Brief Report

Comparison of Nondiabetic Retinal Findings Identified With Nonmydriatic Fundus Photography vs Ultrawide Field Imaging in an Ocular Telehealth Program

Paolo S. Silva, MD; Jerry D. Cavallerano, OD, PhD; Nour Maya N. Haddad, MD, MS; Dorothy Tolls, OD; Komal Thakore, OD; Bina Patel, OD; Mina Sehizadeh, OD; Ann M. Tolson, BS; Jennifer K. Sun, MD, MPH; Lloyd Paul Aiello, MD, PhD

IMPORTANCE Ultrawide field imaging (UWFI) is increasingly being used in teleophthalmology settings. Given the greater area of the retina imaged, we evaluated the ability of UWFI vs nonmydriatic fundus photography (NMFP) to detect nondiabetic retinal findings in a teleophthalmology program.

OBSERVATION We conducted a retrospective single-center comparative cohort study from January 1, 2011, to June 30, 2013, imaging 3864 and 3971 consecutive teleophthalmology patients (7728 and 7942 eyes) using NMFP and UWFI, respectively. Standard diabetic retinopathy evaluation and nondiabetic findings were compared between the 2 imaging modalities. In patients without diabetic retinopathy (2243 by NMFP and 2252 by UWFI), the rate of identification of nondiabetic findings by NMFP (451 patients [20.1%]) and UWFI (490 [21.8%]) were comparable ($P = .19$). Ultrawide field imaging increased the identification of choroidal nevi by 27% (406 eyes [5.3%] by NMFP vs 545 eyes [6.9%] by UWFI; $P < .001$) and chorioretinal atrophy or scarring by 116% (50 eyes [0.6%] by NMFP vs 101 eyes [1.3%] by UWFI; $P < .001$). No peripheral retinal findings were identified with NMFP, while UWFI detected 25 retinal tears (0.3%; $P < .001$), 54 lattice and peripheral degenerations (0.7%; $P < .001$), and 142 cases of vitreous detachment or floaters (1.8%; $P < .001$). Data analysis was performed from November 1, 2013, to May 1, 2014.

CONCLUSIONS AND RELEVANCE In eyes without diabetic retinopathy, approximately 20% may have ocular findings identified on retinal imaging, which emphasizes the role of retinal imaging in patients with diabetes mellitus type 1 and type 2 regardless of the severity of retinopathy. In this cohort, UWFI increased the identification of peripheral retinal and vitreous pathologic findings.

JAMA Ophthalmol. 2016;134(3):330-334. doi:10.1001/jamaophthalmol.2015.5605
Published online January 21, 2016.

Author Affiliations: Beetham Eye Institute, Joslin Diabetes Center, Boston, Massachusetts (Silva, Cavallerano, Haddad, Tolls, Thakore, Patel, Sehizadeh, Tolson, Sun, Aiello); Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts (Silva, Cavallerano, Aiello); Teleophthalmology and Image Reading Center, Philippine Eye Research Institute, University of the Philippines, Manila, Philippines (Silva); New England College of Optometry, Boston, Massachusetts (Patel).

Corresponding Author: Paolo S. Silva, MD, Beetham Eye Institute, Joslin Diabetes Center, One Joslin Place, Boston, MA 02215 (paoloantonio.silva@joslin.harvard.edu).

Diabetes mellitus affects the retinal vasculature and manifests primarily as diabetic retinopathy (DR). However, prior reports from telemedicine programs have found that approximately 26% to 40% of patients with diabetes have ocular abnormalities other than DR.[1,2] Imaging modalities used by telemedicine programs for DR have evolved in the past decade. Traditional flash-based fundus photography is used by the majority of telemedicine programs. During the past 5 years, there has been growing use and adoption of ultrawide field retinal imaging (UWFI). The agreement between UWFI and standard Early Treatment Diabetic Retinopathy Study 7-field color photography in identifying DR and diabetic macular edema has been established.[3-5] Furthermore, UWFI has been shown to reduce the rates of ungradable images by more than 70%, decrease image evaluation time by 25%, and increase the rate of identification of DR by 10%.[6] The nearly 4-fold greater area captured by UWFI may allow identification of additional peripheral, nondiabetic retinal disease that would have otherwise not have been identified with traditional 30° to 50° field fundus photography. When compared with Early Treatment Diabetic Retinopathy Study standard photography, UWFI identifies 1.9 times more neovascularization[7] and provides greater prognostic information with regard to progression of DR.[8] The use of UWFI has been reported in the management of patients with a wide range of retinal pathologic findings other than DR, such as retinal vein occlusion,[9,10] retinal detachment and retinal tears,[11] and choroidal tumors.[12]

Given the potential advantages of UWFI, we compared the ability to identify nondiabetic retinal findings in patients with

diabetes via either nonmydriatic fundus photography (NMFP) or UWFI in an established teleophthalmology program using validated methods of retinal imaging.

Key Points

Question: What nondiabetic retinal findings are identified on nonmydriatic fundus photography compared with ultrawide field imaging in an ocular telehealth program?

Findings: Nonmydriatic fundus photography and ultrawide field imaging identified nondiabetic retinal findings in approximately 20% of patients without diabetic retinopathy.

Meaning: Ultrawide field imaging in teleophthalmology settings may allow the identification of peripheral retinal disease that is otherwise not readily observed.

Methods

The Joslin Vision Network is a validated American Telemedicine Association category 3 ocular telehealth program for DR with established protocols for acquiring and grading nonmydriatic retinal images.[3,13] The study design was consistent with the tenets of the Declaration of Helsinki,[14] and the Joslin Diabetes Center Committee on Human Studies approved the retrospective review of records.

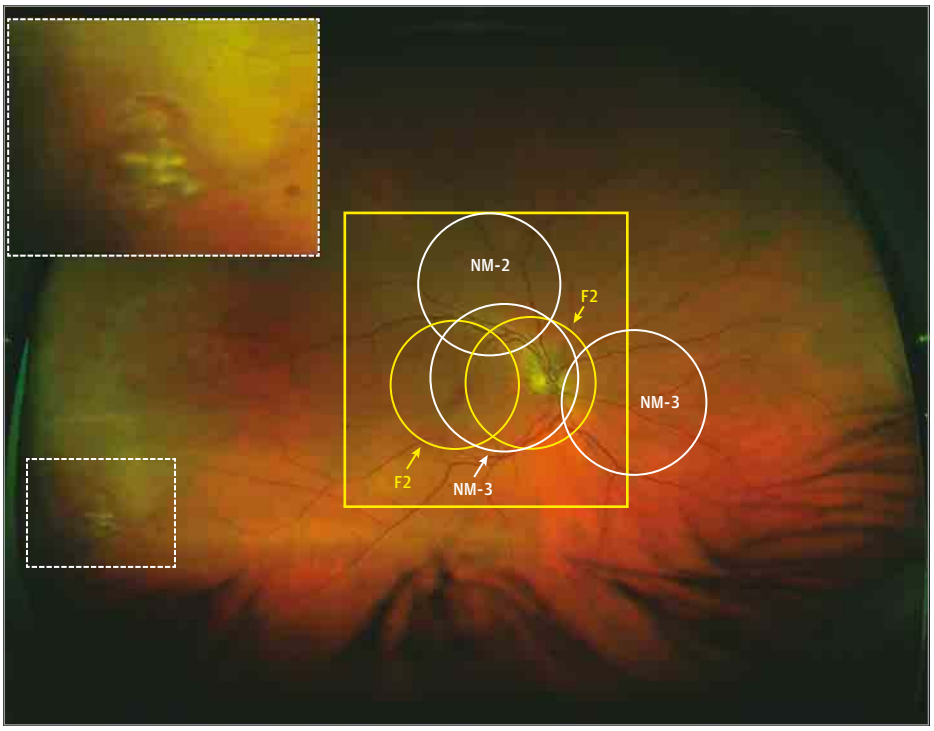
We reviewed the electronic records of all patients receiving Joslin Vision Network retinal imaging at the Joslin Diabetes Center in Boston, Massachusetts, from January 1, 2011, to June 30, 2013. From January 1, 2011, to March 31, 2012, all patients were imaged using lowlight-adapted NMFP. Stereoscopic pairs of three 45° and two 30° retinal fields were acquired according to a prescribed protocol, which has been previously validated to compare favorably with mydriatic Early Treatment Diabetic Retinopathy Study 7 standard fields (**Figure**).[13] From April 1, 2012, to June 30, 2013, all patients were imaged using UWFI, which was acquired using a previously validated image acquisition protocol[3] of stereoscopic pairs of 100° and 200° retinal images for each eye using the Optos P200MA/P200C (Optos, plc) (Figure). All images were graded following a standard protocol at a centralized reading center under supervision by a retina specialist (P.S.S.). All data were recorded using standardized electronic templates.

Nonparametric analyses (Wilcoxon rank sums) were used to compare distributions of continuous variables between groups. The χ^2 and Fisher exact test were used to compare frequencies of categorical variables. All analyses were performed using SAS, version 9.3 (SAS Institute Inc). Data analysis was performed from November 1, 2013, to May 1, 2014.

Results

A total of 3864 and 3971 consecutive patients (7728 and 7942 eyes) were imaged using NMFP and UWFI, respectively. There were no statistically significant differences between groups in age, sex, ethnicity, or insulin use (**Table 1**). Patients imaged with UWFI had a longer mean (SD) duration of diabetes compared with patients imaged with NMFP (13.3 [11.1] vs 12.3 [10.5] years; $P < .001$). Consistent with prior reports,[3,6] the rates of ungradable images using UWFI for DR and diabetic macular edema

Figure. Multifield Nonmydriatic Fundus Photography Compared With Ultrawide Field Imaging



A 200° retinal ultrawide field image with the 100° image area outlined in yellow. The circles (F1, F2: 30° fields; NM-1, NM-2, NM-3: 45° fields) indicate the area imaged via multifield nonmydriatic fundus photography. Dotted lines highlight a horseshoe-shaped retinal tear; inset shows a ×2.25 magnified view of the tear. F indicates field; NM, nonmydriatic.

Table 1. Demographic Characteristics, Diabetic Retinopathy Severity Levels, and Nondiabetic Retinal Findings

Characteristic	Value[a] NMFP (n = 3864)	UWFI (n = 3971)	*P* Value
Age, mean (SD), y	53.4 (16.6)	53.9 (16.3)	.31
Diabetes duration, mean (SD), y	12.3 (10.5)	13.3 (11.1)	<.001
Female sex	1743 (45.1)	1715 (43.2)	.09
White race	2168 (80.8)[b]	2210 (80.0)[b]	.41
Insulin use	2420 (62.6)	2578 (64.9)	.05
Diabetic retinopathy severity			
Absent	2243 (58.0)	2252 (56.7)	
NPDR			
Mild	763 (19.7)	965 (24.3)	
Moderate	198 (5.1)	326 (8.2)	
Severe	41 (1.1)	60 (1.5)	
Very severe	5 (0.1)	5 (0.1)	
PDR	22 (0.6)	25 (0.6)	
High risk	7 (0.2)	8 (0.2)	
Quiescent	105 (2.7)	171 (4.3)	
Ungradable	480 (12.4)	157 (4.0)	<.001
Diabetic macular edema severity			
Absent	3160 (81.8)	3459 (87.1)	
Present, not CSME	125 (3.2)	165 (4.2)	
CSME	126 (3.3)	121 (3.0)	
Ungradable	453 (11.7)	226 (5.7)	<.001
Findings			
Nondiabetic retinal	726 (18.8)	832 (21.0)	.02
Posterior pole			
AMD	331 (8.6)	320 (8.1)	.42
Retinal occlusion			
Artery	0	1 (0.03)	.32
Vein	2 (0.05)	2 (0.05)	.98
Epiretinal membrane	148 (3.8)	123 (3.1)	.08
Optic nerve drusen	14 (0.4)	17 (0.4)	.84
Macular hole	4 (0.1)	4 (0.1)	.97
Hypertensive retinopathy	4 (0.1)	3 (0.08)	.68
Peripheral findings			
Choroidal			
Scar	43 (1.1)	91 (2.3)	<.001
Nevi	356 (9.2)	486 (12.2)	<.001
Retinal			
Emboli	3 (0.08)	11 (0.3)	.04
Tears	0	23 (0.6)	<.001
Lattice and peripheral degenerations	0	39 (1.0)	<.001
Vitreous pathologic findings			
Vitreous detachment or vitreous floaters	0	101 (2.5)	<.001
Asteroid hyalosis	14 (0.4)	25 (0.6)	.09

Abbreviations: AMD, age-related macular degeneration; CSME, clinically significant macular edema; NMFP, nonmydriatic fundus photography; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy; UWFI, ultrawide field imaging.

[a] Data are presented as number (percentage) of patients unless otherwise indicated.

[b] Data on race/ethnicity were available for 2682 patients undergoing NMFP and 2764 of those undergoing UWFI.

were 68.5% and 51.3% lower, respectively, than with NMFP (157 patients [4.0%] vs 480 [12.4%]; $P < .001$, and 226 [5.7%] vs 453 [11.7%]; $P < .001$), and the rates for identification of retinopathy were increased 9.7% with UWFI (1560 [39.2%] vs 1141 [29.5%]; $P < .001$) (Table 1).

Use of NMFP and UWFI identified at least 1 nondiabetic retinal finding in 726 patients (18.8%) and 832 patients (21.0%), respectively ($P = .02$) (Table 1). This increased identification remained significant even after correcting for duration of diabetes. However, in patients without DR (2243 by NMFP and 2252 by UWFI), nondiabetic retinal findings were present in 451 (20.1%) of those imaged with NMFP and 490 (21.8%) imaged with UWFI ($P = .19$).

Nondiabetic retinal findings identified by NMFP and UWFI in all patients are summarized in Table 1 (patient level) and in **Table 2** (eye level) by category: posterior pole disease, periph-

Table 2. Comparison of Nondiabetic Retinal Findings Identified on NMFP and UWFI by Eye and Stratified by Presence or Absence of Retinopathy

Finding	NMFP, No. of Eyes (%)			UWFI, No. of Eyes (%)			*P* Value for NMFP vs UWFI[a]		
	All (n = 7728)	No DR (n = 5352)[b]	DR (n = 1303)[b]	All (n = 7942)	No DR (n = 5649)[b]	DR (n = 1814)[b]	All	No DR	DR
Non-DR findings	2183 (28.2)	1441 (26.9)	390 (29.9)	2146 (27.0)	1538 (27.2)	513 (28.3)	.09	.72	.24
Posterior pole findings									
AMD	543 (7.0)	410 (7.7)	57 (4.4)	549 (6.9)	431 (7.6)	94 (5.2)	.78	.95	.30
RAO	0	0	0	1 (0.01)	0	1 (0.1)	>.99		.40
RVO	5 (0.06)	1 (0.02)	4 (0.3)	10 (0.1)	4 (0.07)	6 (0.3)	.21	.38	.91
Glaucoma suspected	677 (8.8)	477 (8.9)	92 (7.1)	783 (9.9)	557 (9.9)	186 (10.3)	.02	.09	.002
Epiretinal membrane	280 (3.6)	141 (2.6)	88 (6.8)	225 (2.8)	114 (2.0)	104 (5.4)	.005	.03	.24
Optic nerve drusen	14 (0.2)	14 (0.3)	0	17 (0.2)	14 (0.2)	3 (0.2)	.64	.89	.27
Macular hole	4 (0.05)	2 (0.04)	1 (0.08)	4 (0.05)	3 (0.05)	1 (0.06)	>.99	>.99	>.99
HTN retinopathy	6 (0.08)	1 (0.02)	5 (0.4)	6 (0.08)	0	5 (0.3)	.96	.49	>.99
Peripheral findings									
Choroidal									
Scar	50 (0.6)	28 (0.5)	11 (0.8)	101 (1.3)	70 (1.2)	22 (1.2)	<.001	<.001	.32
Nevi	406 (5.3)	319 (6.0)	57 (4.4)	545 (6.9)	414 (7.3)	118 (6.5)	<.001	.004	.01
Retinal									
Emboli	3 (0.04)	3 (0.06)	0	12 (0.2)	7 (0.1)	5 (0.3)	.04	.35	.08
Tears	0	0	0	25 (0.3)	18 (0.3)	7 (0.4)	<.001	<.001	.05
Lattice and peripheral degenerations	0	0	0	54 (0.7)	48 (0.8)	6 (0.3)	<.001	<.001	<.001
Vitreous pathologic findings									
Vitreous detachment or vitreous floaters	0	0	0	142 (1.8)	117 (2.1)	22 (1.2)	<.001	<.001	<.001
Asteroid hyalosis	16 (0.2)	3 (0.06)	6 (0.5)	26 (0.3)	9 (0.2)	4 (0.2)	.15	.10	.33

Abbreviations: AMD, age-related macular degeneration; DR, diabetic retinopathy; HTN, hypertensive; NMFP, nonmydriatic fundus photography; RAO, retinal artery occlusion; RVO, retinal vein occlusion; UWFI, ultrawide field imaging.

[a] χ^2 or Fisher exact test as appropriate.

[b] Includes only eyes that were gradable for presence of diabetic retinopathy.

eral disease, and vitreous pathologic findings. Ultrawide field imaging identified comparable findings within the area covered by NMFP. Only epiretinal membrane differed statistically, being identified more often by NMFP (148 [3.8%] vs 123 [3.1%]; *P* = .08). In contrast, UWFI identified substantially more peripheral abnormalities than did NMFP, including choroidal scars, choroidal nevi, retinal emboli, retinal tears, lattice degeneration, and vitreous detachment. The eye-level findings closely mirror the patient-level findings reported above.

Discussion

In this comparative cohort, nondiabetic retinal lesions were observed using both NMFP and UWFI in approximately 20% of patients with no DR. Ultrawide field imaging substantially increased the identification of nondiabetic findings outside the area imaged by NMFP, including findings such as peripheral lattice degeneration, other retinal degenerations, retinal tears, retinal holes, and choroidal lesions. These disparities result from the differences in the retinal area imaged, being approximately 30% in the combined NMFP fields compared with more than 80% with the single UWFI 200° field (Figure).

Both modalities of nonmydriatic retinal imaging are able to identify retinal changes other than DR to an extent comparable with that reported in previous publications.[1,2] Ultrawide field imaging identified 9.7% more DR in the cohort compared with NMFP, which is also consistent with prior reports from the Joslin Vision Network and other independent groups.[6,7,15] These data highlight the additional diabetic and nondiabetic retinal findings that can be observed with UWFI in teleophthalmology programs that may not be identified by standard 30° to 50° retinal imaging and yet are clinically important and necessary to direct optimal patient care in such settings.

A potential limitation of this study is the comparison of 2 imaging modalities derived from 2 different cohorts of patients imaged at different times. However, this issue is minimized by evaluation of large consecutive patient groups who underwent imaging during a relatively short period, one group immediately after the other, within a single established teleophthalmology program. With the exception of mean (SD) duration of diabetes (13.3 [11.1] years with UWFI vs 12.3 [10.5] years with NMFP; *P* < .001), there were no significant differences observed in the demographic characteristics between the 2 cohorts, and the findings were statistically significant even after adjusting for duration of diabetes. Previous publications have shown consistent agreement between retinal imaging and the clinical identification of nondiabetic retinal findings.[1,2] For posterior pole pathologic findings that are similarly imaged by both NMFP and UWFI, no statistically significant differences were observed between either modality. However, important pathologic findings in the retinal periphery are

substantially better identified by UWFI, allowing more comprehensive and accurate eye care in teleophthalmology programs using this imaging modality.

Conclusions

The results of this study suggest that, when using a standardized image acquisition and evaluation protocol, both NMFP and UWFI can similarly identify nondiabetic retinal findings in approximately 20% of patients with diabetes. In eyes without DR, nondiabetic findings were observed in 26.9% imaged by NMFP and 27.2% imaged by UWFI. These findings emphasize the need for retinal evaluation in all people with diabetes regardless of the presence or severity of DR. Furthermore, the use of UWFI in teleophthalmology settings may allow the identification of important peripheral retinal abnormalities that are not readily identified using NMFP.

ARTICLE INFORMATION

Submitted for Publication: September 8, 2015; final revision received October 29, 2015; accepted November 23, 2015.

Published Online: January 21, 2016. doi:10.1001/jamaophthalmol.2015.5605.

Author Contributions: Dr Silva had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Silva, Cavallerano, Aiello.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Silva, Haddad, Aiello.
Critical revision of the manuscript for important intellectual content: Silva, Cavallerano, Tolls, Thakore, Patel, Sehizadeh, Tolson, Sun, Aiello.
Statistical analysis: Silva, Sun, Aiello.
Obtained funding: Aiello.
Administrative, technical, or material support: Silva, Haddad, Thakore, Patel.
Study supervision: Silva, Cavallerano, Tolson, Aiello.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflict of Interest and none were reported.

Funding/Support: This study was supported by the Massachusetts Lions Eye Research Fund (Drs Silva and Aiello). Temporary loan of 2 ultrawide field imaging devices was provided to the Joslin Diabetes Center by Optos plc.

Role of the Funder/Sponsor: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

REFERENCES

1. Cavallerano AA, Cavallerano JD, Katalinic P, Tolson AM, Aiello LP, Aiello LM; Joslin Vision Network Clinical Team. Use of Joslin Vision Network digital-video nonmydriatic retinal imaging to assess diabetic retinopathy in a clinical program. *Retina*. 2003;23(2):215-223.

2. Chow SP, Aiello LM, Cavallerano JD, et al. Comparison of nonmydriatic digital retinal imaging versus dilated ophthalmic examination for nondiabetic eye disease in persons with diabetes. *Ophthalmology*. 2006;113(5):833-840.

3. Silva PS, Cavallerano JD, Sun JK, Noble J, Aiello LM, Aiello LP. Nonmydriatic ultrawide field retinal imaging compared with dilated standard 7-field 35-mm photography and retinal specialist examination for evaluation of diabetic retinopathy. *Am J Ophthalmol*. 2012;154(3):549-559.e2.

4. Kernt M, Hadi I, Pinter F, et al. Assessment of diabetic retinopathy using nonmydriatic ultra-widefield scanning laser ophthalmoscopy (Optomap) compared with ETDRS 7-field stereo photography. *Diabetes Care*. 2012;35(12):2459-2463.

5. Rasmussen ML, Broe R, Frydkjaer-Olsen U, et al. Comparison between Early Treatment Diabetic Retinopathy Study 7-field retinal photos and non-mydriatic, mydriatic and mydriatic steered widefield scanning laser ophthalmoscopy for assessment of diabetic retinopathy. *J Diabetes Complications*. 2015;29(1):99-104.

6. Silva PS, Cavallerano JD, Tolls D, et al. Potential efficiency benefits of nonmydriatic ultrawide field retinal imaging in an ocular telehealth diabetic retinopathy program. *Diabetes Care*. 2014;37(1):50-55.

7. Wessel MM, Aaker GD, Parlitsis G, Cho M, D'Amico DJ, Kiss S. Ultra-wide-field angiography improves the detection and classification of diabetic retinopathy. *Retina*. 2012;32(4):785-791.

8. Silva PS, Cavallerano JD, Haddad NM, et al. Peripheral lesions identified on ultrawide field imaging predict increased risk of diabetic retinopathy progression over 4 years. *Ophthalmology*. 2015;122(5):949-956.

9. Spaide RF. Peripheral areas of nonperfusion in treated central retinal vein occlusion as imaged by wide-field fluorescein angiography. *Retina*. 2011;31(5):829-837.

10. Prasad PS, Oliver SC, Coffee RE, Hubschman JP, Schwartz SD. Ultra wide-field angiographic characteristics of branch retinal and hemicentral retinal vein occlusion. *Ophthalmology*. 2010;117(4):780-784.

11. Meyer CH, Saxena S. Non-mydriatic imaging of a giant retinal tear with the Optos Optomap Panoramic 200MA. *Clin Experiment Ophthalmol*. 2010;38(4):427.

12. Jain A, Shah SP, Tsui I, McCannel TA. The value of Optos Panoramic 200MA imaging for the monitoring of large suspicious choroidal lesions. *Semin Ophthalmol*. 2009;24(1):43-44.

13. Silva PS, Walia S, Cavallerano JD, et al. Comparison of low-light nonmydriatic digital imaging with 35-mm ETDRS seven-standard field stereo color fundus photographs and clinical examination. *Telemed J E Health*. 2012;18(7):492-499.

14. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-2194. doi:10.1001/jama.2013.281053.

15. Silva PS, Cavallerano JD, Sun JK, Soliman AZ, Aiello LM, Aiello LP. Peripheral lesions identified by mydriatic ultrawide field imaging: distribution and potential impact on diabetic retinopathy severity. *Ophthalmology*. 2013;120(12):2587-2595.