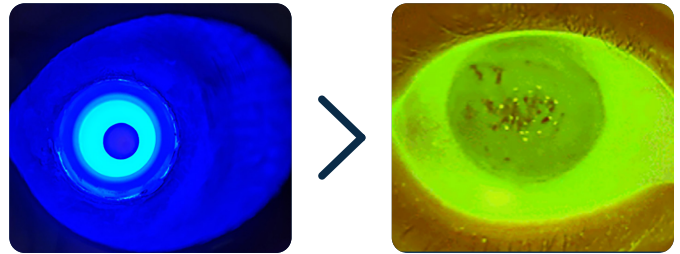


# Ora Ocular Protection Index

The Ora Ocular Protection Index 2.0 System<sup>®</sup> and the associated algorithm-run analysis provide a precise and novel measurement of the tear film breakup phenomenon and a functional endpoint in a clinical trial.

- The Ora OPI 2.0 system is a more clinically relevant measure of tear film instability. We provide quantitative (TFBUT) measurements as well as qualitative (mean surface breakup area). Providing stronger data sets for our partners.
- OPI 2.0 has been validated as a secondary endpoint in the United States.
- The Ora OPI 2.0 system can evaluate ocular surface protection under normal visual conditions. The new approach allows a more advanced method to analyze tear film dynamics.



Above: Ora EyeCup<sup>™</sup> adapted with blue filter for fluorescein detection > fluorescein image of the eye showing tear film break up (dark patches)

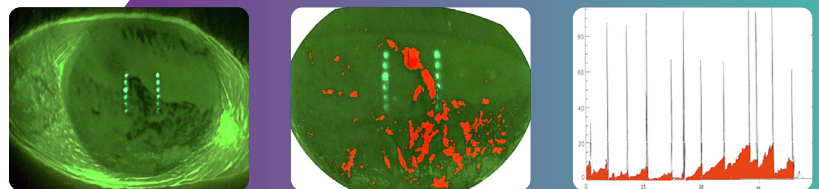
At Ora Clinical, the researchers and R&D team are constantly working to evolve our current methodology and technology to assess DED. The evolution of the OPI measurement into OPI 2.0 is a beautiful example of the ever-improving tests utilized by Ora. OPI 2.0 was designed to address three nuances of the original methodology.

- TFBUT and IBI measurements are performed at different times.
- TFBUT is evaluated using the forced-stare technique, which is not indicative of the natural physiological action of the unaltered blink pattern.
- The original OPI test provided no information on what occurs on the ocular surface between actual tear film breakup and the next blink.

Dry Eye Disease (DED) is a long-lasting and incapacitating condition that impacts the surface of the eye, affecting millions of people globally. Interruption of the delicate homeostasis of the tear film resulting from insufficiencies in either the quality or quantity of its components can lead to tear-film instability and subsequent surface damage. Consequently, the many pathophysiology's of DED will manifest in such individuals.

The relationship between the interblink interval (IBI), the time between consecutive blinks, and tear film breakup time (TFBUT), time from the end of a blink to the appearance of the first dry spot on the cornea, defines the integrity of the ocular surface<sup>1-5</sup>. Therefore, both IBI and TFBUT are insightful variables to measure in efforts to better understand DED.

The ocular protection index (OPI) was developed by researchers at Ora to capture the nature of the relationship between blinking and TFBUT. Since its inception, the OPI methodology has been used in numerous observational studies and clinical trials<sup>6-9</sup>. OPI is calculated by dividing the TFBUT by the IBI<sup>10</sup>.



Above: Fluorescein Image > Mean Breakup area (red patches=exposed cornea) > Data Analysis (y-axis=% Exposed Cornea/x-axis=time (seconds)).

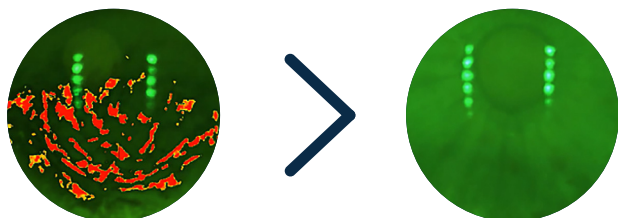
As a result, the Ora OPI 2.0 system was developed to evaluate ocular surface protection under normal visual conditions. The new approach allows a more advance method to analyze tear film dynamics due to the:

- 1 Automated and real-time measurement of the percent of the cornea exposed (fluorescein staining of tear film break up) for each IBI frame during a 1-minute video.
- 2 Simultaneous measurement of TFBUT and IBI.
- 3 The mean breakup area (MBA) and OPI 2.0 measurement, defined as  $MBA/IBI$ , are calculated and analyzed automatically.

A recent study done by Ora R&D proved the feasibility of performing real-time, home-based assessment of tear film stability and ocular surface protection using the Ora EyeCup™ technology. Patients were asked to blink normally during video capture to provide natural IBI and TFBUT measurements. OPI was calculated by dividing the TFBUT by the IBI. This proof-of-concept study demonstrates the usefulness of this technology in clinical trials involving DED outside of the laboratory and clinical setting<sup>11</sup>.

Most importantly, the OPI 2.0 technology provides several benefits to our Ora customers and sponsors.

- OPI 2.0 is a more clinically relevant measure of tear film instability. We provide TFBUT measurements and mean surface breakup area, providing stronger data sets for our partners.
- OPI 2.0 captures a precise and real-time measurement of dynamic TFBUT between blinks. Thus providing a greater opportunity to demonstrate therapeutic efficacy related to tear film stability.
- OPI 2.0 has the capacity to evaluate both the immediate therapeutic benefit (e.g., single eyedrop of an artificial tear) and long term-dosing and disease modification (e.g., prescription product).



Left: Fluorescein Image showing mean breakup area before and after treatment.

## References

1. Abelson MB, Ousler GW 3rd, Nally LA, Welch D, Krenzer K. Alternative reference values for tear film break up time in normal and dry eye populations. *Adv Exp Med Biol.* 2002;506 (Pt B):1121-1125.
2. Holly FJ. Formation and rupture of the tear film. *Exp Eye Res.* 1973; 15(5):515-525.
3. Lemp MA. Breakup of the tear film. *Int Ophthalmol Clin.* 1973; 13(1):97-102.
4. Lemp MA, Goldberg M, Roddy MR. The effect of tear substitutes on tear film break-up time. *Invest Ophthalmol.* 1975;14(3):255-258.
5. Smith J, Nichols KK, Baldwin EK. Current patterns in the use of diagnostic tests in dry eye evaluation. *Cornea.* 2008;27(6):656-662.
6. Crampton HJ, Abelson MB, Ousler GW 3rd, et al. Correlation of the controlled adverse environment (CAE) model with a murine model of experimental dry eye in assessing the ability of topical doxycycline to prevent corneal barrier disruption. *Invest Ophthalmol Vis Sci.* 2007;48:E-abstract 402.
7. D'Arienzo P, Ousler GW 3rd, Schindelar MR. A comparison of two marketed artificial tears in improvement of tear film stability as measured by tear film break-up time (TFBUT) and ocular protection index (OPI) [Poster presentation]. *Tear Film and Ocular Surface Society Meeting; 2007; Taormina, Sicily; 2007.*
8. Ousler GW, Emory TB, Welch D, Abelson MB. Factors that influence the inter-blink interval (IBI) as measured by the ocular protection index (OPI). *Invest Ophthalmol Vis Sci.* 2002;43:E-abstract 56.
9. Wilcox Hagberg KA, Ousler GW 3rd, Casavant JS, Welch D, Abelson MB. Effects of menopause on the ocular protection index (OPI) in a population of dry eye patients of Ashkenazi Jewish descent. *Invest Ophthalmol Vis Sci.* 2005;45:E-abstract 79.
10. Ousler GW 3rd, Hagberg KW, Schindelar M, Welch D, Abelson MB. The ocular protection index. *Cornea.* 2008;27(5):509-513.
11. Bensinger E, Rodriguez J, Wallstrom G, Deiter K, Abelson MB. Tear film stability measure with the Ocular Protection Index (OPI) Acquired with Ora EyeCup Phone. [Poster presentation]. *The Association for Research in Vision and Ophthalmology (ARVO); 2022.*



Ora is a global full-service ophthalmic drug and device development firm with vast capabilities through all steps of clinical research, including preclinical, clinical, CMC & regulatory, and patient and site evaluations. Through Ora's 40+ years of experience, the company has assisted in bringing more than 80 products to market. Ora's team of experts utilizes global regulatory strategies, integrated research operations, and extensive site and patient engagement to accelerate product development in anterior and posterior segment, as well as ophthalmic devices.