

Developing portable widefield fundus camera for teleophthalmology: Technical challenges and potential solutions

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Impact statement

Prompt eye disease diagnosis and reliable treatment assessment are important for effective prevention of visual losses. Better development of teleophthalmology has been a well-accepted concept to reduce the disparity of eye care in rural areas and underserved regions. This review article summarizes the technical challenges and potential solutions of developing portable widefield fundus camera to foster teleophthalmology.

Abstract

A portable, low cost, widefield fundus camera is essential for developing affordable teleophthalmology. However, conventional trans-pupillary illumination used in traditional fundus cameras limits the field of view (FOV) in a snapshot image, and frequently requires pharmacologically pupillary dilation for reliable examination of eye conditions. This minireview summarizes recent developments in alternative illumination approaches for widefield fundus photography. Miniaturized indirect illumination has been used to enable compact design for developing low cost, portable, widefield fundus camera. Contact mode trans-pars-planar illumination has been validated for ultra-widefield fundus imaging of infant eyes.

Contact-free trans-pars-planar illumination has been explored for widefield imaging of adult eyes. Trans-palpebral illumination has been also demonstrated in a smartphone-based widefield fundus imager to foster affordable teleophthalmology.

Keywords: Fundus camera, fundus photography, retina, choroid, eye, ophthalmology

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Introduction

As a posterior layer of the eye, the retina consists of a neurovascular complex to capture light, convert photon energy to bio-electronic activation, and to initiate visual signal processing. Major eye conditions, including diabetic retinopathy (DR), glaucoma, age-related macular degeneration (AMD), etc., can cause chorioretinal dysfunctions. Fundus examination of the chorioretinal complex is important for eye disease detection, progression monitoring, and treatment outcome evaluation. Because anterior segment of the eye is optically transparent, multiple optical imaging modalities, such as fundus camera, scanning laser ophthalmoscope (SLO), optical coherent tomography (OCT) and OCT angiography (OCTA) systems, have been developed for clinical detection and management of eye diseases. Different imaging modalities have different merits and limitations for clinical applications. For example, SLO and OCT can provide enhanced image contrast and resolution, compared to traditional fundus camera. However, color

fundus camera is relatively simple and costly effective, particularly for screening purpose of eye diseases.^{1,2}

There have been active efforts to develop portable handheld^{3,4} or smartphone^{5–7} fundus cameras for pursuing affordable teleophthalmology. The portable imagers have been successfully demonstrated for DR screening,^{5,8} optic nerve evaluation,^{9,10} and retinopathy of prematurity (ROP) assessment,¹¹ etc. However, one potential concern is the small field of view (FOV) in these systems, which may affect the performance of teleophthalmology. In principle, diagnostic markers such as microaneurysms for DR detection or neurovascular markers for ROP assessment can exist at both the central and peripheral parts of the eye fundus. Therefore, widefield fundus assessment is essential for prompt detection and clinical management of DR,^{12,13} ROP,^{14,15} sickle cell retinopathy (SCR),^{16,17} and other eye conditions which can cause chorioretinal abnormalities at both central and peripheral parts of the fundus. However, it is technically difficult to develop widefield fundus camera. Traditional fundus cameras, including the portable imaging devices, have field of view

(FOV), typically limited at 30° or 45° visual angle in a snapshot image. In order to provide reliable fundus evaluation, mydriatic ETDRS 7-field testing protocol has been developed for DR detection.¹⁸ The traditional mydriatic ETDRS 7-field photography requires pharmacologically pupillary dilation and careful image registration to provide montage image. For telemedicine, particularly in rural or underserved area, one widefield nonmydriatic fundus camera, which can cover both central and peripheral retinal region required for the screening purpose in a single snapshot image, is desirable. In this article, we will summarize the technical challenges and potential solutions of developing one widefield fundus camera to meet the need of affordable telemedicine. Before addressing the details of fundus camera systems, the relationship of visual-angle and eye-angle will be explained.

Visual-angle and eye-angle for FOV quantification

Visual-angle degree is the conventional unit for FOV quantification in fundus imaging. Recently, eye-angle degree has been used as the unit in emerging widefield fundus imaging devices, such as Optos and RetCam systems. The mixed usages of visual-angle θ_v and eye-angle θ_e units have created confusions for FOV quantification in imaging system design and clinical outcome interpretation. Precise conversion between the θ_v and θ_e requires two parameters, i.e. the location of the nodal point and the radius of the eyeball.¹⁹ Figure 1(a) illustrates the eye model to represent average values of human eye.^{20–22} Figure 1(b) verifies that the posterior surface of the crystalline lens as the nodal point of the ocular optics. Figure 1(c) shows the geometric correlation of the visual-angle θ_v and eye-angle θ_e . To simplify the discussion, the half visual-angle θ_v' and half eye-angle θ_e' ,

corresponding to the half space above the optical axis in Figure 1(c), are illustrated. The same correlation is applicable to another half space below the optical axis. Therefore, the full space FOV value is twofold of the half space values in Figure 1(c), i.e. $\theta_v = 2\theta_v'$ and $\theta_e = 2\theta_e'$. Based on the optical parameters in Figure 1(a) and geometric relationship in Figure 1(c), the correlation between the visual-angle θ_v and eye-angle θ_e can be quantified as follows¹⁹

$$\theta_e = \theta_v + 2\sin^{-1}(0.51\sin(\theta_v/2)) \quad (1)$$

According to equation (1), Figure 1(d) depicts the visual-angle θ_v versus eye-angle θ_e graph. In Figure 1(e), the conversion ratio θ_e/θ_v can be used to convert the traditional visual-angle θ_v into eye-angle θ_e . As shown in Figure 1(e), the FOV conversion ratio θ_e/θ_v is not linear from the central to peripheral fields. For central part, e.g. FOV <75° visual-angle, it is reasonable to use the conversion ratio $\theta_e/\theta_v \sim 1.5$ for eye-angle conversion. In contrary, the conversion factor gradually decreases with enlarged FOV, up to 1.34 for 180° visual-angle. The angular conversion ratio $\Delta\theta_e/\Delta\theta_v$ is also included in Figure 1(e) to confirm the nonlinear change of angular relationship. At the central part, 1.0° visual-angle is corresponding to 1.51° eye-angle. In contrary, 1.0° visual-angle increment is corresponding to 1.0° eye-angle change at the far peripheral region.

Technical difficulties of constructing widefield fundus camera

The most challenging factor for widefield fundus imaging is how to provide efficient illumination to the back of the eye. Trans-pupillary illumination, delivering the light

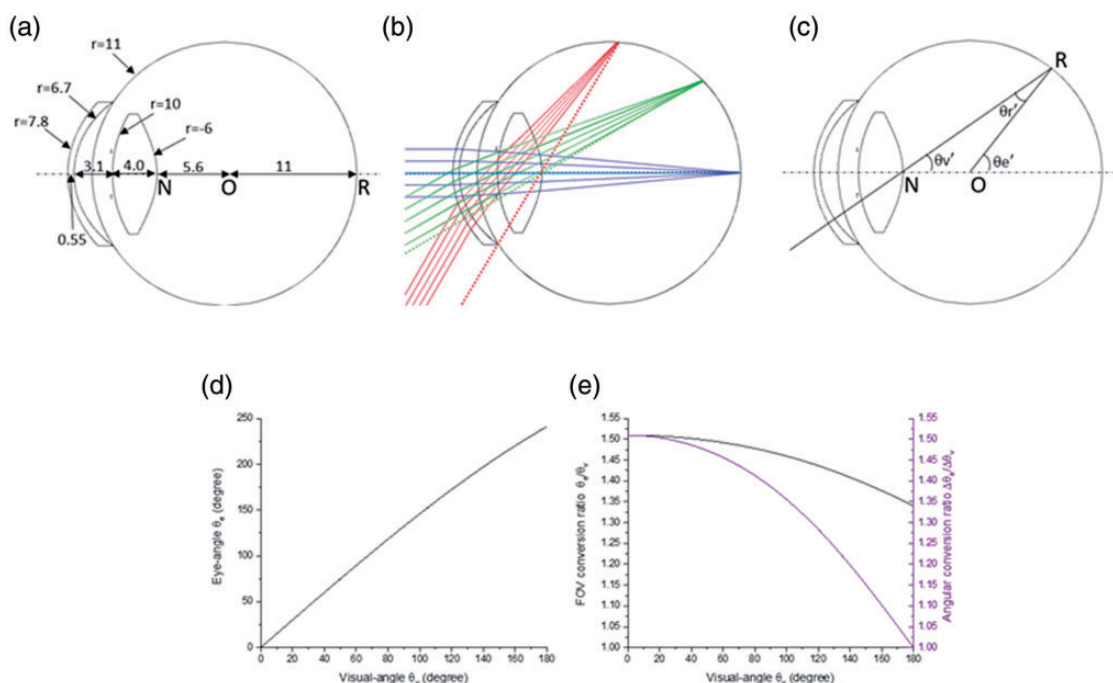


Figure 1. (a) Geometric illustration and major parameters of the eye model. (b) Ray tracing simulation. (c) Illustration of the relationship between the visual-angle and eye-angle. (d) FOV conversion ratio θ_e/θ_v . (e) Angular conversion ratio $\Delta\theta_e/\Delta\theta_v$ at different visual fields. Modified with permission from Yao et al.¹⁹ (A color version of this figure is available in the online journal.)

through the pupil (Figure 2), has been employed in conventional fundus cameras. As shown in Figure 2(a), a ring-shaped light pattern, corresponding to the peripheral region of the available pupil, is designed for trans-pupillary illumination. According to the Gullstrand-Principle,²⁵ the pupil regions used as illumination window, i.e. for delivering illumination light, and observation window, i.e. for collecting imaging light, should be separated from each other. In fact, these illumination and observation pathways should overlap at neither the cornea nor the first surface of crystalline lens (Figure 2(a)). Otherwise, the reflectance artifact from these surfaces can be hundreds of times stronger than the interested scattering light from the fundus of the eye. In order to minimize the potential reflectance artifact, a certain buffer range between the illumination and observation (i.e. imaging) windows at the pupil plane should be considered (Figure 2(a2)). In order to separate the illumination and imaging/observation windows, a popular design is to deliver the ring-shaped illumination through the peripheral region of a hollow mirror, with the transparent hole at the central region for collecting imaging light (Figure 2(b)). In order to ensure the fundus region illuminated corresponding to the same area covered by the camera sensor, a tradeoff between the pupil regions used for light illumination and imaging observation should be carefully designed. Therefore, a traditional fundus camera has a typical FOV range within 30° (Figure 3(a))–45° visual-angle.²⁷ Careful optical design and delicate system construction are needed to provide mandatory tradeoff of the available pupillary regions used for illumination light delivery and imaging light collection, increasing the instrument complexity and device cost of the fundus camera.

In principle, the fundus camera can be rotated relative to the axis of the eye to image different retinal regions, and thus to expand the effective FOV for comprehensive examination. The variable field examination requires necessary

pupil size for effective light illumination and imaging. Therefore, mydriatic ETDRS 7-field imaging protocol has been developed for DR assessment¹⁸ (Figure 3(b)). The traditional mydriatic ETDRS 7-field recording requires a skilled operator for pharmacologically pupillary dilation and careful image registration to produce montage image.

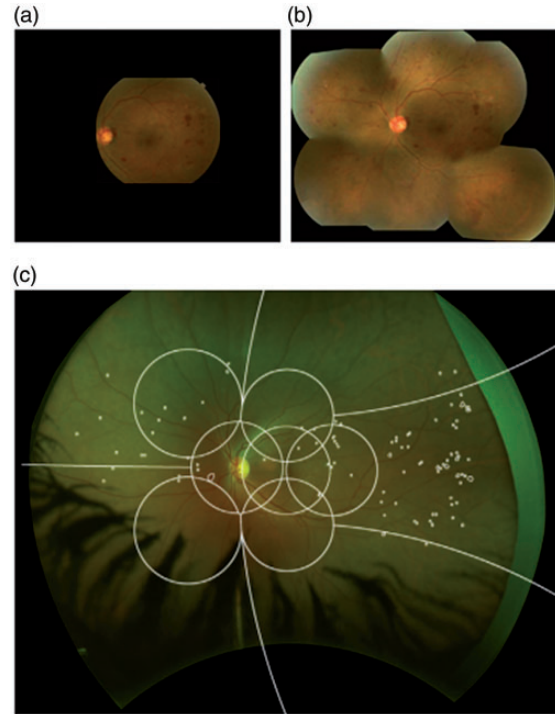


Figure 3. (a) Representative fundus image with a 30° visual-angle FOV. (b) Montage image from the same patient in Figure 3(a) using ETDRS 7-field fundus photography. Images (a) and (b) reprinted with permission from Salz et al.¹⁸ (c) Representative widefield image. Retinal hemorrhage and/or microaneurysm (H/Ma) distributions were annotated on the image. A standardized ETDRS 7-field grid overlay was used to identify the location of the H/Mas. Reprinted from Silva et al.²⁶ (A color version of this figure is available in the online journal.)

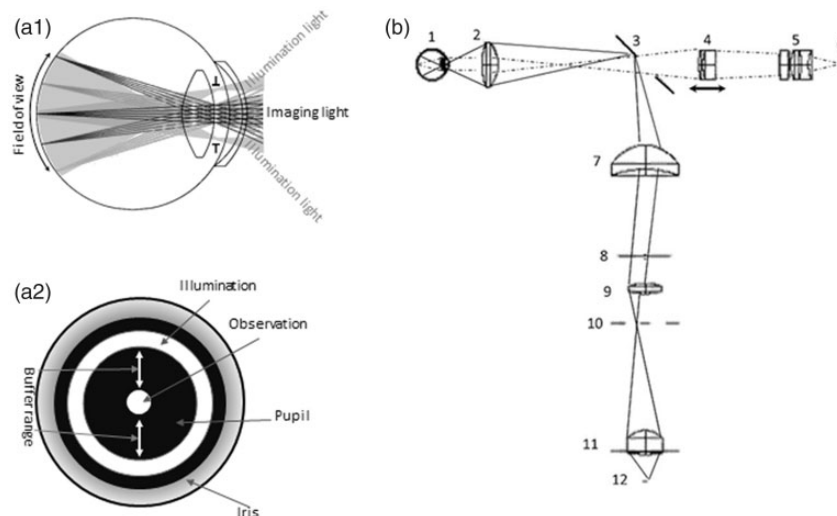


Figure 2. (a) Schematic diagram of ring-shaped trans-pupillary illumination. Side (a1) and front (a2) view illustrations of the pupillary regions for delivering illumination light and collecting imaging light. The ring-shaped illumination pattern corresponds to the periphery part of the pupil, and imaging light is collected through the observation window at the center of the pupil. Reprinted with permission from Toslak et al.²³ (b) Fundus camera system diagram with ring-shaped illumination design. Reprinted with permission from DeHoog et al.²⁴

Ultra-widefield scanning laser ophthalmoscopy (SLO), such as Optos (Figure 3(c)), has been also validated to expand the FOV for better fundus examination.^{28,29} By using two or more lasers with different wavelengths, it is feasible to produce color fundus SLO. However, a dedicated scanning device must be involved. The expensive device cost and professional skills required for system maintenance and operation limit its access to rural or underserved areas for telemedicine.

Miniaturized indirect illumination

Miniaturized indirect illumination has been demonstrated to validate smartphone based widefield fundus camera³⁰ (Figure 4). Figure 4(a) illustrates the indirect illumination pattern, and Figure 4(b) shows the simplified imaging system. There are two unique differences to differentiate the miniaturized indirect illumination system from the optical design used in conventional fundus cameras.

First, instead of using a ring-shaped illumination in conventional fundus camera (Figure 2), a single-spot of the pupil plane is used for indirect illumination of the fundus (Figure 4(a)). For the single-spot illumination in Figure 4(a), roughly a half of the pupil size is required to provide the same buffer range as required in ring-shaped illumination (Figure 2(a)) to minimize the reflectance artifact. Therefore, the FOV of the fundus camera can be readily enhanced, if the same pupil size is available.

Second, the indirect ophthalmoscopy illumination is directly implemented using a miniaturized light source nearby the camera lens (Figure 4(b)). Therefore, the optics in the illumination arm and the hollow mirror in Figure 2(b) is no longer needed, and the imaging system can be simplified significantly to enable a compact design (Figure 4(c)).

In Figure 4(b), the retinal image plane (dashed vertical line RI in Figure 4(b)) is between the lens L1 and lens L2. The retinal image RI is further imaged to the smartphone camera via the lens L2. Using the smartphone fundus camera, a 92° snapshot FOV has been demonstrated.³⁰ With pharmacological pupillary dilation, the smartphone fundus camera can provide real-time video mode to foster easy involvement of skilled ophthalmologists remotely.³⁰ Montage image processing can further increase the effective FOV for comprehensive eye examination (Figure 5(d)).

In cooperation with a near infrared light guidance for retinal focusing, the miniaturized indirect ophthalmology illumination has been also demonstrated for nonmydriatic fundus photography,²³ with snapshot FOV up to 101° eye-angle (Figure 6).

Trans-scleral illumination

Trans-scleral illumination provides one alternative approach to conduct ultra-widefield fundus imaging examination. Instead of delivering illumination light through the pupil in conventional trans-pupillary illumination, trans-scleral illumination delivers the light from the sclera, i.e. a region different from the pupil (Figure 7(a1)). By freeing the available pupil for recording imaging light only, trans-scleral illumination can readily increase the snapshot FOV for widefield fundus photography.

As shown in Figure 7, the trans-scleral illumination based Panoret-1000TM can capture the retinal image covered from the optic disc to the far peripheral region (Figure 7(b)). However, the Panoret-1000TM is commercially discontinued. The Panoret-1000TM might fail due to (1) the bulky design and expensive cost, (2) complication of contact-mode imaging: direct contact of the

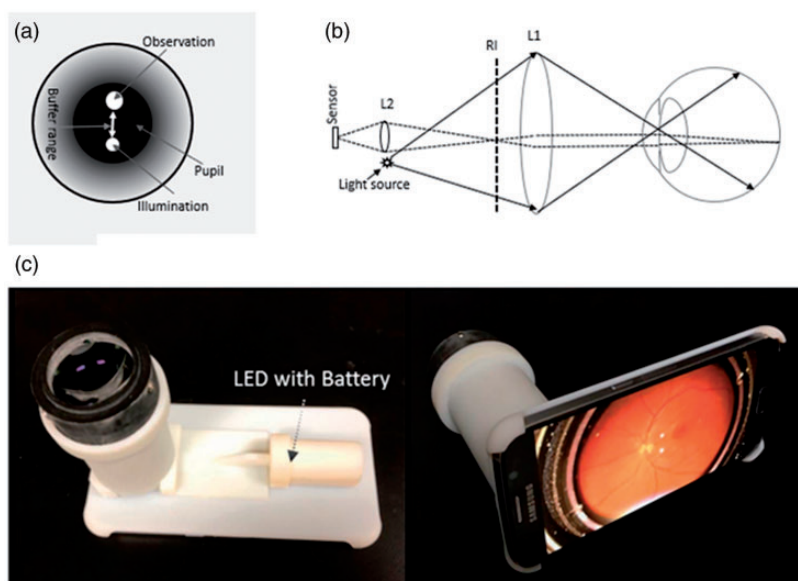


Figure 4. (a) Schematic diagram of miniaturized indirect illumination. Reprinted with permission from Toslak et al.²³ (b) Optical layout of a fundus camera with miniaturized indirect illumination; (c) Representative photographs of a smartphone-based fundus camera with miniaturized indirect illumination. (b) and (c) Reprinted with permission from Toslak et al.³⁰ (A color version of this figure is available in the online journal.)

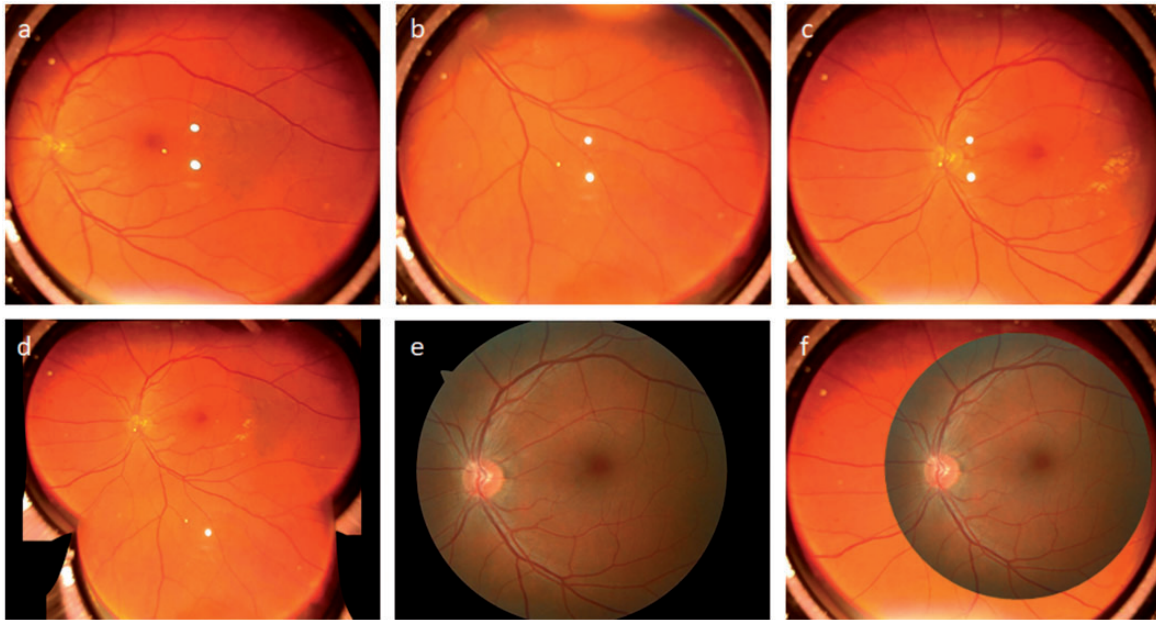


Figure 5. (a) to (c) Representative snapshot fundus images with the fundus camera in (d) Montage processing of snapshot images shown in Figure 5(a) to (c). (e) Comparative fundus image from the same subject acquired with a clinical device (Cirrus Photo 800, Zeiss) with 45° visual-angle (67.5° eye-angle) FOV. (f) Comparative illustration of Figure 5(c) and (e). Reprinted with permission from Toslak et al.³⁰(A color version of this figure is available in the online journal.)

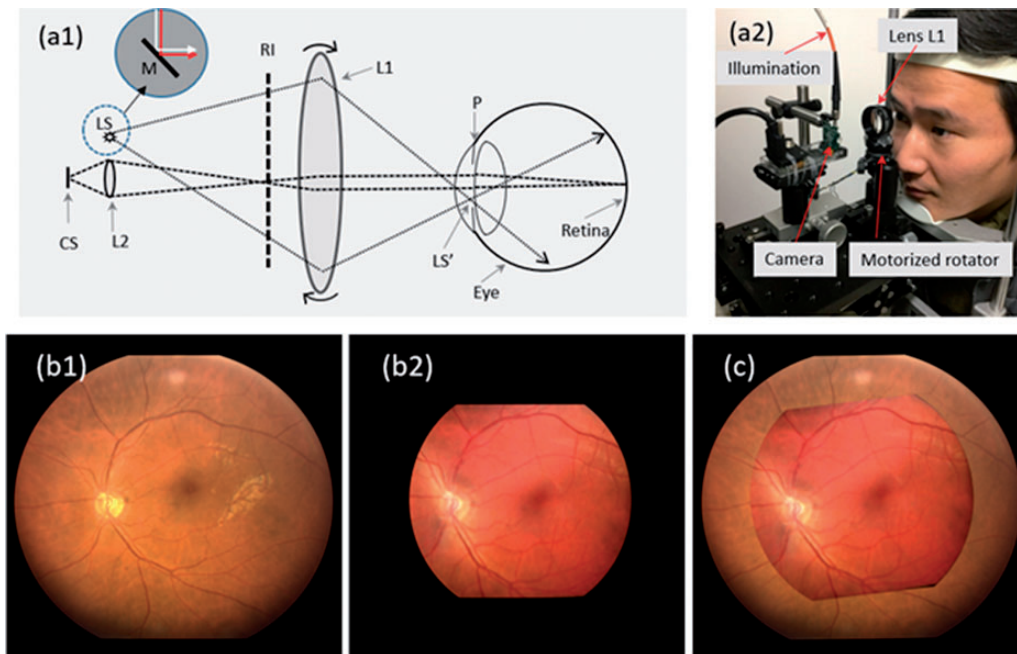


Figure 6. (a) Optical layout (a1) and photograph (a2) of the miniaturized indirect illumination-based fundus camera. (b) Comparative imaging with the prototype device (b1) and a commercial fundus camera (b2). (c) FOV comparison of the images (b1) and (b2) from the same subject. Modified with permission from Toslak et al.²³(A color version of this figure is available in the online journal.)

illuminator and image probe to the eyeball is not favorable and careful sterilization is required to minimize cross-contamination, and (3) difficulty of obtaining good retinal images: the illumination efficiency and image quality are highly dependent on the scleral location for light delivery.

Trans-palpebral illumination

Trans-palpebral illumination has been demonstrated as one alternative to the trans-scleral illumination for widefield fundus photography.³³ Instead of directly contacting the illuminator to the sclera in trans-scleral illumination, the

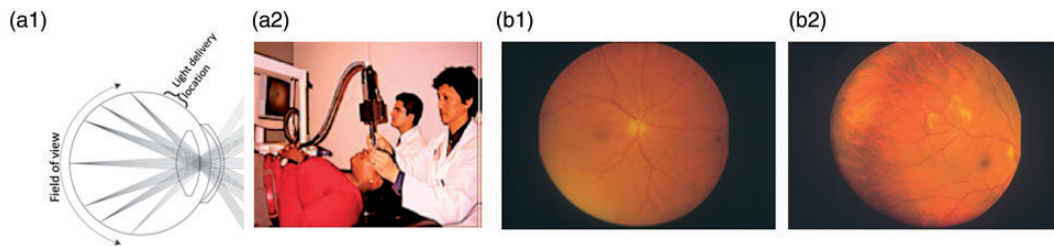


Figure 7. (a) Schematic diagram of trans-scleral illumination (a1) used in Panoret-1000™ (a2). (b) Representative fundus images of eyes with DR (b1) and sclero-choroidal calcification (b2) employing trans-scleral illumination. Image a2 reprinted from reference.³¹ (b1) and (b2) reprinted from Shields et al.³² (A color version of this figure is available in the online journal.)

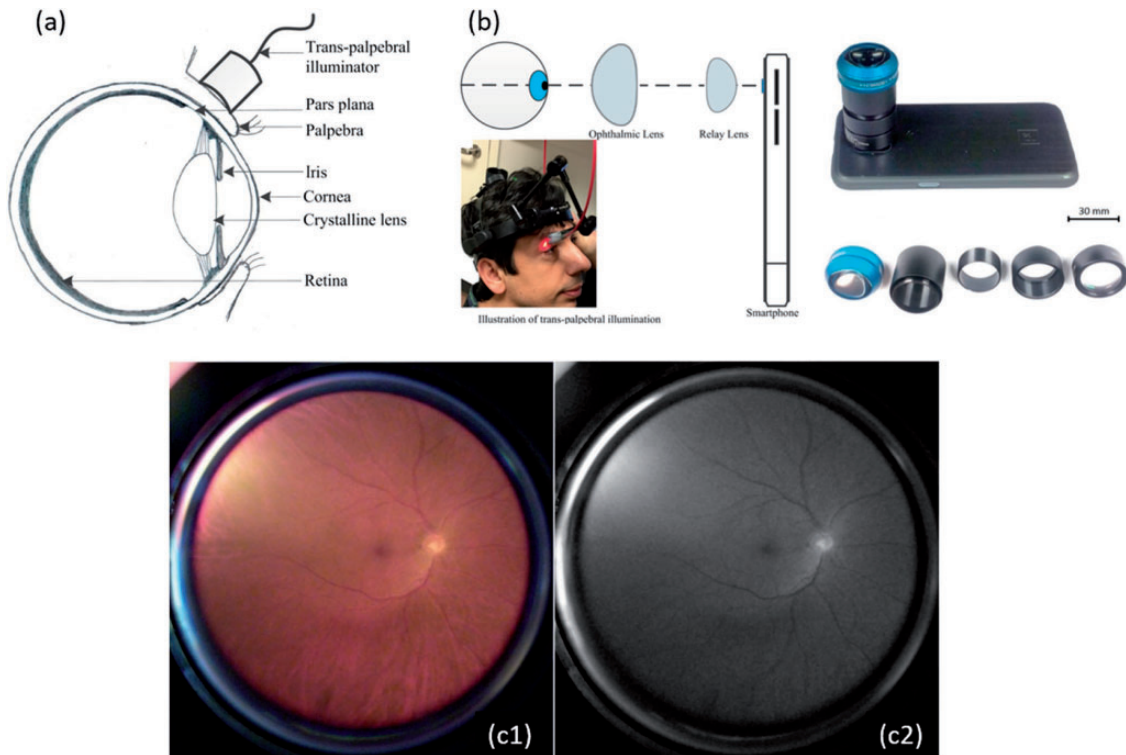


Figure 8. (a) Schematic illustration of trans-palpebral illumination. (b) Optical layout and photograph of the smartphone fundus camera with trans-palpebral illumination. (c) Representative color fundus (c1) and green channel (c2) images taken with smartphone fundus camera using trans-palpebral illumination. Modified with permission from Toslak et al.³³ (A color version of this figure is available in the online journal.)

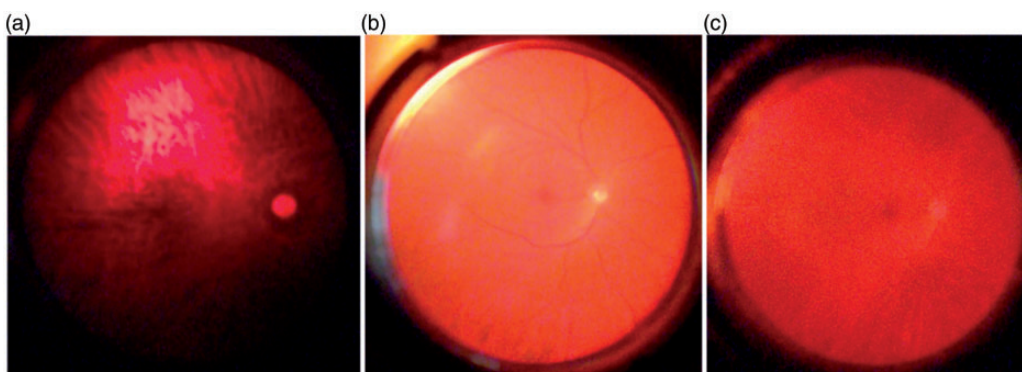


Figure 9. Representative images acquired with trans-palpebral illumination from the (a) posterior, (b) center, and (c) anterior of the pars plana. Reprinted with permission from Toslak et al.³³ (A color version of this figure is available in the online journal.)

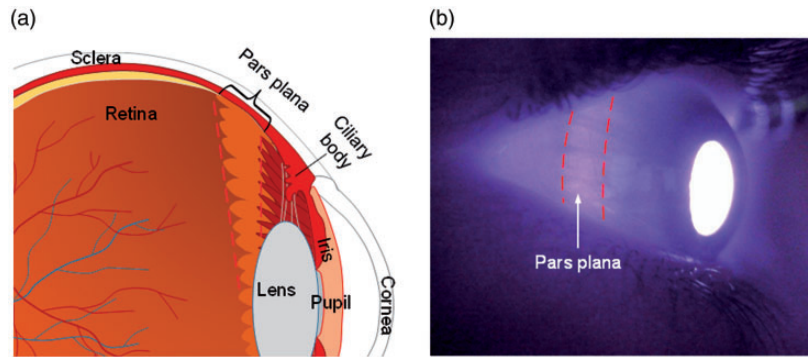


Figure 10. Schematic diagram (a) and photographic illustration (b) of pars plana. Reprinted with permission from Wang et al.³⁴ (A color version of this figure is available in the online journal.)

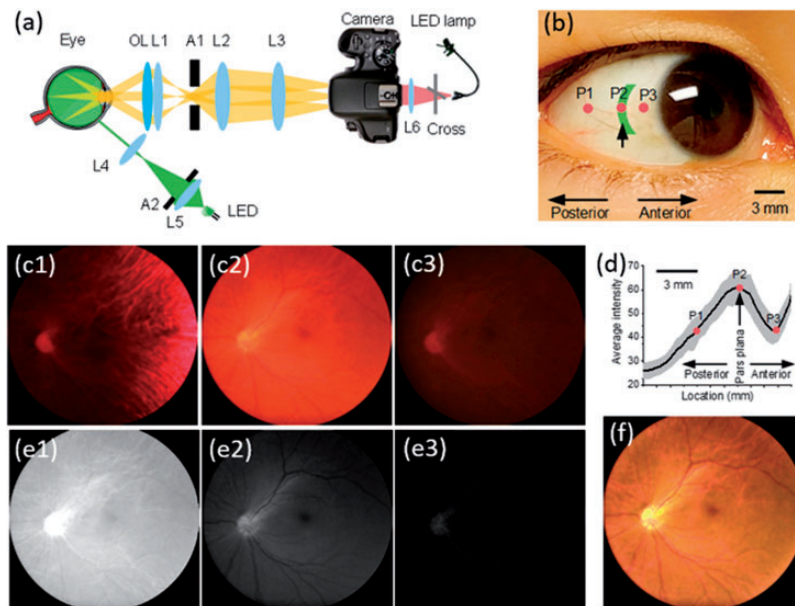


Figure 11. Contact-free fundus imaging using trans-pars-planar illumination. (a) Schematic diagram of a benchtop fundus camera with trans-pars-planar illumination. (b) Illustration of posterior, center, and anterior regions for comparative fundus imaging. (c) Retinal images (c1) to (c3) correspond to illumination locations P1–P3 in (b). (d) Comparative analysis of location dependency of the illumination efficiency. P1–P3 show illumination locations for recording images (c1) to (c3). (e) Separate illustration of red, green, and blue channels of the color image (c2). (f) Color brightness balanced image of (c2). Modified with permission from Wang et al.³⁴ (A color version of this figure is available in the online journal.)

trans-palpebral illuminator delivers the light through the eyelid. Moreover, the smartphone fundus camera is for contact-free imaging, compared to the contact-mode imager in Figure 7. Without direct contact of the illuminator and imager to the eyeball, the trans-palpebral illumination-based smartphone fundus camera promises a simple solution to achieve affordable widefield imaging. Figure 8 shows representative fundus imaging with a 152° eye-angle FOV in a snapshot image.³⁴ Figure 9 shows representative images acquired with illumination light delivered from the (a) posterior, (b) center, and (c) anterior of the pars plana.

Trans-pars-planar illumination

As shown in Figure 9, the illumination efficiency and image quality are dependent on the location for trans-scleral or trans-palpebral illumination.³³ In other words, the optical

property of the sclera is not homogeneously distributed. Figure 10 shows schematic (Figure 10(a)) and photographic (Figure 10(b)) illustration of the pars plana. The pars plana is one posterior portion of the ciliary body (Figure 10(a)), with a $\sim 3\text{--}4$ mm distance posterior to the limbus and a ~ 4 mm band width.^{35,36} The pars planar region has relatively low density of muscle, blood vessels, and pigmentation, compared to other scleral area.³³ Hence, its light transparency is better than other scleral regions, providing a unique window for delivering light into the eye.³⁴

Contact-free “trans-pars-planar” illumination has been recently demonstrated for nonmydriatic widefield photography.³⁴ As shown in Figure 11, the illumination can be projected to the sclera without direct contact. The fundus images collected with illumination light delivered through the posterior (Figure 11(c1)), center (Figure 11(c2)), and anterior (Figure 11(c3)) of the pars plana is consistent to the observation in Figure 9. The brightness analysis of

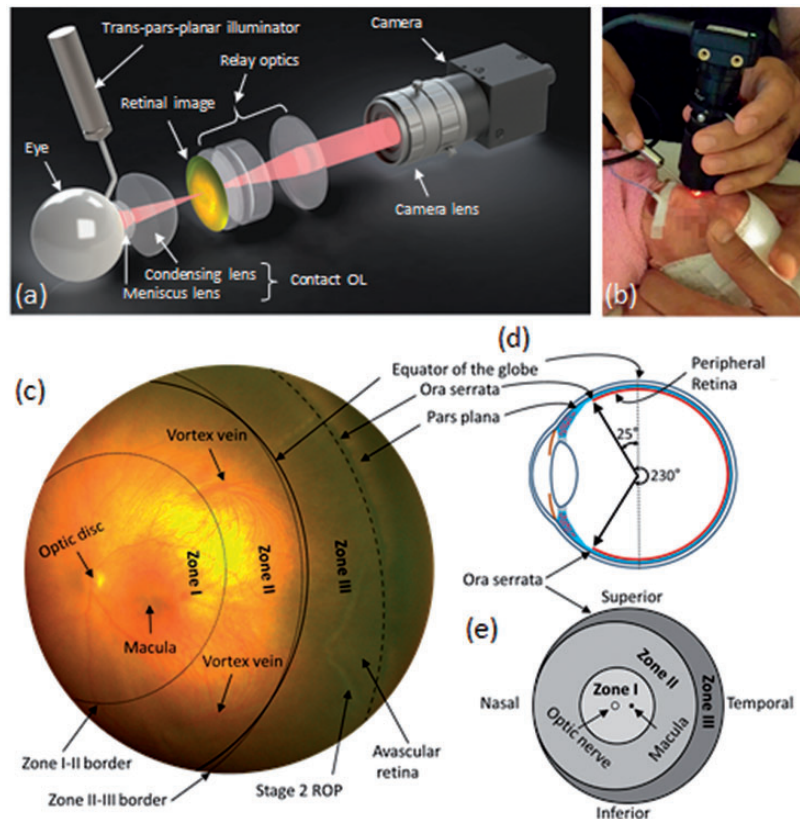


Figure 12. (a) Optical diagram of the lab prototype PedCam. (b) Photographic illustration of the prototype device for retinal examination. (c) Representative retinal images collected with the PedCam from one eye with zone III stage 2 ROP. (d) Schematic illustration of the cross-section of the eye. (e) Schematic illustration of the fundus, illustrating three retinal zones for ROP detection and classification. Modified with permission from Toslak et al.³⁷ (A color version of this figure is available in the online journal.)

fundus images collected from different locations further confirms the transparency of the pars plana (Figure 11 (d)). The coefficients of light absorption and scattering are known to be wavelength dependent. As shown in Figure 11 (c), the fundus image is red dominant because the red light is much more efficient than that of the shorter wavelength green and blue light. Spectral analysis of the fundus image, i.e. separate evaluation of the red, green, and blue channels, confirms the different color efficiencies of the trans-pars-planar illumination (Figure 11(e)). Figure 11(f) shows normalized illustration of the Figure 11(c2), with digitally brightness balance of color channels.

Portable fundus camera based on trans-pars-planar illumination

Contact-mode trans-pars-planar illumination has been also validated in a portable pediatric camera (PedCam).³⁷ Since the trans-pars-planar illumination significantly simplifies the system requirement, a low weight handheld PedCam can be readily achieved (Figure 12). For proof-of-concept experiment, all off-the-shelf parts were used to construct the lab prototype system in Figure 12. By freeing the available pupil for recording imaging light only, the trans-pars-planar illumination-based PedCam provides a 200° FOV, allowing comprehensive evaluation from the central retina to peripheral region up to the ora serrata. The lab prototype PedCam has been validated for retinal imaging

of the eyes with ROP and retinoblastoma treatments (Figure 13).

Moreover, the multispectral trans-pars-planar illumination has been also validated for selective imaging of the retinal and choroidal structures.³¹ Figure 14 show representative images of the choroidal layer, with near infrared light illumination.

Discussion

Prompt diagnosis and reliable treatment assessment of eye conditions are important for effective prevention of vision losses. Better development of teleophthalmology has been a well-accepted concept to reduce the disparity of eye care in rural areas and underserved regions. With the COVID-19 pandemic, the increasing demand has been emphasized for providing homecare telemedicine even in urban areas, fostering social-distancing to minimize potential infections. It is known that eye diseases may affect any part of the chorioretinal system. Therefore, a widefield fundus camera is essential to provide sufficient information for teleophthalmology. Moreover, the widefield fundus camera should be affordable and easy to use, because the access to expensive devices and skilled operators is typically limited in rural and underserved areas.

Conventional trans-pupillary illumination delivers a ring-shaped light pattern through the peripheral region of the available pupil, and careful tradeoff between the

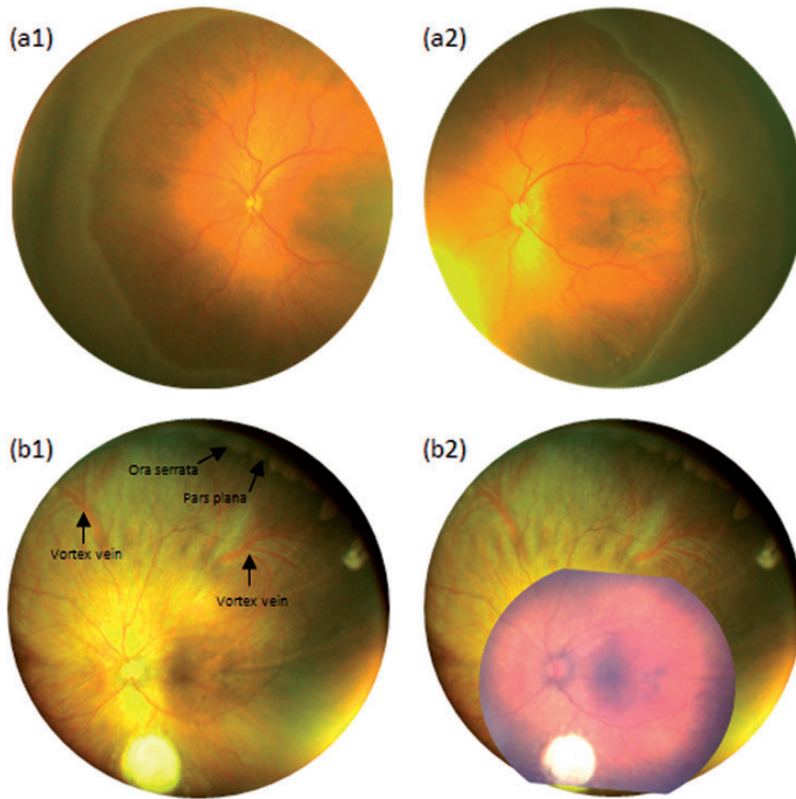


Figure 13. Representative 200° PedCam images captured from patients with ROP (a) and retinoblastoma (b). Comparative 130° clinical RetCam image is overlapped on the 200° PedCam image in (b2). Modified with permission from Toslak et al.³⁷(A color version of this figure is available in the online journal.)

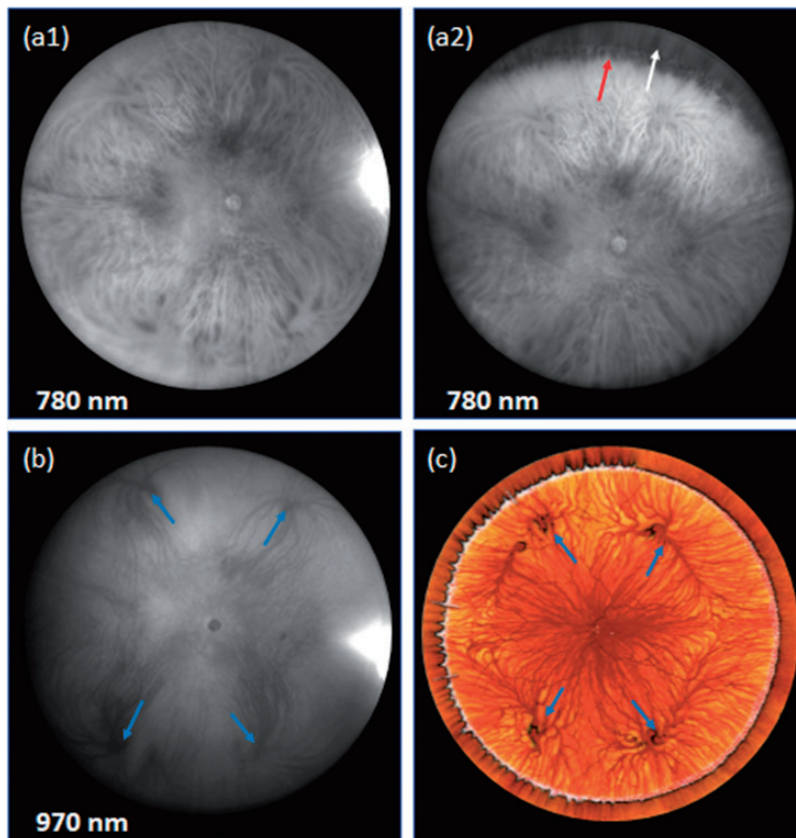


Figure 14. Choroidal images collected with 780 nm (a) and 970 nm (b) near infrared illumination. (c) Schematic illustration of the fundus of young adult. The red and white arrows in a2 point to the ora serrata and pars plana, respectively. The blue arrows in b in c indicate vortex vein ampullas. Reprinted with permission from Toslak et al.³⁸ (A color version of this figure is available in the online journal.)

illumination and observation pathways is required to minimize the reflectance artifacts at the cornea and crystalline lens (Figure 2).

The miniaturized indirect illumination provides a feasible strategy to expand the FOV in a single snapshot image³⁰ (Figure 4). With the NIR imaging guidance, the miniaturized indirect illumination has been validated for nonmydriatic fundus imaging, with snapshot FOV up to 101° eye angle²³ (Figure 6). We anticipate that further optimization of the miniaturized indirect illumination may provide a practical solution to enable a nonmydriatic fundus camera with a snapshot FOV that can cover the whole fundus region in traditional mydriatic ETDRS 7-field photography.¹⁹ The simplified illumination strategy excludes the need of the separate illumination path in traditional fundus camera, and thus enables smartphone-based fundus camera³⁰ (Figure 4) and compact benchtop device²³ (Figure 6). The simple, compact design is essential for cost control to foster telemedicine deployments in rural areas and underserved regions.

Trans-scleral illumination provides one alternative strategy for developing ultra-widefield fundus cameras (Figure 7). By freeing the whole available pupil for collecting imaging light only, trans-scleral illumination can readily achieve a snapshot FOV beyond the equator of the eye. It is aware of that the illumination efficiency and image quality depend on the illumination location, and the pars plana provides a relatively transparent window for optimal illumination³⁴ (Figures 9 and 10) Using the trans-pars-planar illumination, a 200° snapshot FOV has been achieved in a portable contact-mode PedCam (Figures 12 and 13).³⁷ The multispectral trans-pars-planar illumination has been also used to validate ultra-widefield imaging of the retina and choroid (Figure 14).³⁸ The contact mode is favorable for pediatric imaging, particularly for ROP screening of newborns, to reduce the effect of eye movements. However, the contact-mode imaging is not favorable for adult patients, such as for DR screening and diagnosis, because the direct contact of the illuminator and imager to the eyeball is not comfortable, with potential risk of inflammation due to cross-contamination. Moreover, the contact-mode imaging may increase the operation cost due to special training for eyeball contact handling and the device sterilization required. These complications may provide challenges for telemedicine deployments in rural areas and underserved regions.

By projecting the illumination pattern to the sclera without physical contact, contact-free trans-pars-planar illumination has been demonstrated for nonmydriatic widefield photography, with a 90° snapshot FOV³⁴ (Figure 11). Compared to the 200° snapshot FOV in contact-mode imaging,^{37,38} the contact-free trans-pars-planar illumination provides a compromised FOV. This results from the distance between the eye and imaging optics and the space required for illumination light projection (Figure 11(a)).

Trans-palpebral illumination has been also validated in a nonmydriatic smartphone fundus camera, with a 152° snapshot FOV.³³ The trans-palpebral illumination involves only eyelid contact which is relatively simple and the sterilization complication significantly low, compared to

eyeball contact in contact-free trans-pars-planar illumination. The 152° snapshot FOV covers a fundus region larger than that in traditional mydriatic ETDRS 7-field photography. One disadvantage of the trans-palpebral illumination is the lowered light efficiency due to the illumination light should pass through the eyelid before the pars plana. However, the image quality with the preliminary prototype fundus camera is promising to reveal retinal vasculatures (Figure 8). In principle, there is great room to further enhance the image performance by using pulsed light illumination with increased power. Moreover, multispectral imaging of the retina and choroid is also possible by employing independent visible and NIR illumination light controls³⁸ (Figure 14).

Conclusions

In conclusion, miniaturized indirect illumination provides a feasible strategy to enable compact design for developing low cost, portable widefield fundus camera. Contact-mode trans-pars-planar illumination allows ultra-widefield fundus camera for pediatric imaging application. Contact-free trans-pars-planar illumination is possible with a reduced FOV, compared to contact-mode imaging. Trans-palpebral illumination can provide a tradeoff between light efficiency and FOV for developing portable, widefield fundus camera to foster affordable teleophthalmology.

AUTHORS' CONTRIBUTIONS

XY drafted the article. TS and JM contributed to the article preparation.

DECLARATION OF CONFLICTING INTERESTS

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REFERENCES

- Xiao B, Liao Q, Li Y, Weng F, Jin L, Wang Y, Huang W, Yi J, Burton MJ, Yip JL. Validation of handheld fundus camera with mydriasis for retinal imaging of diabetic retinopathy screening in China: a prospective comparison study. *BMJ Open* 2020;10:e040196

2. Tuulonen A, Airaksinen PJ, Montagna A, Nieminen H. Screening for glaucoma with a non-mydratic fundus camera. *Acta Ophthalmol (Copenh)* 1990;**68**:445-9
3. Jin K, Lu H, Su Z, Cheng C, Ye J, Qian D. Telemedicine screening of retinal diseases with a handheld portable non-mydratic fundus camera. *Bmc Ophthalmol* 2017;**17**:89
4. Wang S, Jin K, Lu H, Cheng C, Ye J, Qian D. Human visual system-based fundus image quality assessment of portable fundus camera photographs. *IEEE Trans Med Imaging* 2016;**35**:1046-55
5. Tan CH, Kyaw BM, Smith H, Tan CS, Tudor Car L. Use of smartphones to detect diabetic retinopathy: scoping review and meta-analysis of diagnostic test accuracy studies. *J Med Internet Res* 2020;**22**:e16658
6. Palacios DR, Shen K, Baig S, Wang JH, Zhang C, Chen D, Wang MR. Widefield of view handheld smart fundus camera for telemedicine applications. *J Med Imaging* 2021;**8**:26001
7. Russo A, Morescalchi F, Costagliola C, Delcassi L, Semeraro F. A novel device to exploit the smartphone camera for fundus photography. *J Ophthalmol* 2015;**2015**:823139
8. Queiroz MS, de Carvalho JX, Bortoto SF, de Matos MR, das Gracas Dias Cavalcante C, Andrade EAS, Correa-Giannella ML, Malerbi FK. Diabetic retinopathy screening in urban primary care setting with a handheld smartphone-based retinal camera. *Acta Diabetol* 2020;**57**:1493-9
9. Bastawrous A, Giardini ME, Bolster NM, Peto T, Shah N, Livingstone IA, Weiss HA, Hu S, Rono H, Kuper H, Burton M. Clinical validation of a smartphone-based adapter for optic disc imaging in Kenya. *JAMA Ophthalmol* 2016;**134**:151-8
10. Wintergerst MWM, Brinkmann CK, Holz FG, Finger RP. Undilated versus dilated monoscopic smartphone-based fundus photography for optic nerve head evaluation. *Sci Rep* 2018;**8**:10228
11. Wintergerst MWM, Petrak M, Li JQ, Larsen PP, Berger M, Holz FG, Finger RP, Krohne TU. Non-contact smartphone-based fundus imaging compared to conventional fundus imaging: a low cost alternative for retinopathy of prematurity screening and documentation. *Sci Rep* 2019;**9**:19711
12. Pugh JA, Jacobson JM, Van Heuven WA, Watters JA, Tuley MR, Lairson DR, Lorimor RJ, Kapadia AS, Velez R. Screening for diabetic retinopathy. The wide-angle retinal camera. *Diabetes Care* 1993;**16**:889-95
13. Chalam KV, Brar VS, Keshavamurthy R. Evaluation of modified portable digital camera for screening of diabetic retinopathy. *Ophthalmic Res* 2009;**42**:60-2
14. Fierson WM, Capone A Jr; American Academy of Pediatrics Section on O, American Academy of Ophthalmology AAoCO. Telemedicine for evaluation of retinopathy of prematurity. *Pediatrics* 2015;**135**:e238-54
15. Wang SK, Callaway NF, Wallenstein MB, Henderson MT, Leng T, Moshfeghi DM. SUNDROP: six years of screening for retinopathy of prematurity with telemedicine. *Can J Ophthalmol* 2015;**50**:101-6
16. Alabduljalil T, Cheung CS, VandenHoven C, Mackeen LD, Kirby-Allen M, Kertes PJ, Lam WC. Retinal ultra-widefield colour imaging versus dilated fundus examination to screen for sickle cell retinopathy. *Br J Ophthalmol* 2020;**105**:1121-6
17. Linz MO, Scott AW. Widefield imaging of sickle retinopathy. *Int J Retina Vitreous* 2019;**5**:27
18. Salz DA, Witkin AJ. Imaging in diabetic retinopathy. *Middle East Afr J Ophthalmol* 2015;**22**:145-50
19. Yao X, Toslak D, Son T, Ma J. Understanding the relationship between visual-angle and eye-angle for reliable determination of the field-of-view in ultra-widefield fundus photography. *Biomed Opt Express* 2021;**12**:6651-9
20. Liou HL, Brennan NA. Anatomically accurate, finite model eye for optical modeling. *J Opt Soc Am A Opt Image Sci Vis* 1997;**14**:1684-95
21. Artal P. Optics of the eye and its impact in vision: a tutorial. *Adv Opt Photon* 2014;**6**:340-67
22. Wu Q, Tang Y, Chen X, Ma C, Yao F, Liu L. Method for evaluating ophthalmic lens based on eye-lens-object optical system. *Opt Express* 2019;**27**:37274-85
23. Toslak D, Liu C, Alam MN, Yao X. Near-infrared light-guided miniaturized indirect ophthalmoscopy for nonmydratic widefield fundus photography. *Opt Lett* 2018;**43**:2551-4
24. DeHoog E, Schwiegerling J. Fundus camera systems: a comparative analysis. *Appl Opt* 2009;**48**:221-8
25. Gullstrand A. New methods of reflexless ophthalmoscopy. *Berichte Deutsche Ophthalmologische Gesellschaft* 1910;**36**:326
26. Silva PS, El-Rami H, Barham R, Gupta A, Fleming A, van Hemert J, Cavallerano JD, Sun JK, Aiello LP. Hemorrhage and/or microaneurysm severity and count in ultrawidefield images and early treatment diabetic retinopathy study photography. *Ophthalmology* 2017;**124**:970-6
27. Panwar N, Huang P, Lee J, Keane PA, Chuan TS, Richhariya A, Teoh S, Lim TH, Agrawal R. Fundus photography in the 21st century - a review of recent technological advances and their implications for worldwide healthcare. *Telemed J E Health* 2016;**22**:198-208
28. Nagiel A, Lalane RA, Satta SR, Schwartz SD. Ultra-widefield fundus imaging: a review of clinical applications and future trends. *Retina* 2016;**36**:660-78
29. Aboshiha J, Dubis AM, van der Spuy J, Nishiguchi KM, Cheeseman EW, Ayuso C, Ehrenberg M, Simonelli F, Bainbridge JW, Michaelides M. Assessment of accuracy and precision of quantification of ultra-widefield images. *Ophthalmology* 2015;**122**:864-6
30. Toslak D, Ayata A, Liu C, Erol MK, Yao X. Widefield smartphone fundus video camera based on miniaturized indirect ophthalmoscopy. *Retina* 2018;**38**:438-41
31. Leung EH, Rosen R. Fundus imaging in widefield a brief historical journey. In: Kozak I and Arevalo JF (eds), *Atlas of widefield retinal angiography and imaging*. Cham: Springer, 2016, p.21
32. Shields CL, Materin M, Shields JA. Panoramic imaging of the ocular fundus. *Arch Ophthalmol* 2003;**121**:1603-7
33. Toslak D, Thapa D, Chen Y, Erol MK, Paul Chan RV, Yao X. Transpalpebral illumination: an approach for wide-angle fundus photography without the need for pupil dilation. *Opt Lett* 2016;**41**:2688-91
34. Wang B, Toslak D, Alam MN, Chan RVP, Yao X. Contact-free transpars-planar illumination enables snapshot fundus camera for non-mydratic widefield photography. *Sci Rep* 2018;**8**:8768
35. Stephen FC, Nicolette G. The uvea: anatomy, histology and embryology. In: Foster CS and Vitale AT (eds), *Diagnosis and treatment of uveitis*. Philadelphia: WB Saunders, 2002, p.11
36. Bye L. Anatomy. In: Bye L, Modi N and Stanford M (eds), *Basic sciences for ophthalmology*. Oxford: OUP, 2013, p.51
37. Toslak D, Chau F, Erol MK, Liu C, Chan RVP, Son T, Yao X. Transpars-planar illumination enables a 200 degrees ultra-widefield pediatric fundus camera for easy examination of the retina. *Biomed Opt Express* 2020;**11**:68-76
38. Toslak D, Son T, Erol MK, Kim H, Kim TH, Chan RVP, Yao X. Portable ultra-widefield fundus camera for multispectral imaging of the retina and choroid. *Biomed Opt Express* 2020;**11**:6281-92