Smart Eye Camera: A Validation Study for Evaluating the Tear Film Breakup Time in Human Subjects

Eisuke Shimizu1,2, Hiroyuki Yazu1–3, Naohiko Aketa1,2, Ryota Yokoiba2, Shinri Sato1, Taiichiro Katayama1, Akiko Hanyuda1, Yasunori Sato4, Yoko Ogawa1, and Kazuo Tsubota1

1 Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan
2 OUI Inc., Tokyo, Japan
3 Department of Ophthalmology, Tsurumi University School of Dental Medicine, Kanagawa, Japan
4 Department of Preventive Medicine and Public Health, School of Medicine, Keio University, Tokyo, Japan

Correspondence: Eisuke Shimizu, Department of Ophthalmology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan. e-mail: ophthalmolog1st.acek39@keio.jp

Received: December 21, 2020
Accepted: March 13, 2021
Published: April 26, 2021

Keywords: dry eye disease (DED); smart eye camera (SEC); slit-lamp; tear film breakup time (TFBUT); corneal epithelium


Purpose: This study aimed to demonstrate the efficacy of a “Smart Eye Camera (SEC)” in comparison with the efficacy of the conventional slit-lamp microscope by evaluating their diagnostic functionality for dry eye disease (DED) in clinical cases.

Methods: This retrospective study included 106 eyes from 53 adult Japanese patients who visited the Ophthalmology outpatient clinics in Keio University Hospital from June 2019 to March 2020. Tear film breakup time (TFBUT) and corneal fluorescence score (CFS) measurements for the diagnosis of DED were compared between the conventional slit-lamp microscope and SEC.

Results: The objective findings of DED showed that there was a strong correlation between the conventional slit-lamp microscope and SEC with respect to TFBUT and CFS results (Spearman’s $r = 0.887$, 95% confidence interval [CI] = 0.838–0.922, and $r = 0.920$, 95% CI = 0.884–0.945, respectively). The interobserver reliability between the conventional slit-lamp microscope and SEC showed a moderate agreement (weighted Kappa $\kappa = 0.527$, 95% CI = 0.517–0.537 and $\kappa = 0.550$, 95% CI = 0.539–0.561 for TFBUT and CFS, respectively). The diagnostic performance of the SEC for Asia Dry Eye Society diagnostic criteria showed a sensitivity of 0.957 (95% CI = 0.841–0.992), specificity of 0.900 (95% CI = 0.811–0.927), positive predictive value of 0.880 (95% CI = 0.774–0.912), and negative predictive value of 0.964 (95% CI = 0.869–0.993). Moreover, the area under the receiver operating characteristic curve was 0.928 (95% CI = 0.849–1.000).

Conclusions: Compared with the conventional slit-lamp microscope, SEC has sufficient validity and reliability for diagnosing DED in the clinical setting.

Translational Relevance: The SEC can portably evaluate TFBUT in both basic research and clinical care.

Introduction

Dry eye disease (DED) is a common ocular complaint and one of the main reasons for visiting an ophthalmology department. It is reported that 7.4% to 33.4% of the worldwide population has been diagnosed with DED.1 It is estimated that 560 million to 2.54 billion people currently have DED. DED is characterized by low tear volume and/or instability of the tear film.2–5 It has been proposed that the tear film breakup time (TFBUT) is one of a key objective finding for diagnosing DED, and that the progression of TFBUT is clearly associated with both a reduction in visual performance and a decline in optical quality.6 In particular, severe DED manifests in patients with Sjögren’s syndrome,7 Stevens-Johnson syndrome / toxic epidermal necrolysis,8 ocular cicatricial pemphigoid,9 and ocular graft-versus-host disease.10 Nevertheless, both severe and mild DED can decrease productivity, quality of sleep, and subjective happiness.11 Küçük et al. demonstrated...
that the morbidity of DED in patients with chronic stroke with hemiplegia was high. Moreover, DED symptoms even tend to affect inpatients admitted to the intensive care unit (ICU). Based on the increased incidence of DED, the diagnostic criteria for DED were renewed by the Asia Dry Eye Society. They highlight the importance of assessing TFBUT as an objective finding in DED cases. The majority of TFBUT evaluations are performed with a conventional nonportable slit-lamp microscope, however, it is difficult to record a uniform video using this device. There are several video recording camera attachments for conventional slit-lamp microscopes. However, mobility problems remain. Conversely, there are various portable slit-lamp microscopes sold on the market; however, the recordability problem persists. Therefore, some patients with DED may not be diagnosed by an ophthalmological examination because of either mobility and recordability problems in conventional devices. To resolve both the mobility and recordability issues, our study group invented a portable smartphone attachment, referred to as the “Smart Eye Camera (SEC).” We previously demonstrated the diagnostic ability of the SEC in a murine DED model and hypothesized that filming the TFBUT in humans would be possible with a mobile phone. Moreover, the SEC has been registered as a medical device in Japan in June 2019 (13B2 × 10198030101; Fig. 1). The SEC irradiates a blue light at a wavelength of 488 nm when an acrylic resin blue filter (PGZ 302K 302, Kuraray Co, Ltd., Japan) is placed above the light source of the smartphone. Moreover, a convex macro lens (focal length = 20 mm, magnification = × 20) is placed above the camera to adjust the focus. The frame was manufactured from polyamide 12 on a 3D printer (Multi Jet Fusion 3D Model 4210; Hewlett-Packard Company, Palo Alto, CA, USA). The iPhone 7 (Apple Inc., Cupertino, CA, USA) was used to make the recordings.

Diagnostic Instruments

The conventional nonportable slit-lamp microscopes (700GL; Takagi Seiko Co., Ltd., Nagano, Japan; or SL 130; Carl Zeiss AG, Oberkochen, Germany) and the SEC (SEC-i07; OUI Inc., Tokyo Japan) were both used as diagnostic instruments in this study. The SEC is a smartphone attachment medical device that fits above the light source and camera lens of the smartphone (Pharmaceuticals and Medical Devices Agency resisted Japan medical device number: 13B2 × 10198030101; Fig. 1). The SEC irradiates a blue light at a wavelength of 488 nm when an acrylic resin blue filter (PGZ 302K 302, Kuraray Co, Ltd., Japan) is placed above the light source of the smartphone. Moreover, a convex macro lens (focal length = 20 mm, magnification = × 20) is placed above the camera to adjust the focus. The frame was manufactured from polyamide 12 on a 3D printer (Multi Jet Fusion 3D Model 4210; Hewlett-Packard Company, Palo Alto, CA, USA). The iPhone 7 (Apple Inc., Cupertino, CA, USA) was used to make the recordings.

Study Design

A corneal fellow (author T.K.) reviewed the EHR (HOPE EGMAIN-GX; Fujitsu Limited, Tokyo, Japan and Cl aio, FINDEX Inc., Tokyo, Japan) to screen for eligible cases to enroll into our study. We enrolled (1) Japanese adult men and women (over 20 years of age) who had visited the DED, ocular allergy, or cornea specialty outpatient clinics in Keio University Hospital from June 2019 to March 2020 (examined by authors Y.O., E.S., H.Y., and N.A.), (2) cases with good structure of corneal and conjunctival videos taken by the SEC, and (3) cases with the TFBUT and corneal fluorescence scores (CFS) were both recorded in the EHR. The TFBUT and CFS measurements were both performed by the conventional slit-lamp microscopes and the SEC on the same day as the routine examination procedures. The following cases were excluded: (1) patients who had done the Schirmer’s test or Cochet-Bonnet corneal esthesiometer before slit-lamp

Methods

Ethics and Information Governance

This retrospective study adhered to the tenets of the Declaration of Helsinki and was conducted in compliance of the protocols approved by the Institutional Ethics Review Board (IRB) of Keio University School of Medicine, Tokyo, Japan (IRB No. 20170350). The Japanese Ministry of Health, Labor, and Welfare, as well as the IRB, approved a waiver or exemption for the collection of informed consent because of the retrospective study design and lack of personally identifiable information being published. Moreover, according to the guidelines of the IRB, we have provided detailed written guidelines and an ethical statement on the present study on our department website. Patient data were anonymized before access and / or analysis.
Figure 1. Characteristics of the Smart Eye Camera (SEC) invented for the evaluation of dry eye disease. (A) The hardware, which contains the basal component which fits into the iPhone 7. The blue filter fits above the light source, and a convex macro lens is placed above the camera. (B) The SEC equipped to the iPhone 7. (C) The recording interfaces.

Examinations and Diagnostic Criteria

Examinations by the conventional slit-lamp microscope and the SEC were performed by same method, which will be detailed later. For the SEC examination only, the SEC was placed 4 cm from the corneal apex by the DED specialist or fellows. This distance is important because the convex lens in front of the camera was designed to be in the best focus by 4 cm. Each video has taken at least three blinks in order to record good image of the ocular surface. The resolution of the video was 4K, with a frame rate of 30 frames per second. For the DED examination, 2.0 μl of 0.5% sodium fluorescein solution was administered into the lower conjunctival fornix with a micropipette (P2: F144801; Gilson Inc., Villiers le Bel, France) prior to the evaluation. Both the TFBUT and CFS were evaluated using the enhancement of fluorescence staining exposed by 488 nm wavelength blue light in the dark examination room. The TFBUT was evaluated after the individual had blinked a few times to ensure that the fluorescein solution had permeated the whole conjunctival sac. The time taken for dry areas to appear after each blink was measured. For the evaluation, a TFBUT shorter than 5 seconds was defined as tear film instability. The CFS, examined from the recorded photograph taken by the conventional slit-lamp microscope and the SEC, ranged between zero and nine points because the cornea was divided into three vertical sectors. Each sector was then graded from zero to three points, and the total number of points were added together. The OSDI questionnaire was selected to evaluate subjective DED symptoms. An OSDI score ≥ 13 was defined as positive for subjective DED symptoms according to previous studies. Consequently, the cases that had both an unstable tear film (TFBUT < 5 seconds) and
were positive for subjective sign were classed as DED according to the renewed DED diagnostic criteria by the Asia Dry Eye Society.2,3

Statistical and Data Analysis
The sample size was calculated according to our previous study.18 The difference between two dependent means of the TFBUT (2.4 ± 0.55 vs. 2.2 ± 0.84, average ± SD) and correlation coefficient (0.934) was used to calculate an effect size of 0.52. A statistical power of 0.95 and a significance level of 0.05 was applied to calculate the total sample size of 51. All of the data were analyzed using SPSS statistics software (version 25; International Business Machines Corporation, Armonk, NY, USA). To compare the differences in age, OSDI score, TFBUT, CFS, and record-}

Results

Baseline Characteristics
A total of 53 Japanese cases were divided into the DED and non-DED groups according to the renewed DED diagnostic criteria of the Asia Dry Eye Society.2 They diagnosed the DED cases based on the positive subjective symptoms plus short TFBUT (<5 seconds).3 There were 25 cases in the DED group (14 men and 11 women) and 28 cases in the non-DED group (14 men and 14 women). The mean age was higher in the DED group than in the non-DED group (55.80 ± 13.74 vs. 44.64 ± 16.80 years of age, respectively, P = 0.011). The OSDI score for subjective symptoms of DED was higher in the DED group than in the non-DED group (38.69 ± 21.60 vs. 5.72 ± 6.94 points, respectively, P < 0.001). The TFBUT was shorter in the DED group than in the non-DED group (3.00 ± 1.10 vs. 5.30 ± 2.41 seconds, respectively, P < 0.001). The CFS were higher in the DED group than in the non-DED group (2.04 ± 2.24 vs. 0.23 ± 0.66 points, respectively, P < 0.001). In contrast, the recording time of each video using the SEC did not significantly differ between the DED and non-DED groups (45.20 ± 11.98 vs. 50.46 ± 11.08 seconds, respectively, P = 0.104; Table 1). A comparison of the visual characteristics of DED between the slit-lamp microscope and the SEC is shown in Figure 2.

Correlation of DED Signs Between the Conventional Slit-Lamp Microscope and the SEC
We compared objective DED signs of TFBUT and CFS between the conventional slit-lamp microscope and the SEC. There was a strong correlation between the conventional slit-lamp microscope and SEC with respect to TFBUT and CFS, the Spearman’s correlation coefficient was performed. A weighted Kappa coefficient with a 95% confidence interval (CI) was used to evaluate the interobserver reliability assessment of five observers (authors Y.O., E.S., H.Y., N.A., and S.S.) between the conventional slit-lamp microscope and SEC. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to define the performance of the SEC against the conventional slit-lamp microscope.

DED Diagnostic Performance
The diagnostic performance for DED was assessed according to the renewed DED diagnostic criteria between the conventional slit-lamp microscope and the SEC, which showed a sensitivity of 0.957 (95% CI = 0.864–0.992), a specificity of 0.900 (95% CI = 0.811–0.927), a PPV of 0.880 (95% CI = 0.744–0.912), and an NPV of 0.964 (95% CI = 0.869–0.993). Moreover, the area under the receiver operating characteristic curve (AUC) was 0.928 (95% CI = 0.849–1.000; Fig. 4). In addition, Figure 5 shows the 5 tear-film-oriented diagnosis (TFOD) breakup patterns, spot break (Fig. 5A), area break (Fig. 5B), dimple break (Fig. 5C), line break (Fig. 5D), and random break (Fig. 5E).
Table 1. Baseline Characteristics of Patients With or Without Dry Eye Disease

<table>
<thead>
<tr>
<th></th>
<th>DED</th>
<th>Non-DED</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>25</td>
<td>28</td>
<td>-</td>
</tr>
<tr>
<td>Age</td>
<td>55.80 ± 13.74</td>
<td>44.64 ± 16.80</td>
<td>0.011</td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
<td>14</td>
<td>-</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
<td>14</td>
<td>-</td>
</tr>
<tr>
<td>OSDI points</td>
<td>38.69 ± 21.60</td>
<td>5.72 ± 6.94</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TFBUT, seconds</td>
<td>3.00 ± 1.10</td>
<td>5.30 ± 2.41</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CFS points</td>
<td>2.04 ± 2.24</td>
<td>0.23 ± 0.66</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Recording time, seconds</td>
<td>45.20 ± 11.98</td>
<td>50.46 ± 11.08</td>
<td>0.104</td>
</tr>
</tbody>
</table>

DED, dry eye disease; OSDI, Ocular Surface Disease Index; TFBUT, tear film breakup time; CFS, corneal fluorescence score.

Figure 2. Comparison of the visual characteristics of dry eye disease between the slit-lamp microscope and the Smart Eye Camera. Clinical photos of the left eye in the same case, which involved a 53-year-old patient with severe ocular graft-versus-host disease with a broad pseudomembrane in the conjunctiva, obvious meibomian gland dysfunction in the lower eyelid, and corneal epitheliopathy. (A), (B), and (C) were recorded using the conventional slit-lamp microscope. (D), (E), and (F) were video recorded using the Smart Eye Camera. A and D show superior tarsal plate with a broad pseudomembrane in the conjunctiva with the diffuse illumination method. B and E show the lower conjunctiva and eyelid with pseudomembranes and meibomian gland dysfunction with the diffuse illumination method. D and F show the corneal epithelial disorder, both with a score of five out of nine points each (upper 2, middle 1, and lower 2) by the blue light illumination method.

Discussion

This study aimed to evaluate the diagnostic ability of SEC for DED through objective findings in the clinical setting. In the current study, DED cases were diagnosed based on the presence of subjective symptoms and a low TFBUT by either the conventional slit-lamp microscope or SEC. Both the OSDI score for the subjective DED symptoms and the objective findings, such as the TFBUT, were statistically worse in the DED group than in the non-DED group. Moreover, the CFS, like other objective findings, was also worse in the DED group as expected. These findings suggested that our recruited cases were eligible for further discussion.

We performed validity and reliability assessments to evaluate the diagnostic efficacy of the SEC in comparison with that of the conventional slit-lamp microscope for DED.

Diagnostic performances for the DED in the SEC and the conventional slit-lamp microscope showed high value (sensitivity = 0.957, specificity = 0.900, PPV = 0.880, and NPV = 0.964). Furthermore, the AUC.
Table 2. Correlations of Objective Findings for Dry Eye Disease Between the Conventional Slit-Lamp Microscope and the Smart Eye Camera, Analyzed Using Spearman’s Correlation Coefficient

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>r</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFBUT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right eye</td>
<td>53</td>
<td>0.891</td>
<td>0.818 0.936</td>
</tr>
<tr>
<td>Left eye</td>
<td>53</td>
<td>0.884</td>
<td>0.806 0.932</td>
</tr>
<tr>
<td>Both eyes</td>
<td>106</td>
<td>0.887</td>
<td>0.838 0.922</td>
</tr>
<tr>
<td>CFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right eye</td>
<td>53</td>
<td>0.894</td>
<td>0.823 0.938</td>
</tr>
<tr>
<td>Left eye</td>
<td>53</td>
<td>0.937</td>
<td>0.893 0.964</td>
</tr>
<tr>
<td>Both eyes</td>
<td>106</td>
<td>0.920</td>
<td>0.884 0.945</td>
</tr>
</tbody>
</table>

CI, confidence interval; TFBUT, tear film breakup time; CFS, corneal fluorescence score.

showed a high value of 0.928. A previous report, which compared the applicability of noninvasive corneal topography and the conventional method for measuring the TFBUT, showed similar high sensitivity and specificity values, with a standardized cutoff value.29 These results suggest that the SEC is a valid diagnostic tool for DED compared with the conventional slit-lamp microscope. The interobserver reliability for the diagnostic performance of SEC compared with that of the conventional slit-lamp microscope was moderate in terms of the TFBUT (κ = 0.527) and CFS (κ = 0.550). Moreover, a strong correlation between the TFBUT (r = 0.887) and CFS (κ = 0.920) was observed. Lee et al. also assessed the interobserver reliability of alternative imaging diagnostic methods for DED using weighted Kappa statistics.30 They also noticed a moderate interobserver reliability agreement and strong correlation coefficients. Moreover, Wang et al. demonstrated a high correlation between white light clinical interferometry, and different type of keratoscopes in a TFBUT assessment.31 These results suggest that the SEC has similar reliability to the conventional slit-lamp microscope for diagnosing DED.

Table 3. Interobserver Reliability Assessment Using a Weighted Kappa Coefficient Between the Slit-Lamp Microscope and the Smart Eye Camera for Assessment of Dry Eye Disease

<table>
<thead>
<tr>
<th></th>
<th>κa</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFBUT</td>
<td>0.527</td>
<td>0.517 0.537</td>
</tr>
<tr>
<td>CFS</td>
<td>0.550</td>
<td>0.539 0.561</td>
</tr>
</tbody>
</table>

CI, confidence interval; TFBUT, tear film breakup time; CFS: corneal fluorescence score.
aBetween the conventional slit-lamp microscope and the Smart Eye Camera.

Figure 3. Consecutive corneal photographs taken by the Smart Eye Camera invented for the evaluation of dry eye disease (DED). The photographs have been obtained for a DED case with positive objective signs and a short tear film breakup time (TFBUT). (A) Just after opening the eye, the fluorescence enhanced tear spread into the whole cornea. (B) One second after opening the eye, the superior extension of the tear film can be observed (Gibbs–Marangoni effect). (C) Two seconds after opening the eye, tear film breakup was still not observed. (D) Three seconds after opening the eye, a dry spot of the tear film was observed in the left part of the cornea. (E) Four seconds after opening the eye, the dry spot was clearly observed in several parts of the cornea. (F) Five seconds after opening the eye, the area of the dry spot expanded, suggesting a line break in the breakup pattern.
The TFBUT is a method for determining the stability of the tear film.\textsuperscript{2-4} Evaporation is observed under the slit-lamp microscope until tiny dry spots develop after blinking.\textsuperscript{32} Recently, Yokoi et al. characterized subtypes of DED according to the fluorescein breakup patterns, leading to a TFOD.\textsuperscript{33-35} They categorized the breakup pattern into the following five breaks: spot break, area break, dimple break, line break, and random break. They evaluated the TFOD breakup patterns with the conventional slit-lamp microscope.\textsuperscript{5} We were able to show the efficacy of the SEC in evaluating all five TFOD breakup patterns of DED (see Fig. 5).

There are many studies that have reported the negative effects of smartphone use on DED,\textsuperscript{36,37} as well as its implications on the ocular surface, including the tear film.\textsuperscript{38,39} However, there are limited reports that indicate the diagnostic possibility of smartphones in other ocular settings, such as grading nuclear cataracts,\textsuperscript{15} corneal endothelium quantification,\textsuperscript{40} assessment of vertical cup-to-disc ratios for glaucoma screening,\textsuperscript{41} and for non-mydriatic fundus photography.\textsuperscript{42} However, smartphone diagnostics for DED has not yet been established. Therefore, to the best of our knowledge, this study will be the first to have investigated the efficacy of a smartphone in combination with a SEC for diagnosing DED in the clinical setting.

Our study had several limitations. First, as this was a retrospective study, the DED group and the non-DED group had different average ages. Age is said to be one of the risk factors for DED and an increasing age reduces tear production.\textsuperscript{43} Our study only evaluated the recorded videos and objective findings from the slit-lamp microscope, so that the effect of age on our results was kept to a minimum. Moreover, we have assessed the correlation according to the groups of objective DED findings between the conventional slit-lamp microscope and the SEC (Supplementary Table S1). We found similar strong correlations in TFBUT and CFS according to the DED group and non-DED group. Therefore, these results suggest the minimum effect of age in the current study. However, an age adjusted prospective study will be needed in the future. Second, we only evaluated Japanese adult men and women. Therefore, we applied the diagnostic criteria from the Asia Dry Eye Society,\textsuperscript{2,3} which is believed to be the best criteria for Japanese adult patients with DED. Thus, further studies using suitable DED criteria according to the subject’s demographic characteristics will be necessary to assess the diagnostic ability of the SEC. Third, this study only assessed the diagnostic findings TFBUT and CFS for DED. Other DED examinations include conjunctival epithelial staining, tear meniscus height, and the degree of meibomian gland dysfunction are needed. In addition, cases with DED including autoimmune diseases, such as ocular graft-versus-host disease, is characterized by fibrosis and hyperemia in their conjunctiva.\textsuperscript{10,44} Therefore, other DED examinations could be the next target for further analysis. At last, there is a disparity between our high correlation and moderate Kappa scores. We can speculate that this is the result of (1) interobserver differences, as the conventional slit-lamp was evaluated by the four specialists (authors Y.O., E.S., H.Y., and N.A.) and SEC was evaluated by a different specialist (author S.S.); and (2) differences in the wide appraisal scales, as TFBUT values range from 0 to 10 and CFS values range from 0 to 9. A similar study by Lee et al. found a strong correlation with moderate Kappa value (0.788 and 0.467, respectively). They used a narrower scale from zero to five, which suggests smaller disparity than that in our study.\textsuperscript{30} Therefore, interobserver and evaluation scale differences could be the explanation.

In addition, there are wide possibilities in terms of the external validity of the study. We used the SEC for prescreening before the ophthalmological examination and/or postexamination to confirm the diagnosis by the attending specialists or education to the residents. Because the SEC is a portable device, it can be used outside the ophthalmology department (e.g. bedridden patient in a ward, ICU, emergency unit, etc.).
Moreover, diagnosing DED requires the measurement of the time of the tear film stability; therefore, a video recording system is necessary for telemedicine and artificial intelligence to auto-diagnose DED in the future.

We previously demonstrated the diagnostic efficacy of the SEC for DED in a murine model. In the current study, we hypothesized that the SEC would be as effective in diagnosing DED as the conventional slit-lamp microscope. We demonstrated that, compared with the conventional slit-lamp microscope, the SEC has sufficient validity and reliability for detecting objective findings and diagnosing DED in the clinical setting. However, some limitations still remain, which need to be investigated through further study by taking into account the age, races, alternative objective DED findings, and the distinction between high correlation and moderate Kappa scores.

Acknowledgments

This is one of the Cross-ministerial strategic innovation promotion projects “AI hospital” at Keio University Hospital (Tokyo, Japan), supported by the Cabinet Office, Government of Japan. The authors thank Masahiro Jinzaki and Shigeru Ko, who are in charge of the AI hospital at Keio University Hospital, for providing helpful advice. All data associated with this study can be found in the server of the Department of Ophthalmology, Keio University School of Medicine.

Disclosure: E. Shimizu, OUI Inc. (P), The Japan Agency for Medical Research and Development (F), Uehara Memorial Foundation (F), Hitachi Global Foundation (F), Kondo Memorial Foundation (F), Eustylelab (F), Kowa Memorial Foundation (F);
H. Yazu, OUI Inc. (P), Casio Science Promotion Foundation (F); N. Aketa, OUI Inc. (P); R. Yokoiwa, OUI Inc. (P); S. Sato, None; T. Katayama, None; A. Hanyuda, None; Y. Sato, None; Y. Ogawa, Kissei Pharmaceutical (P), Alcon (F); K. Tsubota, Tsubota lab (R), JIN (F), Santen (F), Kowa (F), Otsuka Pharmaceutical (F), Rohto Pharmaceutical (F) Fuji Xerox (F), Sucampo Pharma (F), Ophthece (F) Wakasa Seikatsu (F), Pfizer (F), Alcon (F), QD laser (F) Kao Corporation (R), Thea (R, P)

References


**Supplementary Material**

**Supplementary Video S1.** To watch the DED video, please click the link below. [https://www.youtube.com/watch?v=mJDyaaTkXK8&list=PLnU2MWEekv5he8mCwk0EE7SYiS0oIrEcE&index=5&time=0s](https://www.youtube.com/watch?v=mJDyaaTkXK8&list=PLnU2MWEekv5he8mCwk0EE7SYiS0oIrEcE&index=5&time=0s).