinically significant cystoid macular edema (significant CME, according to the ETDRS criteria[12]). DR was then graded according to the International Clinical Diabetic Retinopathy Disease Severity scale[13]: no apparent retinopathy, mild nonproliferative DR (NPDR, microaneurysms only), moderate NPDR (more than just microaneurysms but less than severe NPDR), severe NPDR (more than 20 intraretinal hemorrhages in each of the 4 quadrants, definite venous beading in 2 or more quadrants, and prominent intraretinal microvascular abnormalities in 1 or more quadrants), or proliferative DR (neovascularizations and vitreous/preretinal hemorrhage).

• **SMARTPHONE OPHTHALMOSCOPY:** After pharmacologic dilation, a retinal specialist (L.D.) performed a comprehensive dilated fundus examination with a final prototype (Figure 1) of the D-Eye adapter (Si14 S.p.A., Padova, Italy; http://www.d-eyecare.com) attached to an iPhone 5 (Apple Inc, Cupertino, California, USA). The images were captured on 3264 × 2448 pixels of the camera's sensor. Thus, direct fundus ophthalmoscopy was performed using live images displayed on the smartphone's screen (a video showing the acquisition procedure is available as Supplemental Material at AJO.com).

FIGURE 1. Depiction of the D-Eye prototype magnetically attached to the smartphone.

When the pupil is dilated, the device captures a field of view of approximately 20 degrees in a single fundus image at a distance of 1 cm from the patient's eye. An acquisition protocol was therefore followed to pan the retina, starting from the posterior pole and then moving to the upper, nasal, inferior, and nasal peripheral retina to the equator. Color digital images and videos of the retina were obtained, encompassing the posterior pole, including the macula, optic disc, and peripheral retina.

• **DILATED FUNDUS BIOMICROSCOPY:** Twenty minutes after smartphone ophthalmoscopy, a retinal specialist (A.R.), masked to the findings of smartphone ophthalmoscopy, performed a comprehensive dilated fundus examination with a slit-lamp biomicroscope. For this study, dilated fundus biomicroscopy was considered the gold standard for

TABLE 1. Assessment of Diabetic Retinopathy Severity by Smartphone Ophthalmoscopy and Biomicroscopy

	Dilated Slit-Lamp Biomicroscopy						
Smartphone Ophthalmoscopy	No Apparent DR	Mild NPDR	Moderate NPDR	Severe NPDR	Proliferative DR	Not Gradable	Total
No Apparent DR	110 (45.8%)	12 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	122 (50.8%)
Mild NPDR	5 (2.1%)	44 (18.3%)	5 (2.1%)	3 (1.2%)	0 (0%)	0 (0%)	57 (23.8%)
Moderate NPDR	0 (0%)	0 (0%)	27 (11.2%)	5 (2.1%)	0 (0%)	0 (0%)	32 (13.3%)
Severe NPDR	0 (0%)	0 (0%)	0 (0%)	11 (4.6%)	1 (0.4%)	0 (0%)	12 (5%)
Proliferative DR	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (3.3%)	0 (0%)	8 (3.3%)
Not Gradable	0 (0%)	3 (1.2%)	1 (0.4%)	1 (0.4%)	0 (0%)	4 (1.7%)	9 (3.8%)
Total	115 (47.9%)	59 (24.6%)	33 (13.8%)	20 (8.3%)	9 (3.8%)	4 (1.7%)	240 (100%)

DR = diabetic retinopathy; NPDR = nonproliferative diabetic retinopathy.

TABLE 2. Sensitivity and Specificity of Comparison Between Slit-Lamp Biomicroscopy and Smartphone Ophthalmoscopy for Diabetic Retinopathy Stages

	Sensitivity (95% CI)	Specificity (95% CI)
No apparent DR	0.96 (0.90-0.98)	0.90 (0.83-0.95)
Mild NPDR	0.75 (0.61-0.85)	0.93 (0.88-0.96)
Moderate NPDR	0.82 (0.64-0.92)	0.98 (0.94-0.99)
Severe NPDR	0.55 (0.32-0.76)	0.99 (0.97-1)
Proliferative DR	0.89 (0.51-0.99)	1 (0.98-1)

CI = confidence interval; DR = diabetic retinopathy; NPDR = nonproliferative diabetic retinopathy.

adjudication of differences in DR grading between smartphone ophthalmoscopy and biomicroscopy.

• **ANALYSIS OF DATA:** Descriptive statistics were used to present the demographic and ocular baseline characteristics. Overall agreement, sensitivity, and specificity of the 2 ophthalmoscopy techniques were calculated and compared. To assess the agreement between smartphone and slit-lamp ophthalmoscopy, the κ statistic was used, which was also adopted by the ETDRS.[14] Statistical analyses were performed using SPSS software version 20 (SPSS Inc, Chicago, Illinois, USA).

RESULTS

OF THE 120 PATIENTS WITH DM WHO UNDERWENT SMARTphone ophthalmoscopy and slit-lamp biomicroscopy, 55 (45.8%) were men and 28 (23.3%) had type I DM. The mean age at examination was 58.8 ± 16.4 years, and mean duration of DM was 11.6 ± 9.7 years.

• **GRADING OF DIABETIC RETINOPATHY:** The eye fundus was not gradable for DR in 9 eyes (3.75%) by smartphone ophthalmoscopy and in 4 eyes (1.7%) by biomicroscopy because of cataract and/or small pupil diameter.

The clinical level of DR found with both techniques is reported in Table 1. An exact agreement was found in 204 of 240 eyes (85%) and an agreement within 1 step was observed in 232 eyes (96.7%). Simple κ was 0.78 (95% confidence interval 0.71-0.84; $P < .001$), showing a substantial agreement[15] for the grading of DR between smartphone ophthalmoscopy and slit-lamp biomicroscopy. In 82% of 1-step disagreements and 93% of disagreements by 2 or more steps, the severity level was higher by biomicroscopy grading.

Table 2 reports the sensitivity and specificity associated with the comparison.

Figure 2 shows representative images of healthy and pathologic retinas. Mean duration of the smartphone ophthalmoscopy procedure was 37.8 ± 6.3 seconds per eye.

• **DIABETIC MACULAR EDEMA:** Table 3 compares the findings of smartphone ophthalmoscopy and slit-lamp biomicroscopy of significant CME. The examiners were asked to note only the presence or absence of significant CME. Seventeen of the 240 eyes (7.1%) were classified as true positive and 4 eyes (1.7%) as false negative (sensitivity 0.81; 95% CI 0.57-0.94); 215 eyes (89.6%) were classified as true negative and 4 eyes (1.7%) as false positive (specificity 0.98; 95% CI 0.95-0.99).

Simple κ was 0.79 (95% confidence interval 0.65-0.93; $P < .001$), indicating a substantial[15] agreement between the examined techniques.

DISCUSSION

RECENT LITERATURE HIGHLIGHTS THAT SMARTPHONES are valuable tools in the field of ophthalmology and are beginning to play a central role as medical diagnostic tools in general.[10,11,16] In fact, owing to the portability, data storage capability, and wireless connectivity of smartphones, it is plausible that a smartphone's fundus camera could soon play a significant role in clinical settings. Furthermore, it is estimated that 1 out of every 2 physicians uses a smartphone, and this ratio is expected to rise.[8]

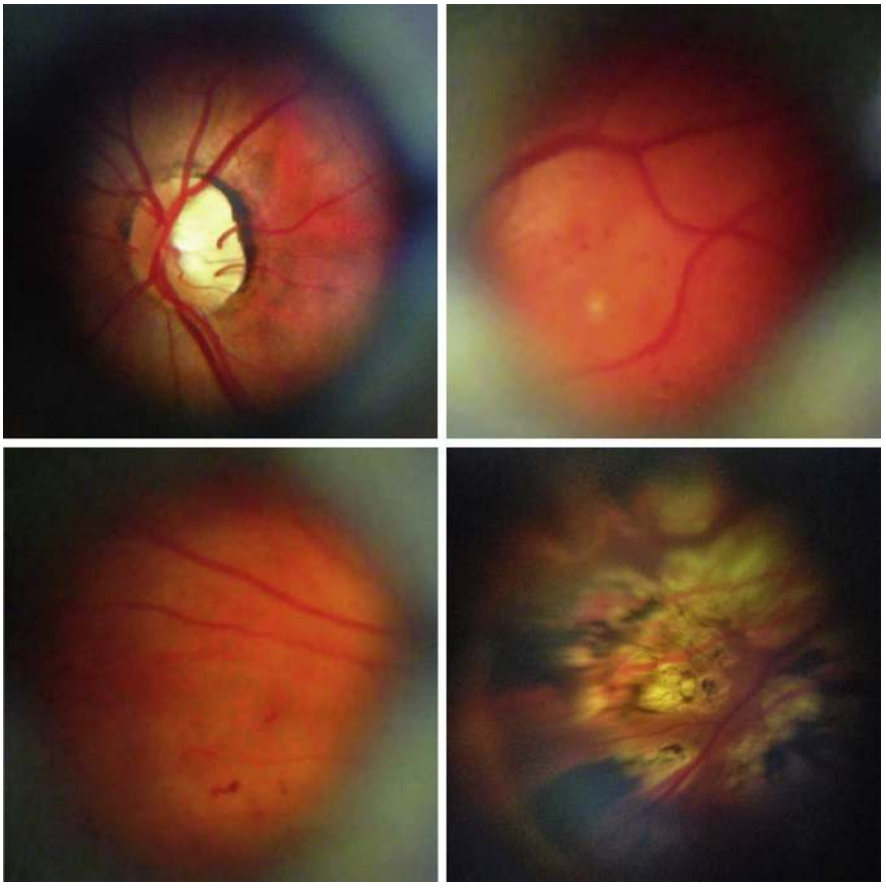

FIGURE 2. Representative retinal images of diabetic retinopathy taken with D-Eye. (Top left) Optic disc in a retina with no apparent diabetic retinopathy. (Top right) Mild nonproliferative diabetic retinopathy. (Bottom left) Moderate nonproliferative diabetic retinopathy. (Bottom right) Panretinal photocoagulation scars in a proliferative diabetic retinopathy.

The classification of DR requires a comprehensive fundus examination and is therefore a reliable index of the clinical capabilities of smartphone ophthalmoscopy performed with the D-Eye device, as the effectiveness of lesion identification in any imaging system is of paramount importance.

In this study, clinical grading of DR between the gold-standard slit-lamp biomicroscopy and smartphone ophthalmoscopy techniques showed a substantial agreement, according to Landis and Koch's recommendations for unweighted κ interpretations.[15] Similarly, a substantial agreement was found with regard to the presence or the absence of significant CME, with sensitivity and specificity comparable to those of a high-end fundus camera.[17] However, the findings of ophthalmoscopy performed with the D-Eye device were more sensitive to media opacities and pupil diameter, since 9 eyes were nongradable vs only 4 eyes for biomicroscopy. This can be explained by the direct ophthalmoscopy design of the device, which lacked a condensing lens that is much more subjective to the pupil diameter and lens transparency. Indeed, the resolution achievable with the D-Eye device combined with an iPhone 5 (8-megapixel camera) is approximately 150 pixels per retinal degree, significantly exceeding the image resolution benchmarks of 6 megapixels and 30 pixels per degree set forth by the United Kingdom's National Health Service for effective retinopathy screening and detection of DR-related pathology.[18]

We believe that smartphone ophthalmoscopy using the mobile D-Eye system offers specific practical advantages over the currently available tabletop fundus cameras and other portable ophthalmic imaging devices. First, the ergonomic usability makes this direct ophthalmoscopy technique easier than traditional direct ophthalmoscopy, since the examiner does not need to bring his or her face too close to the patient, but can position himself or herself at a convenient distance and focus the smartphone's camera on the patient's eye by looking at the smartphone's screen. Second, the portability of the system together with the wireless connectivity of smartphones presents a unique opportunity for applications such as telemedicine even in nonhospital or rural settings. Developments in telemedicine networks, along with advances in cloud storage, electronic medical records accessible by smartphones, and encryption technology, now present the prospect for a wholly smartphone-based teleophthalmology system.

TABLE 3. Comparison of Smartphone Ophthalmoscopy and Slit-Lamp Biomicroscopy for the Assessment of Clinically Significant Macular Edema

	Dilated Slit-Lamp Biomicroscopy		Total
Smartphone Ophthalmoscopy	CSME Absent	CSME	
CSME Absent	215 (89.6%)	4 (1.7%)	219 (91.2%)
CSME	4 (1.7%)	17 (7.1%)	21 (8.8%)
Total	219 (91.2%)	21 (8.8%)	240 (100%)

CSME = clinically significant macular edema.

Third, owing to the relatively low hardware and production costs, the final retail price could be less than $300, making the device suitable for community vision screening by a variety of nonophthalmic medical personnel. A drawback of D-Eye system is the need for dilating eye drops to conveniently visualize the peripheral retina, owing to the direct ophthalmoscopy design of the device.

Our study has some limitations. The smartphone ophthalmoscopy was performed by a retina specialist; therefore the reported results cannot be linearly transposed to a nonophthalmologist technician. Secondly, the generalization of the results must take into account that we reported the agreement between only 2 retina specialists, although masked to each other. Further studies with a variety of physicians using the device are needed to deeper validate the clinical use of smartphone ophthalmology.

In conclusion, this study shows that smartphone ophthalmoscopy with the D-Eye system can accurately detect retinal lesions for grading DR and might be used as a screening tool for diabetic retinopathy. The combination of affordability, portability, connectivity, and easy-to-use features of this ophthalmoscopy system provides a foundational platform, based on which a number of revolutionary screening programs can potentially be designed.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST and none were reported. The authors indicate no funding support. Contributions of authors: design of study (A.R., F.M., C.C., F.S.); conduct of study (A.R., L.D., F.S.); data collection (A.R., L.D.); management, analysis, and interpretation of the data (A.R., C.C., L.D., F.S.); preparation of the manuscript (A.R., F.M., C.C., L.D., F.S.); review of the manuscript (A.R., F.M., C.C., L.D., F.S.); and approval of the manuscript (A.R., F.M., C.C., L.D., F.S.).

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Biosketch

Andrea Russo, MD, is a PhD-candidate researcher in clinical ophthalmology with the Eye Clinic, University of Brescia, Italy. He has authored or co-authored numerous articles based on clinical investigations of glaucoma and retina diseases. Dr Russo received his medical degree from the University of Brescia, Italy, and served an Observership at Moorfields Eye Hospital, London, UK.

Comparison of Smartphone-based Ophthalmoscopy versus Dilated Ophthalmic Examination to Detect Ocular Pathologic Features

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BACKGROUND: Retinal imaging has improved considerably since the first photographic images of the ocular fundus were taken near the end of the 19th century. Traditionally, this approach has relied upon expensive and bulky tabletop units, operated by a trained technician in a hospital/clinic setting. These units are complex optical assemblies that require patients to be seated upright, which is often difficult for hospitalized or bedridden patients. Portable fundus cameras have recently become commercially widespread, but these are often costly or remain difficult to use in an ergonomic, hand-held manner.
To overcome these limitations, we took advantage of physicians' pervasive adoption of smartphones, which are equipped nowadays with state-of-the-art cameras. We developed a small optical device, which attaches magnetically to a smartphone, to conveniently examine and record videos or photographs of the retina. This attachment, which we call D-Eye, leverages the portability and wireless connectivity of current smartphones, making it possible to acquire retinal pictures even in remote areas, for viewing and evaluation in a clinical setting. In this article, we evaluate the ability of smartphone-based imaging to detect ocular pathologic features compared to dilated ophthalmic examination by retinal specialist ophthalmologists.

MATERIALS AND METHODS: Overall, 160 outpatients underwent dilated examination and smartphone ophthalmoscopy. Dilating eyedrops (0.5% tropicamide and 10% phenylephrine) were administered to outpatients attending the outpatient service at Spedali Civili di Brecia, Italy. After 20 minutes smartphone ophthalmoscopy was performed in these patients by a retinal specialist (AR). Subsequently another retinal specialist, masked to the findings of the smartphone ophthalmoscopy, performed a retinal slit-lamp examination according to normal clinical practice.
Smartphone Ophthalmoscopy: after pharmacological dilation, a retinal specialist (AR) performed a comprehensive dilated fundus examination with a final prototype (Figure 1) of the D-Eye adapter attached to an iPhone 5 (Apple Inc., Cupertino, CA). The images were captured on 3264 × 2448 pixels of the camera's sensor. Thus, direct fundus ophthalmoscopy was performed using live images displayed on the smartphone's screen. When the pupil is dilated, the device captures a field of view of approximately 20° in a single fundus image at a distance of 1 cm from the patient's eye. Color digital images and videos of the retina were obtained, encompassing the posterior pole, including the macula, optic disc, and peripheral retina.

Figure 1 - Picture of the prototype magnetically attached to an iPhone 5 (Apple, Cupertino, CA).

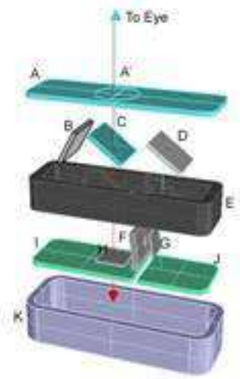
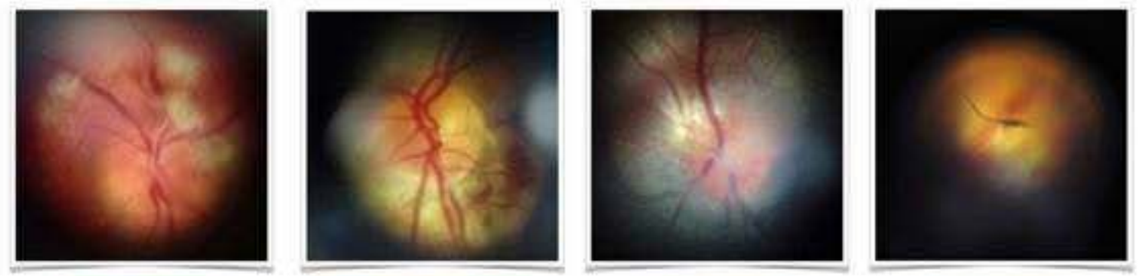


Figure 2 - Exploded view of the D-Eye module (angles and distances between components are approximated). Retinal images are acquired using co-axial illumination and imaging paths thanks to a beam splitter (C). The blue arrow depicts the path of the light; red arrow depicts the path of fundus imaging. Device components are: glass platelet (A) with imprinted negative lens (A'); photo-absorbing wall (B); beam splitter (C); mirror (D); plastic case (E); diaphragm (F); polarized filters (G, H); flash and camera glass (J, I); magnetic external ring (K).

RESULTS: Ocular pathologic features identified by digital smartphone imaging, standard clinical examination, or both included cataract; glaucoma suspicion; age-related maculopathy; chorioretinal atrophy, scar, or both; evidence of systemic disorder (hypertensive or diabetic retinopathy); retinitis pigmentosa; posterior vitreous detachment; retinal detachment.
K values for all lesions (k ≥ 0.66) demonstrated substantial agreement between smartphone-based imaging and clinical examination.

Macular Hole | Posterior Vitreous Detachment | Retinal Detachment | Retinitis Pigmentosa



Grade IV Hypertensive Retinopathy | Choroidal Neovascularization in Choroidal Osteoma | Optic Disc Glioma | Vitreous Floater

DISCUSSION: Recent literature emphasizes smartphones as valuable tools in the field of ophthalmology, while they are also beginning to play a central role as medical diagnostic tools in general. In fact, owing to the portability, data storage capability, and wireless connectivity of smartphones, it is plausible that a smartphone's fundus camera could soon play a significant role in clinical settings. Furthermore, it is estimated that more than one out of every two physicians already uses a smartphone.
In conclusion, this study demonstrates that smartphone ophthalmoscopy with the D-Eye system can be a front line tool to screen patients for ocular pathologic features.
Particularly, smartphone-based ophthalmoscopy shows promise as an alternative to the direct ophthalmoscope for improving access to eye screenings and examinations, as its portability and wireless connectivity enable potential applications such as telemedicine, even in non-hospital or rural settings.

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BACKGROUND: In ophthalmology, images are used extensively for disease documentation, treatment monitoring, and educational purposes. Traditionally, fundus images have been obtained with expensive and bulky tabletop units operated by a trained technician in a hospital clinic setting. The pervasive adoption of smartphones by physicians and their ever-improving built-in camera technology has raised much interest in their use for medical and ophthalmic imaging. The portability and immediate connection capabilities of smartphones make them an attractive device for acquiring retinal pictures in remote non-hospital settings. Indeed, telemedicine has the potential to reach patients and communities that currently receive no or suboptimal eye care as a result of geographic and/or sociocultural barriers.

In the past decade, retinal screening programs for common eye diseases, such as diabetic retinopathy (DR), glaucoma, and age-related macular degeneration, have experienced rapid growth. The application of these screening programs in rural, nurse-operated, highly remote primary care facilities highlights the importance of having access to an inexpensive, portable, easy-to-operate, and high-image-quality fundus camera.

We developed a small optical device, which attaches magnetically to a smartphone, to conveniently examine and record videos or photographs of the retina. This attachment, which we call D-Eye, is a novel, inexpensive, and very portable optical device designed to be magnetically attached to a smartphone.

The purpose of this study was to validate the efficacy of D-Eye device to screen for diabetic retinopathy in the community. We compared the ability of smartphone ophthalmoscopy with that of dilated retinal biomicroscopy to grade DR in patients with diabetes mellitus (DM).

MATERIALS AND METHODS: Overall, 120 consecutive patients with diabetes, new to Diabetes Center's outpatient clinic, underwent dilated retinal digital imaging with a smartphone ophthalmoscope, as a part of their routine examination for diabetes.

Dilating eyedrops (0.5% tropicamide and 10% phenylephrine) were administered to outpatients with diabetes, who were scheduled for an examination at the Diabetes Center. After 20 minutes, smartphone ophthalmoscopy was performed in these patients by a retinal specialist (AR). Subsequently, retinal slit-lamp examination, according to normal clinical practice, was performed by another retinal specialist (FM) who was masked to the findings of smartphone ophthalmoscopy.

Smartphone Ophthalmoscopy: After pharmacological dilation, a retinal specialist (AR) performed a comprehensive dilated fundus examination with a final prototype (Figure 1) of the D-Eye adapter attached to an iPhone 5 (Apple Inc., Cupertino, CA). The images were captured on 3264 × 2448 pixels of the camera's sensor. Thus, direct fundus ophthalmoscopy was performed using live images displayed on the smartphone's screen (a video showing the acquisition procedure is attached). When the pupil is dilated, the device captures a field of view of approximately 25° in a single fundus image at a distance of 1 cm from the patient's eye. Color digital images and videos of the retina were obtained, encompassing the posterior pole, including the macula, optic disc, and peripheral retina.

Figure 1 - Picture of the prototype magnetically attached to an iPhone 5 (Apple, Cupertino, CA).

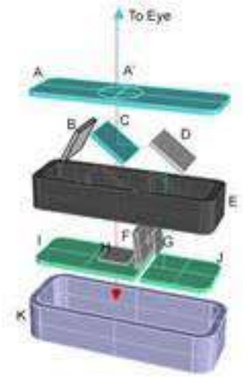

Figure 2 - Exploded view of the D-Eye module (angles and distances between components are approximated). Retinal images are acquired using co-axial illumination and imaging paths thanks to a beam splitter (C). The blue arrow depicts the path of the light; red arrow depicts the path of fundus imaging. Device components are: glass platelet (A) with imprinted negative lens (A'); photo-absorbing wall (B); beam splitter (C); mirror (D); plastic case (E); diaphragm (F); polarized filters (G, H); flash and camera glass (J, I); magnetic external ring (K).

RESULTS: Of the 120 patients with DM who underwent smartphone ophthalmoscopy and slit-lamp biomicroscopy, 55 (45.8%) were men and 28 (23.3%) had type I DM. The mean age at examination was 58.8 ± 16.4 years, and mean duration of DM was 11.6 ± 9.7 years.

Grading of Diabetic Retinopathy: the eye fundus was not gradable for DR in 9 eyes (13.3%) by smartphone ophthalmoscopy and in 4 eyes (3.3%) by biomicroscopy because of cataract and/or small pupil diameter. The clinical level of DR found with both techniques is reported in Table 1. An exact agreement was found in 204 (85%) of 240 eyes and an agreement within one step was observed in 232 eyes (96.7%). Simple κ was 0.78 (95% confidence interval 0.71–0.84; P < 0.001), showing a substantial agreement for the grading of DR between smartphone ophthalmoscopy and slit-lamp biomicroscopy. In 82% of one-step disagreements and 93% of disagreements by two or more steps, the severity level was higher by biomicroscopy grading. Figure 3 shows representative images of healthy and pathological retinas.

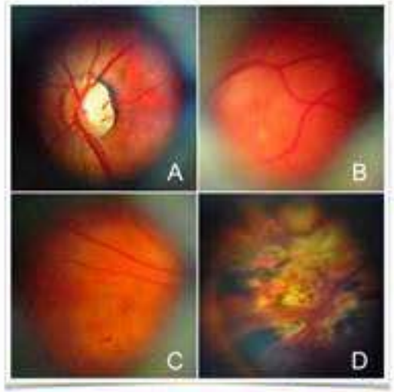

Figure 3 - Representative retinal images taken with D-Eye. (A) Optic disc in a healthy retina. (B) Mild nonproliferative diabetic retinopathy. (C) Moderate nonproliferative diabetic retinopathy. (D) Panretinal photocoagulation scars in a proliferative diabetic retinopathy.

	Smartphone Ophthalmoscopy Number of eyes (%)	Dilated Slit-lamp Biomicroscopy Number of eyes (%)
No apparent retinopathy	122 (50.8%)	115 (47.9%)
Mild nonproliferative diabetic retinopathy	57 (23.8%)	59 (24.6%)
Moderate nonproliferative diabetic retinopathy	32 (13.3%)	33 (13.8%)
Severe nonproliferative diabetic retinopathy	12 (5%)	20 (8.3%)
Proliferative diabetic retinopathy	8 (3.3%)	9 (3.8%)
Not gradable	9 (3.8%)	4 (1.7%)
• Cataract	4 (1.7%)	3 (1.2%)
• Small pupil	6 (2.5%)	1 (0.4%)

Table 1 - Assessment of Diabetic Retinopathy Severity by Smartphone Ophthalmoscopy and Biomicroscopy.

Diabetic Macular Edema: The examiners were asked to note only the presence or absence of clinically significant macular edema. Seventeen eyes (7.1%) were classified as true positive and 4 eyes (1.7%) as false negative (sensitivity 81%); 215 eyes (89.6%) were classified as true negative and 4 eyes (1.7%) as false positive (specificity 98%). Simple κ was 0.79 (95% confidence interval 0.65–0.93; P < 0.001), indicating a substantial agreement between the examined techniques.

DISCUSSION: We believe that smartphone ophthalmoscopy using the mobile D-Eye system offers specific practical advantages over the currently available tabletop fundus cameras and other portable ophthalmic imaging devices. First, the ergonomic usability makes this direct ophthalmoscopy technique easier than traditional direct ophthalmoscopy, since the examiner does not need to bring his face too close to the patient, but can position himself at a convenient distance and focus the smartphone's camera on the patient's eye by looking at the smartphone's screen. Second, the portability of the system together with the wireless connectivity of smartphones presents a unique opportunity for applications such as telemedicine even in non-hospital or rural settings. Developments in telemedicine networks, along with advances in cloud storage, electronic medical records accessible by smartphones, and encryption technology, now present the prospect for a wholly smartphone-based teleophthalmology system.

Third, owing to the relatively low hardware and production costs, the final retail price could be less than $300, making the device suitable for community vision screening by a variety of non-ophthalmic medical personnel.

In conclusion, this study shows that smartphone ophthalmoscopy with the D-Eye system can accurately detect retinal lesions for grading DR. The combination of affordability, portability, connectivity, and easy-to-use features of this ophthalmoscopy system provides a foundational platform, based on which a number of revolutionary screening programs can potentially be designed.

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