The Ocular Surface
A JOURNAL OF REVIEW, LIVING LABORATORY SCIENCE, CLINICAL SCIENCE, AND CLINICAL PRACTICE

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PII: S1542-0124(16)30234-8

DOI: 10.1016/j.jtos.2016.11.003

Reference: JTOS 209

To appear in: *Ocular Surface*

Received Date: 20 April 2016

Revised Date: 14 October 2016

Accepted Date: 28 November 2016

Please cite this article as: Benítez-del-Castillo J, Labetoulle M, Baudouin C, Rolando M, Akova YA, Aragona P, Geerling G, Merayo-Lloves J, Messmer EM, Boboridis K, Visual acuity and quality of life in dry eye disease: Proceedings of the OCEAN group meeting, *Ocular Surface* (2016), doi: 10.1016/j.jtos.2016.11.003.

Visual acuity and quality of life in dry eye disease: proceedings of the OCEAN group meeting

Visual acuity and dry eye disease

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Disclosures

José M. Benítez-del-Castillo has acted as a consultant for Allergan, Bausch & Lomb, Théa, Alcon and Santen. Marc Labetoulle has acted as a consultant for Allergan, Alcon, Bausch & Lomb, Farmigea, MSD, Santen/Novagali and Théa. Christophe Baudouin has received research grants and consulting fees from Alcon, Allergan, Merck, Santen and Théa. Maurizio Rolando declares financial relationships with Allergan, Bausch & Lomb, Farmigea, Théa, Alcon, Eupharma, Santen/Novagali and Alfa Intes. Yonca A. Akova declares financial relationships with Allergan, Théa and Alcon. Pasquale Aragona has acted as a consultant for Allergan, Alcon Italy, Bausch & Lomb, Santen, Medivis, Théa, Eupharmed and Farmigea and has received a research grant from SOOFT Italia and SIFI. Gerd Geerling has acted as a consultant and speaker for Allergan, Alcon, Bausch & Lomb, Chiesi, Oculus, Santen, Théa, TearLab and Tear Science. Jesús Merayo-Lloves has received research grants from Théa and has acted as a consultant for Allergan and Santen. Elisabeth Messmer has acted as an advisor and presenter for Allergan, Alcon, Dompé, Oculus, Santen, Théa and Ursapharm. Kostas G. Boboridis declares financial relationships with Allergan, Alcon, Théa and Santen.

Allergan provided funding for the meetings and for the development of this manuscript. The authors were involved in the entire process, from design to critical revision of the manuscript, and maintained complete control over the direction and content of the paper. Allergan did not have any influence on the manuscript content.

Osmoprotection in Dry Eye Disease – Expert Opinion (OCEAN) is a medical education programme for general ophthalmologists that provides relevant, practical and up-to-date training on the management of dry eye disease. The content of this educational programme is directed and created by the OCEAN faculty (the authors of this paper) with the support of Allergan.

This article was developed from a roundtable meeting held on 16 January 2015 by the OCEAN group in Paris, France. The meeting was supported by an unrestricted grant from Allergan, who had no influence over the faculty discussions or content of this article. This article was further developed through discussion at a subsequent meeting on 11–12 December 2015, Barcelona, Spain, and author participation in teleconferences. All the authors contributed to the drafting of this manuscript, and it represents a consensus of their opinions gathered at the roundtable and subsequent meetings.

Acknowledgements

The authors thank Newton Healthcare Communications for writing and editing support, which was funded by Allergan, UK. The authors thank Dr Minako Kaido (Keio University School of Medicine, Tokyo, Japan) for providing information on the Kowa functional visual acuity measuring system.

Abstract

Dry eye disease (DED) results in tear film instability and hyperosmolarity, inflammation of the ocular surface and, ultimately, visual disturbance that can significantly impact a patient's quality of life. The effects on visual acuity result in difficulties with driving, reading and computer use and negatively impact psychological health. These effects also extend to the workplace, with a loss of productivity and quality of work causing substantial economic losses. The effects of DED and the impact on vision experienced by patients may not be given sufficient importance by ophthalmologists. Functional visual acuity (FVA) is a measure of visual acuity after sustained eye opening without blinking for at least 10 s and mimics the sustained visual acuity of daily life. Measuring dynamic FVA allows the detection of impaired visual function in patients with DED who may display normal conventional visual acuity. There are currently several tests and methods that can be used to measure dynamic visual function: the SSC-350 FVA measurement system, assessment of best-corrected visual acuity decay using the interblink visual acuity decay test, serial measurements of ocular and corneal higher order aberrations, and measurement of dynamic vision quality using the Optical Quality Analysis System. Although the equipment for these methods may be too large or unaffordable for use in clinical practice, FVA testing is an important assessment for DED.

1. Introduction

Dry eye disease (DED) is a multifactorial disease of the tears and ocular surface that results in visual disturbance and tear film instability, among other symptoms (Figure 1). It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.[1,2] The tear film is the first part of the ocular surface that light meets on the pathway to the retina, and the large refractive index step from the air to the tears means that the precorneal tear film has the greatest dioptric power of any optical interface of the eye.[3,4] Furthermore, the tear film compensates for the optical irregularity of the corneal epithelium surface, which is caused by the presence of numerous microvilli; without this compensation by the tear film, the quality of the transmitted light would be poor. As the retinal image depends upon light passing through the optical structures, the composition and homogeneity of the tear film may have a huge impact on the quality of the retinal image.[5]

The tear film is inherently unstable and undergoes irregular disruptions following a blink, causing tear film break-up.[4] The resulting irregularity in the thickness of the tear film across the ocular surface will have a negative effect on the quality of this most important ocular dioptre, which normally has a refractive power of 48.35D.[3,4] It has been well documented that in eyes with a short tear film break-up time (TBUT), optical quality deteriorates significantly more quickly after the blink than it does in normal eyes.[5,6] Patients with DED typically have a shorter TBUT than normal controls,[5,7] and these patients show a reduction in visual acuity over time after holding the eye open for a few seconds.[8] As will be discussed later, an important impact of the short TBUT in patients with DED is an increased blink rate.[9] The use of artificial tears in patients with DED has been shown to significantly improve visual acuity (mean acuity gain of +2.33 optotypes, which was considered to be highly significant in the study) and spatial contrast sensitivity, further supporting the importance of the role of the tear film in visual function.[10,11]

External factors that lead to DED include a low-humidity environment and contact lens use, while internal conditions may include, but are not limited to, Sjögren's syndrome, meibomian

gland dysfunction (MGD), connective tissue disorders, Graves' disease, chronic graft-vs-host disease, pseudoexfoliation syndrome and skin diseases (e.g. ocular rosacea).[12,13]

In this review, we examined the effects of DED on functional visual acuity (FVA) and their impact on the quality of life (QoL) of patients with DED.

2. Reduced visual function can adversely impact quality of life in patients with DED

With increased severity of DED, patients with DED report deficits in perception of overall health and vitality compared with the general population, and the most severely affected patients report the worst health-related QoL over all scales.[14,15] The physical impact of DED appears to be closely related to the concept of DED as a type of chronic pain syndrome, particularly relating to changes in corneal sensitivity,[16] resulting in chronic ocular surface discomfort that impacts a number of aspects of QoL.[17] Patients with DED have reported lower scores for mental health when compared with normal controls, indicating that the disorder has an adverse impact not only on physical health but also on psychological health. Although few published studies have reported the psychological status of patients with DED, these studies showed that patients with DED were more anxious and depressed compared with patients without DED.[18,19] A large (n = 662) cross-sectional, observational clinical study to investigate depression in patients with DED found that depression was common and associated with increased severity of dry eye symptoms ($p \leq 0.001$).[20]

DED may also have a serious impact on sleep and mood; a survey of 730 eye clinic patients who completed a questionnaire containing the Pittsburgh Sleep Quality Index (PSQI) and Hospital Anxiety and Depression Scale (HADS) showed that the prevalence of sleep and mood disorders was significantly higher in patients with DED (n = 247) compared with patients with other ocular conditions (e.g. glaucoma, retinal disease and cataracts).[21] In addition, a cross-sectional survey of 437 participants to assess sleep patterns and DED concluded that sleep disturbance was associated with DED in both men and women (odds

ratio 3.21 [95% confidence interval 1.56–6.63] and 1.74 [95% confidence interval 1.08–2.82], respectively).[22]

The QoL issues experienced by patients with DED extend further than just the discomfort of the dry eye; the significant impact on visual function due to DED can diminish a patient's quality of everyday living.[23] Although best-corrected visual acuity (BCVA) may appear to be normal in most patients with DED,[24] in some patients, DED may reduce BCVA down to near-blindness, for example in those with chronic graft-vs-host disease where visual acuity may be as low as 20/115 (Snellen acuity).[25] Visual function has been shown objectively to be impaired during specific driving situations in patients with DED as compared with normal controls, and reduced driving visual performance was demonstrated to be correlated with ocular optical aberrations and patient-reported QoL.[26] Drivers with DED may experience visual disturbances, particularly on approaches to roundabouts or at crossroads[26] and as they get older,[27] which causes obvious safety concerns. Readers with DED may have lower reading rates compared with readers not suffering from DED,[28,29] and computer users with DED may experience reduced productivity and lower mental performance.[30-32] For the busy general ophthalmologist, the chronic effects of DED may not be well measured and the subsequent impact on patients' vision and QoL may be under-recognised.

An important effect of a decrease in visual acuity is reduced quality of work; presenteeism (productivity loss when an employee comes to work but is not fully productive) is a reported consequence of DED and may be underestimated.[33] Studies of patients with DED suggest that DED interferes with work between 184 and 208 days per year and results in 2–5 days off work per year, suggesting that presenteeism is a greater issue than absenteeism for patients with DED.[34] This interference with daily working life may have a substantial economic impact; one study including 74 patients with DED estimated that DED was responsible for a productivity loss of > US$5000 per patient per year.[35] The increased rates of depression and stress and lower levels of happiness reported by patients with DED

compared with patients without DED may also impact productivity in work and personal tasks.[18,36,37]

3. Detecting visual impairment in DED by measuring Functional Visual Acuity

FVA has been defined as visual acuity measured after sustained eye opening without blinking for at least 10 s using the same spectacles as ordinary BCVA testing.[8] This is supposed to mimic what happens during common daily activities that usually suppress blinking (i.e., activities involving gazing), such as reading, driving and working at a computer.[8,15,17,26] The longer gap between blinks that result from gazing allows a longer time for disruption of the tear film and, hence, vision problems.[2,8] Measuring FVA should allow detection of masked impairment of visual function in patients with DED who complain of decreased visual acuity despite normal conventional visual acuity.[38] In a normal clinical setting, conventional visual acuity tests may not accurately measure all aspects of visual function; patients are able to blink as much as necessary to compensate for a dysfunctional and unstable tear film, and this may result in normal visual acuity measurements using standard testing.[9,39] Indeed, when not gazing, patients with DED blink twice as frequently compared with normal subjects.[9] Patients with more severe DED symptoms may experience difficulty in keeping their eyes open during vision-intensive tasks.[39] This may affect daily activities, such as using laptops or smartphones, with a negative impact on social life and leisure time and a consequent deterioration of the patient's QoL. Furthermore, the area of the exposed ocular surface varies with the task; looking upwards, for example at a television screen, results in a wider palpebral fissure than looking down, for example at a laptop. Greater exposure of the ocular surface results in a higher tear evaporation rate.[40]

The relationship between FVA measurements and dry eye testing methods has been extensively investigated by Tsubota and his research group. In a prospective comparative case series involving 30 patients with DED and 25 patients with normal eyes, the group showed significant correlation between FVA measures made under natural blinking

conditions without topical anaesthesia and dry eye test parameters such as tear quantity, tear stability and ocular surface vital staining scores.[41] In a separate study involving 22 patients with Sjögren's syndrome, they demonstrated that change in FVA was as reliable as wavefront aberration measurements for evaluating visual performance in dry eyes.[42]

One result of the increased rate of blinking is that patients with DED have a significantly greater lid-closure time per minute compared with the general population (4.5% vs 0.7% in controls; $p < 0.001$).[9] Furthermore, during visual tasks, patients with DED have significantly more super extended lid closures of > 0.5 s compared with controls (2.3% vs 0.2% of recorded blinks; $p = 0.023$), with a significantly decreased inter-blink interval of 2.56 vs 5.97 s in controls ($p < 0.004$).[9,43] It would be very interesting to study further whether this increased blink rate and lid-closure time is troublesome for patients with DED.

The alterations in visual function associated with DED are manifestations of tear film instability, as previously noted. A commonly used clinical test to identify tear instability is measuring TBUT.[44] Alternative tests which are also easily accessible to the clinician include tear osmolarity which is closely linked to tear instability.[45]

Ophthalmologists may not be testing visual acuity in patients with DED in the correct way for two main reasons: lack of understanding of the relevance of FVA loss in patients with DED, and lack of suitable, commercially available testing equipment. Questionnaires such as the Ocular Surface Disease Index, Impact of Dry Eye on Everyday Life and the National Eye Institute Visual Function Questionnaire are simple yet valuable tools for initial assessment of the effects of DED on patients' visual function and QoL,[17,46-48] but they only assess the subjective (self-reported) aspects of FVA and probably are not the ideal tools to give an accurate idea of the real, objectively measured FVA (objective, not self-reported).

4. Methods of assessing FVA

There is a clear need for appropriate testing of visual acuity in the clinical setting. This testing needs to be dynamic in order to measure FVA accurately. Table 1 describes dynamic FVA tests that are currently available. Goto *et al*. were the first to develop a way to measure FVA, which is associated with sustained eye opening; this is in contrast to BCVA, which may be accompanied by frequent blinking.[8] After 10 s of sustained eye opening, the surface regularity index (SRI) was measured using corneal topography as a surrogate assessment of visual function. In an interventional, comparative trial of patients with non-Sjögren's syndrome DED, patients with Sjögren's syndrome DED and normal controls, BCVA, as measured by the SRI when blinking freely, did not differ significantly between study groups (1.18, 1.15 and 1.27, respectively).[8] However, FVA, as measured by the SRI 10–20 s after a blink, was significantly decreased compared with BCVA in the two DED patient groups to 0.336 ($p = 0.007$) and 0.228 ($p < 0.00001$), respectively, but in the control group, FVA remained similar to BCVA (1.16).[8] A continuous Functional Visual Acuity Measurement (FVAM) system (SSC-350, NIDEK, Gamagori, Japan) was proposed by Ishida *et al.* in 2005. When FVA was measured in patients with DED at 10, 20 and 30 s after a blink, mean FVA scores were significantly lower than those in normal controls at each time point ($p < 0.05$).[49] As the FVAM system continues to develop, its applications may be expanded to include an assessment of a patient's vision for daily activities in disease states other than DED.[38]

A different FVAM system (Kowa Co Ltd., Nagoya, Japan) has been developed to assess change in visual acuity over time (Figure 2A).[50] The system measures FVA over a 60-s period without topical anaesthesia and with blinking permitted, under normal daily vision correction.[51] The self-contained patient interface device displays black Landolt optotypes on a white screen. Small optotypes are displayed at the start of the assessment; if the patient response is correct, even smaller optotypes are presented. If the responses are incorrect, larger optotypes are presented automatically (Figure 2B).

The key measurements recorded by the Kowa system are baseline visual acuity, FVA (mean value of time-wise changes in visual acuity during examination), visual maintenance ratio (FVA divided by baseline visual acuity value), maximal visual acuity (highest visual acuity during the measurement period), minimal visual acuity (the lowest visual acuity score during the measurement period), response reaction time and blink frequency (Fig 2C).[51] Figure 3 shows representative patterns of FVA in a normal case, a patient with DED and short TBUT and a patient with aqueous deficient DED. Figure 4 shows a representative case of FVA before and after punctal plug insertion. FVA in this patient improved from 0.543 to 1.112 following insertion of punctal plugs (case courtesy of Dr Minako Kaido, Tokyo, Japan).

Contrast sensitivity in patients with DED has been assessed using the Contrast Glare Tester CGT-1000 (Takagi Ophthalmic Instruments, Manchester, UK). Contrast sensitivity, with and without glare, was significantly reduced in patients with DED compared with that in control subjects.[52] The Inter-blink interval Visual Acuity Decay (IVAD) test is a computer-based measure of BCVA decay between blinks and is conducted without the use of an anaesthetic.[53] A rotating Landolt 'C' was presented at the response pace of each patient so that the decay in visual acuity between blinks could be measured. Walker *et al*. reported that, compared with patients with DED, normal age-matched controls were able to maintain their BCVA for significantly longer ($p = 0.0001$). In addition, controls had a longer interblink interval while performing the task than the DED patients ($p = 0.002$).[53] Torkildsen used the IVAD test to investigate the effects of artificial tears on visual decay in patients with DED.[54] By using a standardised test for all patients before and after treatment, the test provided an accurate representation of the effects of DED treatments on visual function.[54]

Degradations of optical quality are known to be affected by light scattering and higher order aberrations (HOAs); a study of 55 patients (35 with DED) demonstrated that ocular forward light scattering and corneal backward light scattering from the anterior cornea were greater in dry eyes compared with normal eyes ($p < 0.05$).[55] Quantitative serial measurements of HOAs and forward light scatter have been used to measure efficacy of eyedrops on optical

quality in patients with DED.[56,57] In addition, a study of 40 patients with DED and 40 age- and gender-matched controls assessed the correlation between the time course of corneal and ocular wavefront HOAs after blinking, and both patient-reported QoL and clinical examination results.[58] Serial measurements of corneal and ocular wavefront aberrations were performed for 10 s after blinking (simulating gazing) using the KR-1W aberrometer (Topcon, Clichy, France). It was demonstrated that the time course of HOAs after a blink accurately correlates with both the clinical examination and patient-centred visual outcomes, suggesting that this assessment could have utility as a method to both diagnose DED and assess efficacy of DED treatments in clinical trials.[58]

Visiometrics (Terassa, Spain) have developed the next generation of the Optical Quality Analysis System (OQAS), the HD Analyzer. This diagnostic system provides a measure of light scatter (objective scattering index [OSI]), which is not measurable using traditional wavefront aberrometry. Therefore, this provides an objective measure that is correlated with visual function.[59] Furthermore, this technique can be used to evaluate the efficacy of treatment, for example the effect of artificial tears on vision.[60] Figure 5 shows the effect of DED on the OSI output and subsequent visual function. The mean OSI score of the control subject (0.54) was lower than that of the patient with DED (4.73). This result would suggest reduced visual function in patients with DED compared with controls. Tan *et al.* have used the OQAS for testing retinal-image quality in patients with DED to evaluate dynamic changes when patients were allowed to blink as normal. Patients with DED had significant alterations in optical quality compared with control subjects, and optical quality was significantly lower in patients with severe disease than in patients with mild disease.[61] It would be very interesting to study further the correlation between the OQAS and other aberrometry measures and FVA from the patient's perspective.

Unfortunately, many of the dynamic assessments for visual acuity are not commercially available, can be challenging to perform or are used largely for research purposes. Moreover, the general ophthalmologist may not be aware that DED-associated reductions in

visual function can only be identified with dynamic rather than classical vision testing, i.e. assessing changes in visual function over time after a blink.

5. Impact of DED-related vision alterations on other ocular conditions

DED is common in patients with glaucoma, often due to eye drops that are used to reduce the intraocular pressure.[62,63] As DED can affect vision due to corneal changes and tear film instability, this may result in misleading visual acuity or visual field test results.[64] A decrease in the visual function of patients with glaucoma may be mistaken for glaucomatous or non-specific visual field defects, when it is in fact caused by DED. It is therefore important that glaucoma patients are treated appropriately for DED and that their condition is not erroneously managed as a deterioration of glaucoma-related visual field defects.[64] Following the administration of artificial tears to patients with glaucoma prior to automated perimetry, both the results and the reliability of visual acuity testing were improved.[64-66]

In a similar way, the presence of DED in patients requiring ocular surgery, e.g. cataract surgery with intraocular lens (IOL) implantation or refractive surgery, may result in incorrect assessments of visual function or keratometric values prior to surgery. For example, when choosing the power of IOL required for a cataract surgery patient, any effect on visual function related to DED needs to be taken into account in order to select the correct power of the lens.[67-69] This is especially true for multifocal lenses. In the postoperative setting, the presence of DED may reduce postoperative visual function below the expected level; DED therapy can improve visual function in patients who were dissatisfied with visual outcomes after multifocal IOL implantation and may reduce the need for more invasive or intensive treatment options.[70,71]

The presence of DED is also an important factor in the preoperative assessment of patients undergoing refractive surgery, such as laser-assisted *in situ* keratomileusis (LASIK) and photorefractive keratectomy; the corneal epithelium can be thinner in dry eyes compared with normal eyes, and this may influence the corneal topography and preoperative

evaluation for refractive surgery in patients with DED.[72] The introduction of automated, non-invasive measures of TBUT in a number of widely available preoperative devices has enabled early assessments of the quality of the tear film surface to be made prior to surgery, thus ensuring that all appropriate allowances for the presence of DED are made.[73]

DED may also have an impact on patients after LASIK surgery; postoperative DED is very common, being reported in up to 50% of patients at 1 week after surgery and 20–40% of patients at 6 months.[74] Indeed, it has been shown that tear secretion may be reduced for up to 9 months post surgery.[75] DED itself is a primary cause of dissatisfaction post surgery[76] and, importantly, may have a negative effect on vision. Patients with low refractive errors following LASIK surgery have improvements in visual function when tear film integrity is restored, e.g. with the insertion of punctal plugs.[77,78]

6. Conclusions

Patients with DED often have poor QoL. This may be due to both the physical effects of DED, such as ocular discomfort, and decreased visual function. There is a negative effect on psychological QoL, which may even lead to depression. In order to assess FVA, visual function needs to be assessed dynamically. There are several methods currently available for dynamic visual testing, but equipment used for these methods may be too large or unaffordable for use in clinical practice. Our hope is that in the future, new, simple and affordable instruments will be developed to test dynamic visual function accurately in patients with DED and that these methods will also be able to test FVA under simulated situations of daily life activities.

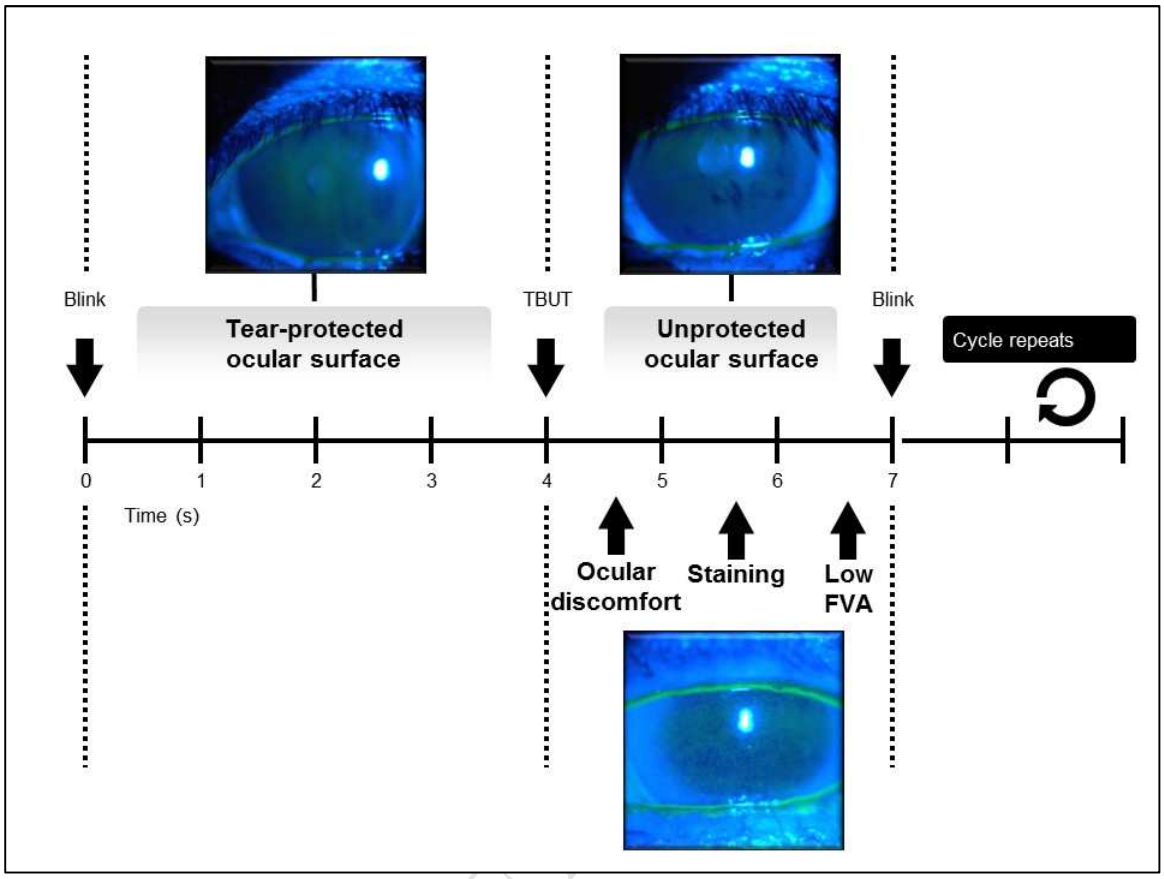
Clinicians and authorities are urged to consider the impact of decreased visual function and the impact on their patients' QoL. The negative effects of DED on visual function may not be considered as a typical DED complaint by the general ophthalmologist, and we would encourage practitioners to consider testing FVA for every patient with DED with methods that are currently available.

Acknowledgements

Newton Healthcare Communications provided writing and editing support, funded by Allergan.

Figures and tables

Figure 1. Dry eye disease – consequences of an unprotected ocular surface



FVA, functional visual acuity; TBUT, tear film break-up time.
Figure adapted from concepts described in Ousler *et al*. 2008.[1] Photographs courtesy of José Benítez-del-Castillo.

Figure 2.

(A) Kowa

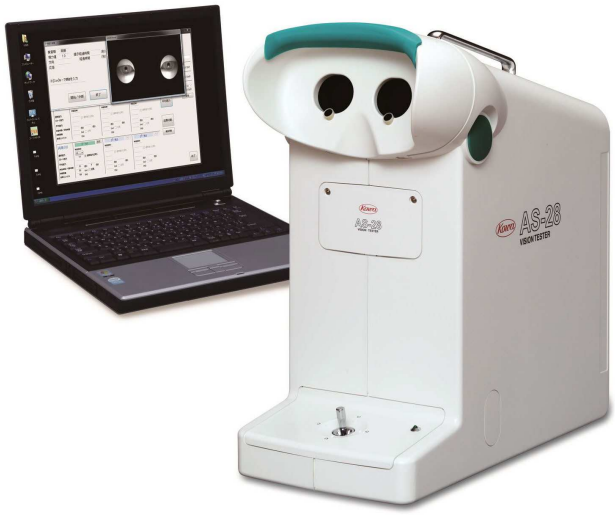


Image reproduced from www.kowa.co.jp.[50]

(B)

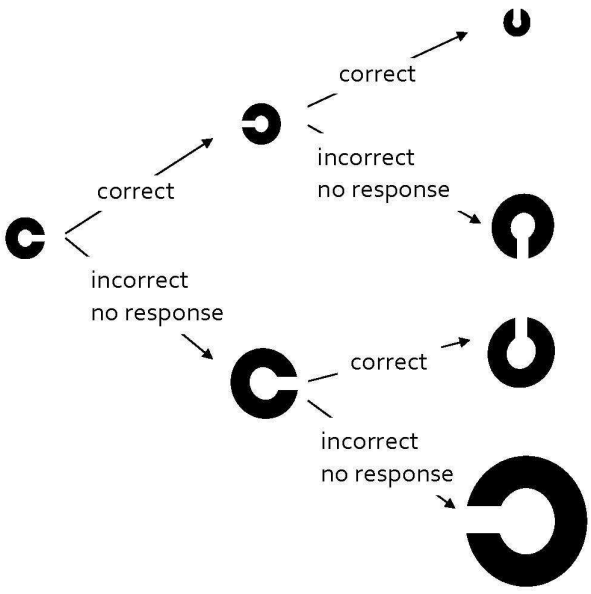
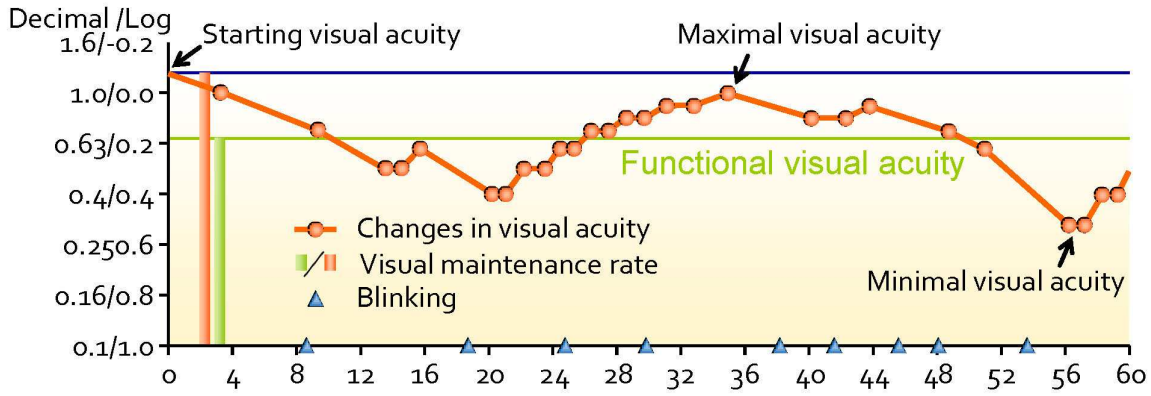


Image reproduced from Kaido et al., J Ocul Pharm Ther 2013[51] [permission to be obtained]

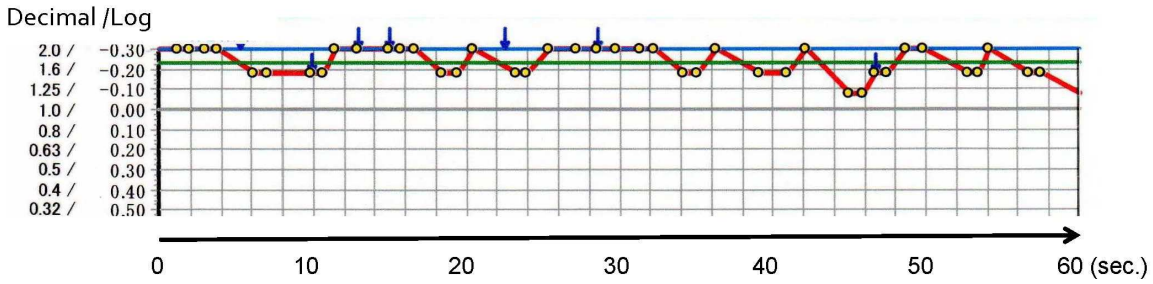
(C)



Triangles represent blinks
Image reproduced with kind permission of Dr Minako Kaido, Keio University School of Medicine, Tokyo, Japan.

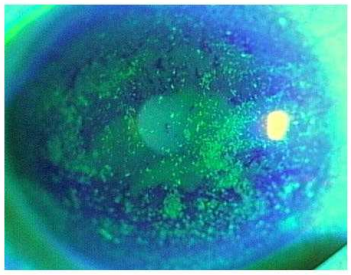
Figure 3. Representative patterns of FVA

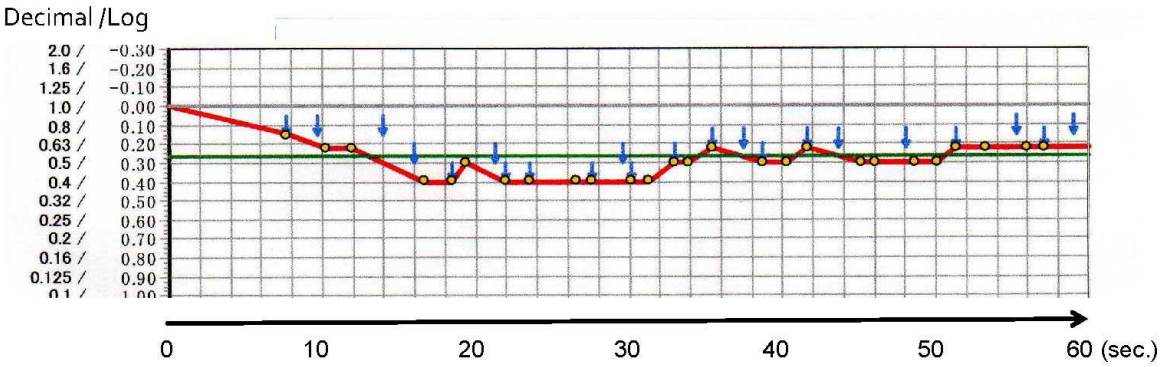
(A) Normal case



Arrows represent blinks

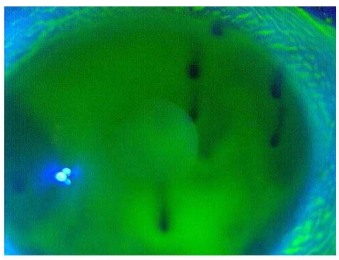
(B) Short TBUT dry eye disease

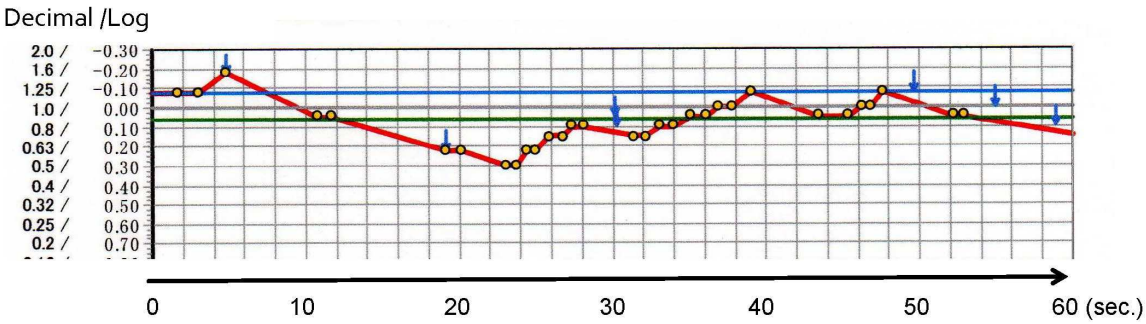




Arrows represent blinks

(C) Aqueous deficient dry eye disease





Arrows represent blinks

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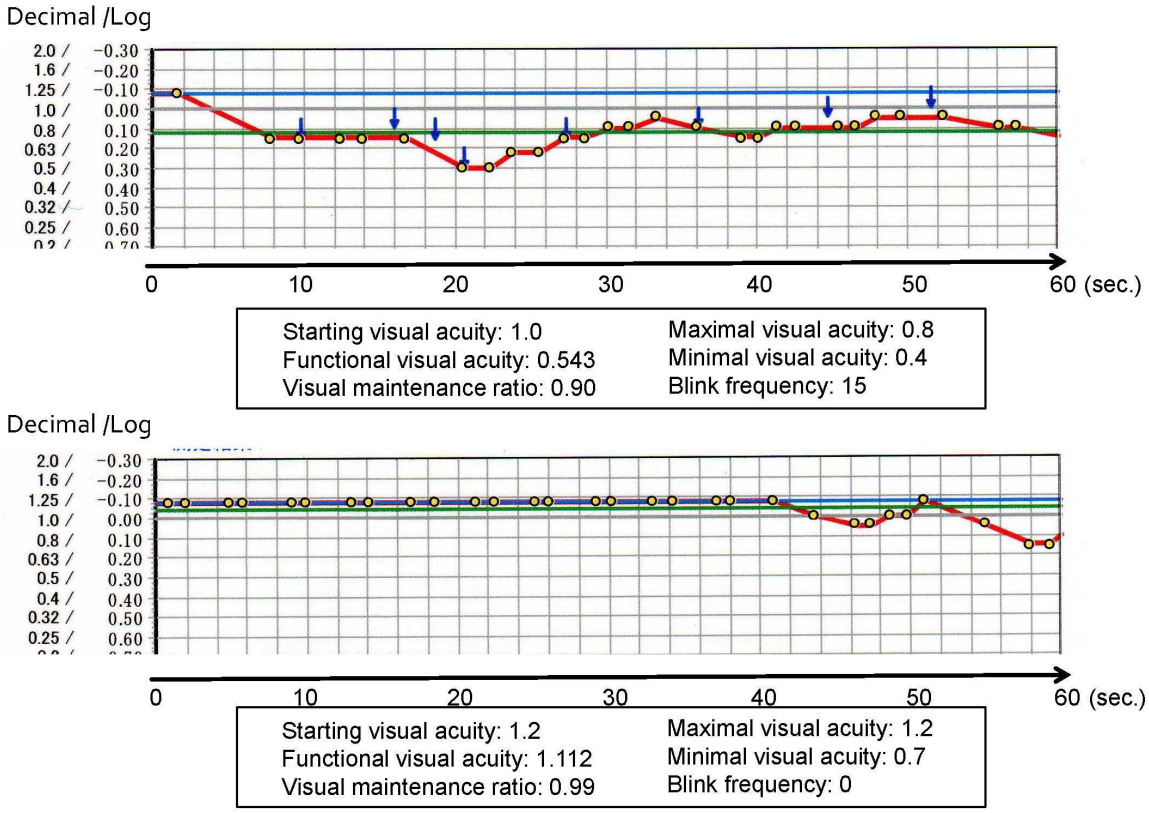
Figure 4. Representative case before (top) and after (bottom) punctal plug insertion



Patient was a 67-year-old female with Sjogren's syndrome. Punctal plugs were inserted in the upper and lower puncta of the left eye. Functional visual acuity (decimal) was improved from 0.543 to 1.112 after punctal plug insertion. Arrows represent blinks.
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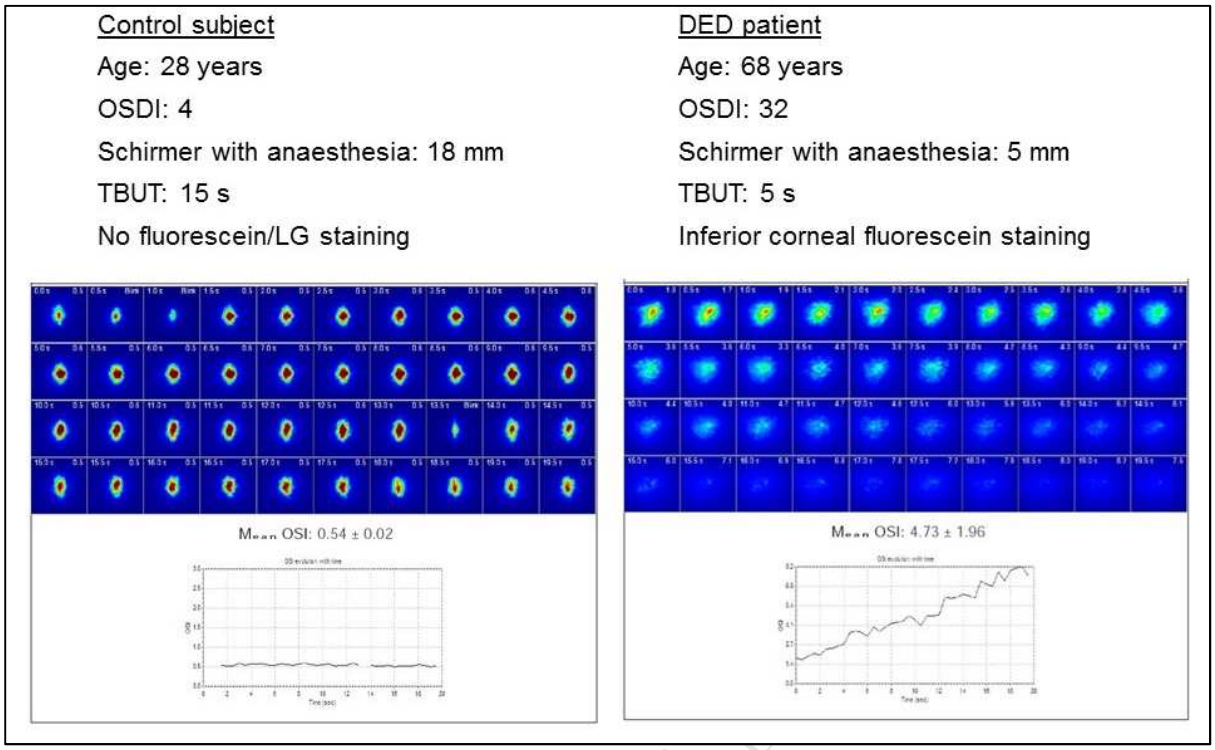
Figure 5. DED is associated with a reduced OSI score



DED, dry eye disease; LG, lissamine green; OSDI, Ocular Surface Disease Index; OSI, objective scattering index; TBUT, tear film break-up time.
Images courtesy of José Benítez-del-Castillo.

Table 1. Dynamic tests to assess FVA

Test	Method description	Results
FVA tester[8]	Using the Snellen chart, visual acuity was measured in patients with DED and controls after sustained eye opening without blinking for 10–20 s (FVA). Oxybuprocaine was applied to the eyes to anaesthetise the ocular surface in order to minimise blinking.	In patients with DED, FVA after sustained eye opening decreased significantly compared with ordinary BCVA, whereas it remained at the same level in normal controls.
FVAM system[49]	The SSC-350 system is a compact device measuring 56 cm in height, 39.6 cm in width and 26.8 cm in depth. Patients are automatically presented with a series of Landolt 'C' rings on a screen at a distance of 1.1 m and asked to delineate the orientation of the rings with a joystick. FVA was measured at 10, 20 and 30 s and compared between patients and control subjects. Topical anaesthesia was administered to minimise blinking.	Mean FVA scores were significantly lower in patients with DED than in controls at each time point.
FVAM system (Kowa)[50,51]	The patient views a screen within the desktop device on which black Landolt optotypes are displayed on a white background. Small optotypes	When used to assess the efficacy of diquafosol tetrasodium eye drops, the FVAM system detected

	are displayed at the start of the assessment; if the patient response is correct, even smaller optotypes are presented. If the responses are incorrect, larger optotypes are presented automatically	improvements in functional, minimal, and maximal visual acuities,
IVAD[53]	The IVAD test is a computer-based measure of BCVA decay between blinks. A rotating Landolt 'C' is presented at the response pace of each patient so that the decay in visual acuity between blinks can be measured. The IVAD test is conducted without the use of an anaesthetic.	Normal controls were able to maintain their BCVA for significantly longer than patients with DED, $p = 0.0001$.
HOAs[58]	Serial measurements of ocular and corneal HOAs after blinking were performed for 10 s using the KR-1 aberrometer (Topcon, Clichy, France).	In DED, patient-reported visual outcomes and clinical findings of tear film and ocular surface damage correlated with the progression index for corneal HOAs.
OQAS II Visiometrics[59]	The OSI is measured with the OQAS to assess the amount of light that passes through the ocular structures and therefore is correlated with dynamic vision quality. OSI was	The OSI was significantly higher in the DED study group (25 eyes) than in the control group (10 eyes).

	measured just after the patient blinked and then at 0.5-s intervals over 20 s without the patient blinking.	

BCVA, best-corrected visual acuity; DED, dry eye disease; FVA, functional visual acuity; FVAM, functional visual acuity measurement; HOA, higher order aberration; IVAD, Interblink interval Visual Acuity Decay; OQAS, Optical Quality Analysis System; OSI, objective scattering index.

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