# Time Course of Changes in Tear Meniscus Radius and Blink Rate After Instillation of Artificial Tears

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**Purpose.** Using a novel digital meniscometer (PDM), alterations in tear meniscus radius (TMR) were measured simultaneously with blink rate (BR) following the instillation of artificial tears.

**Methods.** Central TMR and BR of 22 subjects (11 male and 11 female; mean age, 24.3 ± 2.6 SD years) were measured at baseline, and 0, 1, 5, 10, and 30 minutes after instillation of an artificial tear containing hydroxypropyl-guar and glycol (SYS) or saline (SAL). A dose of 35 μL was applied in one eye in a randomized order with a washout period between each drop.

**Results.** For SAL, compared to baseline TMR (0.33 ± 0.08 mm), TMR significantly increased with drop instillation (1.55 ± 0.69 mm) and at 1 minute (0.66 ± 0.36 mm; $P < 0.05$), but returned to baseline after 5 minutes. For SYS, TMR (0.32 ± 0.07 mm) remained significantly increased after application (1.62 ± 0.81 mm), and at 1 minute (0.81 ± 0.43 mm) and 5 minutes (0.39 ± 0.08 mm; $P < 0.05$). Compared to baseline BR with SAL (14.8 ± 7.7) and SYS (14.9 ± 9.4), values were significantly increased upon drop instillation (22.5 ± 11.8; 21.3 ± 11.8; $P < 0.05$), but returned to baseline after 1 minute. Dry eye symptoms were correlated with baseline BR ($r = 0.550$, $P = 0.008$).

**Conclusions.** Results indicate that PDM can detect changes in TMR following instillation of artificial tears. Difference in residence time reflects the different viscosity of each drop. An overload with a large drop may result in an initially increased BR.

Keywords: tear meniscus, artificial tears, portable digital meniscometer, blink rate, tear volume loss, dry eye symptoms

Tear fluid, produced by the secretory system, is distributed and mixed with the preocular tear film and menisci with each blink and then lost by evaporation, absorption, and drainage from the menisci through the nasolacrimal passage.[1] Normal tear film dynamics requires a balance between production and elimination of tears from the eye.[2] The lacrimal secretory rate and tear meniscus radius (TMR) are related to tear volume.[3–5] Blinking is important for the distribution and drainage of the tear fluid.[6–8] The blink rate (BR) is influenced by various factors, such as ocular irritation, precorneal tear film condition, visual demands, or environmental conditions.[9–11]

Artificial tears are used commonly to increase tear volume and retention, and to improve tear film quality. The retention time of instilled fluids, like artificial tears, has been studied with different techniques, such as dacryoscintigraphy, reflective meniscometry, or optical coherence tomography (OCT).[12–16] However, the impact of different solutions on the time course of changes in BR and simultaneously on the change in tear volume remains unknown.

Recently, an iPod Touch–based system (Apple, Inc., Cupertino, CA, USA), named the Portable Digital Meniscometer (PDM), has been developed to measure TMR. It has been demonstrated as giving accurate and reliable measurements at the central position, which were correlated significantly with OCT and video-meniscometer values.[17,18] Furthermore, the PDM has shown the capability to detect variations in TMR along the lower lid.[19] However, it is not known how effective this new system is at assessing TMR changes after the instillation of artificial tears.

The aims of this study were to investigate the capability of a novel slit-lamp mounted, PDM to measure alterations in TMR after the instillation of artificial tears, and to evaluate any relationships between TMR alterations and changes in BR.

## Materials and Methods

### Subjects

We recruited 22 healthy subjects (mean age, 24.3 ± 2.6 SD years; male = 11, female = 11) from the staff and students of the Höhere Fachschule für Augenoptik Köln (Cologne School of Optometry), Cologne, Germany. Subjects were excluded if they were pregnant or breast-feeding; had a current or previous condition known to affect the ocular surface or tear film; had a history of previous ocular surgery, including refractive surgery, eyelid tattooing, eyelid surgery, or corneal surgery; had any previous ocular trauma; were diabetic; were taking medication known to affect the ocular surface and/or tear film; and/or had worn contact lenses during the preceding two weeks before the study. Cosmetics use was avoided before the procedure. All subjects gave written informed consent before participating in the study. The procedures obtained the approval of the Cardiff School of Optometry and Vision Sciences Human Ethics


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Committee and were conducted in accordance with the requirements of the Declaration of Helsinki.

### Ocular Surface Disease Index (OSDI)

Each subject's symptoms were evaluated before the application of the drop using the OSDI questionnaire, and afterwards the total OSDI scores were calculated.[20] Analysis of OSDI was masked against TMR and BR measurements.

### TMR Measurement

A newly developed slit-lamp mounted PDM was used to measure the central TMR at the lower eyelid. The PDM is based on an application that creates a series of black and white gratings on the screen of an iPod Touch or an iPhone (Apple, Inc.). The PDM is positioned close to and in front of the eye, and the lower lid tear meniscus acts as a concave mirror, creating an image of the grating (Fig. 1A).[3] This image, when captured or recorded by a digital slit-lamp camera (BQ900 with IM900 digital imaging module; Haag-Streit, Koeniz, Switzerland), can be analyzed using ImageJ 1.46 software (available in the public domain at http://rsbweb.nih.gov/ij) (Fig. 1B). The detailed construction of the PDM has been described previously.[17,18]

With the PDM, a 30-second film of the meniscus was recorded using the digital slit-lamp at baseline, and 0, 1, 5, 10, and 30 minutes after instillation of either an artificial tear containing hydroxypropyl-guar and glycol (Systane Balance [SYS]; Alcon Laboratories, Inc., Fort Worth, TX, USA) with a viscosity of 42 cP, or an isotonic sodium chloride solution (SAL, Lens Plus OcuPure; Abbott Medical Optics, Inc., Santa Ana, CA, USA), viscosity 1 cP. Using a micropipette (Pipetman; Gilson S.A.S., Villiers-le-Bel, France), a defined drop size of 35 μL was applied in the temporal lower fornix of the right eye. This drop size represents an average of ophthalmic solution drop sizes,[21,22] and was used previously in similar studies.[8,12–14] The drops were applied in a randomized order with a washout period of at least 1 week between the different solutions. Care was taken to avoid overspill when applying the drop. An image for analysis, at each time point, was captured from the recorded video of the meniscus two seconds after a spontaneous blink when a stable image was achieved. The images then were exported to ImageJ where TMR was measured.

### Blink Measurement

Each recorded 30-second sequence of subject blinking, at each time point, was viewed in a ×0.25 slow-motion mode with the VLC Media Player 2.06 (available in the public domain at http://www.videolan.org/vlc), and the BR per minute analyzed at baseline, and at 0, 1, 5, 10, and 30 minutes after instillation of the different solutions.

The study was conducted in a room with controlled temperature (20°C–23°C) and humidity (44%–53%). All measurements of the lower tear meniscus radius and BR were taken on the right eye in primary gaze by a single observer. Analysis of tear meniscus radius was masked against BR count. The examiner was masked to the different drops and time points. To minimize diurnal variation, images were recorded in the morning between 10 and 12 o'clock.

### Calculation of Tear Volume Loss (TVL) and Tear Volume Loss Rate (TVLR) per Blink

Total tear volume was calculated by the equation between TMR and tear volume, which was described previously by Yokoi et al.[4]:

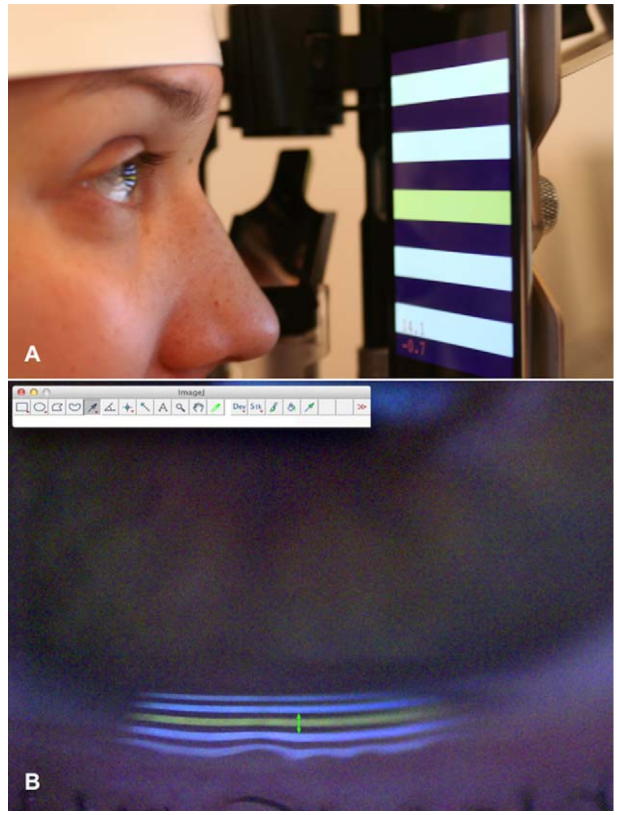


**Figure 1.** **(A)** Patient positioned in front of the portable, slit-lamp mounted PDM. The grid on the screen of the iPod Touch is reflected by the cornea and the lower tear meniscus. **(B)** ImageJ 1.46 software for measurement of line distance on the PDM image.

$$\textit{Total Tear Volume}\ (\mu L) = [(TMR - 0.256)/0.038] + 6.7$$

The TVL was calculated for both solutions for the time intervals between 0 and 1 minute, 1 and 5 minutes, 5 and 10 minutes, and 10 and 30 minutes after the applications. To calculate the TVLR per blink in the different time intervals, the TVL was divided by the BRs that were analyzed for the relevant time interval.

### Statistical Methods

Data were tested for normality using the Shapiro-Wilk test. The time course of changes in TMR and BR was statistically analyzed using 1-way ANOVA on ranks (Kruskal-Wallis test). If significant differences were observed, a Dunnett post hoc test for multiple comparisons was performed to find time points showing a significant difference to the baseline value. Differences between the test solution effects on TMR and BR at various time points were analyzed by the paired *t*-test (for normal distribution) and Wilcoxon signed ranks test (for nonnormal distribution). Correlations between BR and OSDI score were evaluated by Spearman rank order correlation. The data were analyzed using SigmaPlot 12 (Systat Software, Inc., Chicago, IL, USA).

## Results

### Changes in TMR

Compared to baseline values (0.33 ± 0.08 mm) TMR with SAL was significantly increased upon application of drop (1.55 ±

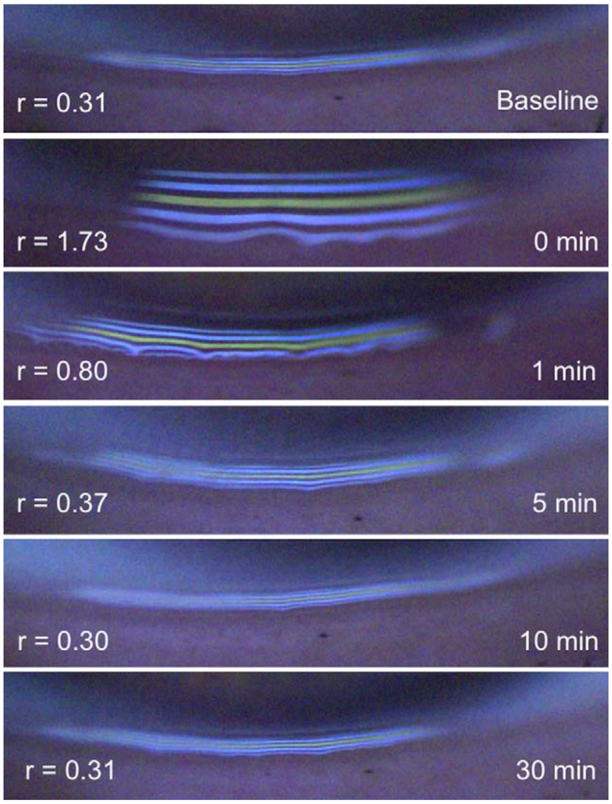


FIGURE 2. Representative PDM images of the dynamic changes in the lower TMR before and after instillation of artificial tears containing SYS.

0.69 mm) and remained significantly greater at 1 minute (0.66 ± 0.36 mm; ANOVA on ranks with Dunnett post hoc test, $P <$ 0.05), but became similar to baseline after 5 minutes (0.34 ± 0.08 mm; $P = 0.417$). In contrast, TMR with SYS (baseline TMR, 0.32 ± 0.07 mm) remained significantly increased after application (1.62 ± 0.81 mm), up until 1 minute (0.81 ± 0.43 mm) and 5 minutes (0.39 ± 0.08 mm; $P < 0.05$, Fig. 2). Compared to SAL, TMR with SYS was significantly flatter at 1 minute (0.15 ± 0.32 mm; $P = 0.044$) and 5 minutes (0.05 ± 0.08 mm; $P = 0.008$, Fig. 3). For all other points in time there was no significant difference between the two solutions.

## Changes in BR

Baseline BRs with SAL (14.8 ± 7.7) and SYS (14.9 ± 9.4) were significantly increased upon application of drops (22.5 ± 11.8 and 21.3 ± 11.8; ANOVA on ranks with Dunnett post hoc test, $P < 0.05$), but became similar to baseline figures after 1 minute ($P > 0.05$, Fig. 4). For all points in time there was no significant difference in BR between the two solutions.

## TVL and TVLR per Blink

The calculated TVL of SAL and SYS in the different time intervals is summarized in the Table.

For both solutions there was no statistically significant difference in the calculated rate of TVL per blink when comparing the first time interval 0 to 1 minute (SAL, 1.24 ± 1.16; SYS, 1.41 ± 1.72 μL/blink) to the second time interval 1 to 5 minutes (SAL, 0.68 ± 1.03; SYS, 0.83 ± 0.79 μL/blink) and the third time interval 5 to 10 minutes (SAL, 0.02 ± 0.11; SYS, 0.12 ± 0.12 μL/blink) to the fourth interval 10 to 30 minutes (SAL 0.07 ± 0.17; SYS 0.08 ± 0.23 μL/blink; ANOVA on ranks

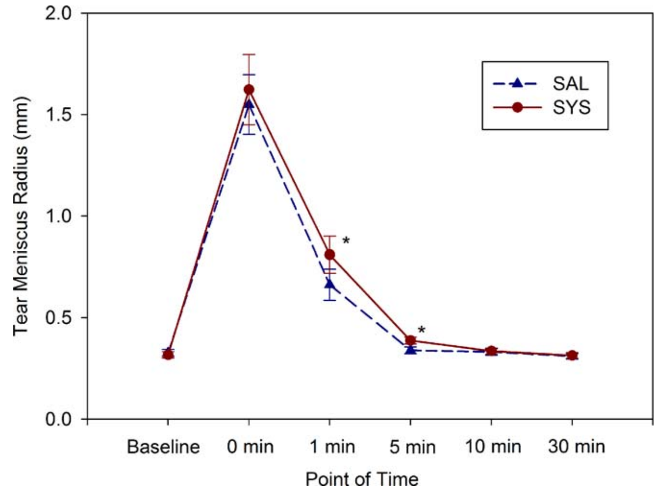


FIGURE 3. Variations in TMR after the instillation of artificial tears. *Indicates a statistically significant difference between the two solutions (paired *t*-test, $P < 0.05$). Values are mean ± SE.

with Dunnett post hoc test, $P < 0.05$). The comparison between all other time intervals (first to third and fourth intervals, and second to third and fourth intervals) showed a statistically significant difference in the rate of TVL per blink ($P < 0.05$, Fig. 5).

## Correlation Between OSDI and BR

Mean OSDI score at baseline was 10.5 ± 7.7 (SD) with a range from 0 to 27.1. The OSDI score was correlated with the BR at baseline (Spearman's rank correlation coefficient, $r = 0.550$; $P = 0.008$; Fig. 6).

## DISCUSSION

We reported the use of a new custom-made PDM to evaluate the dynamic changes of the lower TMR after adding artificial tears. Using the PDM, an increase in TMR (and, therefore, tear

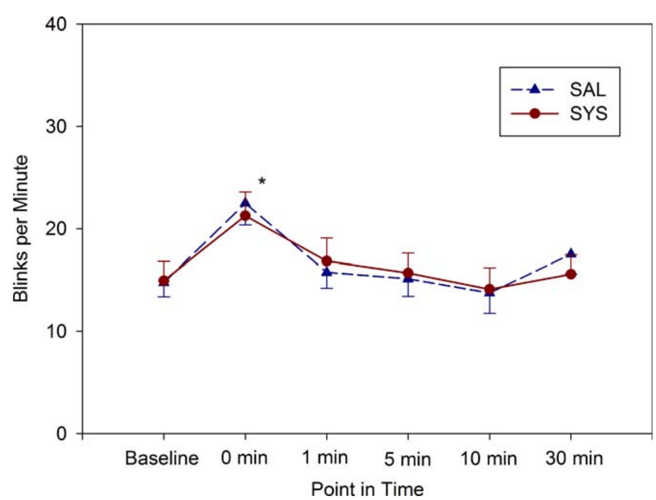


FIGURE 4. Variations in BR after the instillation of artificial tears. *Indicates a statistically significant difference from the baseline values (ANOVA on ranks with Dunnett post hoc test, $P < 0.05$). Values are mean ± SE.

**Table.** Calculated TVL in Microliters (Mean ± SD) in the Different Time Intervals

| Time Interval, µL | 0–1 Min | 1–5 Min | 5–10 Min | 10–30 Min | Total |
|---|---|---|---|---|---|
| SAL | −23.3 ± 16.5 | −11.0 ± 9.0 | −0.1 ± 1.0 | −0.4 ± 1.5 | −34.8 ± 17.8 |
| SYS | −21.4 ± 16.6 | −11.3 ± 10.5 | −1.4 ± 1.3* | −0.6 ± 1.5 | −34.5 ± 22.3 |

* Indicates a statistically significant difference between the two solutions (paired *t*-test, $P < 0.001$).

volume) was found after instillation, with a return to baseline figures after 5 minutes for the SAL solution and after 10 minutes for the artificial tears containing SYS.

Wang et al.[12,14] measured the dynamic changes of tear meniscus height (TMH), TMR, and tear meniscus cross-sectional area (TMA) after artificial tear instillation using a custom-made OCT system. They found the tear meniscus parameter returned to baseline 5 minutes after instillation of saline (viscosity 1 cP), carboxy-methylcellulose sodium (CMC) 0.5% and 1.0% (3 and 70 cP), and propylene glycol 0.3% (10 cP). However, they found an increase in tear film thickness and lower tear meniscus variables at instillation with the more viscous drops in healthy patients. Also using CMC in a concentration of 0.5% and 1.0% in dry eye patients and controls, Wang et al.[13] used a spectral domain OCT to measure TMH and TMA changes. While in the control group the 0.5% and 1% CMC persisted for 1 and 15 minutes, in the dry eye group the artificial tears persisted for 5 and 30 minutes. They suggested that the longer retention time is associated with the viscosity of the drop and, furthermore, that in a dry eye patient, a lower tear clearance rate might prolong the retention time. In this study, when measuring TMR with the PDM in subjects without significant dry eye, a two times longer retention time was found with the more viscous drop compared to saline. Although in this group the differences between the drops were small, but statically significant, a clinically more relevant difference could be expected in dry eye patients, as suggested by Wang et al.[12] Interestingly, the difference of 0.05 mm in TMR after 5 minutes represents a difference in volume of 1.3 µL (see Table). Estimating a total tear volume of 6.2 µL,[5] this represents an increase of approximately 20%, which might be clinically relevant.

Furthermore, the artificial tears we used in this study were formulated specifically to minimize the evaporative loss of tears from the ocular surface, by adding a polar phospholipid surfactant and mineral oil.[23] It is possible, therefore, that a difference in tear evaporation rate between the two drops used will have impacted the changes in TMR.

Yokoi et al.[4] investigated the relationship between tear volume and TMR measured using a video-meniscometer, concluding that there is a linear relationship between the volume of the instilled saline solution and the measured TMR. Applying the video-meniscometer, they showed that a 0.1% hyaluronic acid solution resided longer in the tear meniscus than a solution containing 0.1% KCl and 0.4% NaCl.[15] The PDM in this study is based on the video-meniscometer,[3] where the tear strip acts as a concave mirror, and, likewise, we were able to detect changes in tear volume by measuring the dynamics of TMR.

Besides the volume and the viscosity of the drop, blinking has an important role in the distribution and drainage of instilled fluid. The lacrimal drainage capacity in young individuals was correlated with the BR.[7] Palakuru et al.[8] analyzed the blink outcome, defined as the difference in tear volume before and after a blink, upon the instillation of 35 µL of 1% CMC. Immediately after the drop was applied, the blink outcome of one blink was increased compared to the blink outcome after five minutes. They concluded, that the increase in blink outcome helps to restore balance when the instilled drop overloads the tear system. Zhu and Chauhan[24] used a mathematical model, and calculated a drainage rate of 1.174 µL per blink for the overloaded tear film. Overloading the tear film by repeatedly instilling saline solution into the tear film for 3 minutes, Sahlin et al.[25] reported drainage rates of 1.11 to 4.03 µL per blink. In this study, the volume loss rates of 1.24 and 1.41 µL per blink in the first time interval of 0 to 1 minute are in good agreement with the previously reported values. Interestingly, even though the tear volume after 1 minute was significantly diminished, the volume loss rate per blink in the second interval (1–5 minutes) was not significantly different from that in the first interval. This fact might be explained by the observation of an increase in BR upon

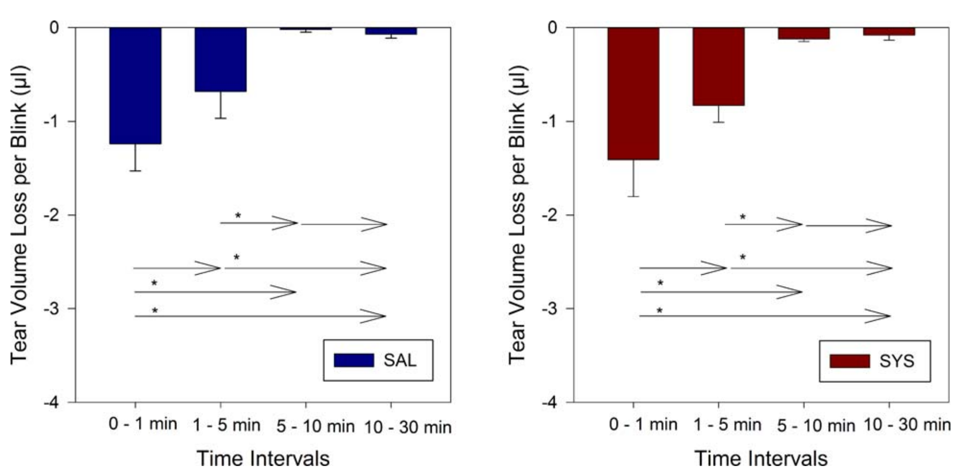


**Figure 5.** Calculated TVL per blink in the different time intervals after the instillation of a 35 µL drop. *Indicating a statistically significant difference between the time intervals (ANOVA on ranks with Dunnett post hoc test, $P < 0.05$). Values are mean ± SE.

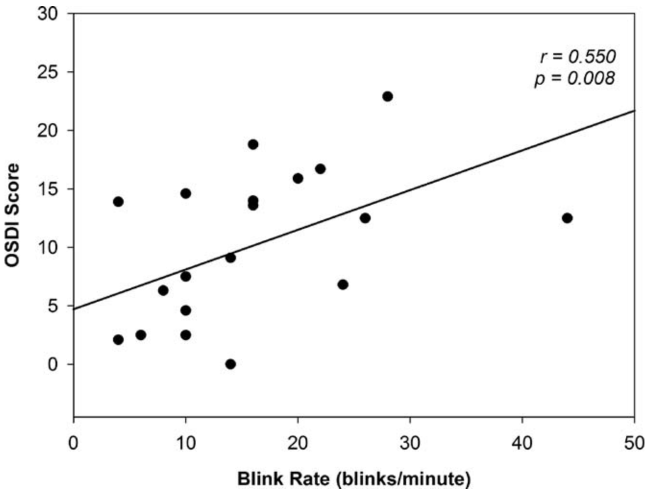


FIGURE 6. Relationship between OSDI score and BR at baseline. (Spearman's rank correlation coefficient, $r = 0.550$, $P = 0.008$).

application of drops with a return to baseline after 1 minute. These results favor the interpretation that, during the initial overload phase, the increase in tear volume results in an increase in BR, but that as soon as the volume is reduced to a certain level, a reduction in BR keeps the volume loss rate per blink nearly constant. Once the overload is removed, the volume loss rate per blink of the normal tear film stays constant (Fig. 5). This mechanism has not been reported previously to our knowledge, although Palakuru et al.[8] argued for a relationship between tear volume and BR output based on the analysis of a single blink.

The spontaneous BR at baseline in this study compares well with the literature.[26,27] Upon drop instillation, the BR increased with no difference in the BRs between the two solutions. Based on these observations, we hypothesized that the viscosity of the drop does not seem to influence the effect. However, the difference in viscosities of the two drops used in this study may be too small and the variations in BRs too large to detect an effect of drop viscosity on BR.

Dry eye patients exhibit an increased BR in response to the drying of the ocular surface.[9,10,28] Although the cohort in this study was very young, we confirmed a correlation between symptoms evaluated by the OSDI scores and the BRs.

A limitation of this study may be that completeness of blink was not assessed. Recent studies suggest that not only the frequency, but also the completeness of blink may have an effect on dry eye symptoms.[26,29] Further studies are needed to examine the effect of different types of blinking on the loss of tear film volume.

In summary, the PDM is able to detect changes in TMR usefully following the instillation of artificial tears. The difference in residence time is likely to reflect the different viscosity and Newtonian properties of these drops. An overload with a large drop may result in an initial increased BR. The BR at baseline was significantly related to dry eye symptoms.

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