Cornea

Noninvasive Assessment of Tear Stability with the Tear Stability Analysis System in Tear Dysfunction Patients

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Purpose. To evaluate tear film stability in patients with tear dysfunction and an asymptomatic control group by using the novel, noninvasive Tear Stability Analysis System (TSAS).

Methods. In this prospective case–control study, 45 patients with dysfunctional tear syndrome (DTS) were stratified into three groups (1, 2, and 3/4) based on clinical severity, with higher scores indicating more severe symptoms; 25 asymptomatic control subjects were evaluated. TSAS measurements were performed with the RT-7000 Auto Refractor-Keratometer (Tomey Corporation, Nagoya, Japan). Images of ring mires projected onto the cornea every second for 6 seconds were captured and analyzed. Focal changes in brightness were calculated as numerical ring breakup (RBU) values, and the elapsed time when the cumulative values (RBU sum) exceeded a threshold was defined as the ring breakup time (RBUT).

Results. RBUTs in the DTS groups were all significantly lower than those in the control subjects, with the lowest values found in DTS 3/4. RBUT was significantly shorter in DTS 3/4 than in DTS 1 ($P < 0.001$). The change in RBU sum over a 6-second period in the DTS groups combined or between the individual groups was statistically significant ($P < 0.001$), as was the difference between the 1- and 6-second values. For distinguishing between asymptomatic controls and DTS, the sensitivity and specificity of a 5.0-second RBUT cutoff were 82.0% and 60.0%, respectively.

Conclusions. The TSAS may be a useful, noninvasive instrument for evaluating tear stability and for classifying DTS severity. (*Invest Ophthalmol Vis Sci.* 2011;52:456–461) DOI: 10.1167/iovs.10-5292

Dry eye and tear dysfunction are among the most common ocular diseases, estimated to affect 14% to 33% of adults and increasing with age.[1-5] The air–tear film interface is the primary refractive surface of the eye, and thus its integrity and stability are crucial for maintaining high-quality vision and ocular comfort.[1-5] Traditionally, the precorneal tear film has been thought to consist of separate mucin, aqueous, and lipid layers. Soluble mucins are important structural components of the precorneal tear film, and the hydrated mucus layer accounts for most of the film's thickness.[6-8] The instability of tear film may be due to qualitative or quantitative abnormalities of any of these components. Other factors that can also affect tear film stability include concentrations of stabilizing factors (e.g., mucins), integrity of the surface epithelia and overlying lipid layer, activity of proteolytic enzymes in tears, and reflex blink mechanisms.[9]

The tear breakup test with fluorescein is one of the most commonly used measures of tear stability.[10,11] However, it has numerous limitations, including the need to instill fluorescein, lack of standardization of fluorescein concentration, induction of reflex tearing, subjective assessment, and difficulty in simultaneous assessment of tear breakup across the entire cornea.[11] It is possible to assess tear breakup with noninvasive methods that include tear film lipid layer interferometry,[12,13] the xeroscope, and the tearscope (Keeler, Windsor, UK).[14] A limitation of these methods is that they do not provide a standardized objective measurement of tear stability.

Topographic regularity indices of the corneal topography instrument (TMS-2N; Tomey Corporation, Nagoya, Japan) have also been used as objective diagnostic parameters of tear stability and corneal surface regularity in patients with tear dysfunction,[15-17] but these topographic examinations provide data at only one time point. For kinetic noninvasive assessment of tear stability, Tear Stability Analysis System (TSAS) software was developed for the TMS-2N, and its utility for measuring tear stability in dry eye was studied.[18] This software is not commercially available; however, a modified version has been developed for the RT-7000 Auto Refractor-Keratometer (Tomey Corporation). This system works on the principle of capturing images of mire rings projected onto the cornea every second for up to 10 seconds. Points along a radial line are converted into a wave pattern based on the light intensity of the reflected points at that second. The instrument's software uses these waves to calculate tear stability parameters.

The purpose of this study was to use the novel, noninvasive TSAS on the RT-7000 instrument to evaluate tear film stability in patients with dysfunctional tear syndrome (DTS) and to compare the results with those in normal control subjects.

METHODS

This study was approved by the Baylor College of Medicine Institutional Review Board (IRB). It adhered to the tenets of the Declaration of Helsinki for clinical research, and written informed consent was obtained from all the participants after explanation of the purpose and possible consequences of the study.

Forty-five consecutive patients with newly diagnosed DTS, who met the inclusion criteria were enrolled in the study at the Ocular Surface Center (Baylor College of Medicine, Houston, TX). Patients were excluded if they used any topical medications other than preservative-free artificial tears, wore contact lenses, had undergone ocular surgery in the past year, or had evidence of any other ocular surface diseases, systemic disease, or medications that would alter the ocular surface. Twenty-five subjects were recruited as asymptomatic controls. Inclusion criteria for the control subjects were absence of corneal and conjunctival dye staining and a symptom severity score ≤20. Diagnosis of DTS was based on patients' reports of eye discomfort (symptom severity score, >20; tear breakup time [TBUT], ≤7 seconds).

DTS patients recruited for this study were referred by three members of the cornea service in our department. Asymptomatic control subjects and DTS patients all underwent the same ocular surface and tear evaluations. Patients completed a dry eye symptom severity questionnaire, followed by a complete ocular surface examination of both eyes in the following sequence: TSAS of the right eye by the RT-7000 Auto Refractor-Keratometer (Tomey Corporation), topographic measurement of the surface regularity index (SRI) in both eyes (right eye followed by the left eye), biomicroscopic examination of the lid margins and meibomian glands, fluorescein TBUT, corneal fluorescein staining, conjunctival lissamine green staining, and Schirmer I test. With the exception of the TSAS, these tests were performed by a single investigator (SCP), as described elsewhere.[19] Symptom severity score was measured by the ocular surface disease index (OSDI) questionnaire, which contains 12 questions for evaluating the character and severity of dry eye symptoms. Briefly, the questionnaire inquired about the frequency of occurrence of each symptom, rating it from *none* to *all the time*. The questionnaire scores ranged from 12 (no symptoms) to a maximum of 59. Criteria for grading DTS severity were modified from the Dry Eye Workshop (DEWS) based on the symptom severity scores, TBUT values, and corneal and conjunctival staining scores (Table 1).[20] If all criteria of a severity group were not met, assignment to a severity grading was based on the worst parameter. Meibomian gland disease (MGD) was diagnosed by evidence of dysfunction (lack of expressible meibum from ≥75% of glands on the central lower lid margin) and the presence of one or more morphologic changes in the meibomian glands, including acinar atrophy and vascular dilation on or scalloping of the posterior lid margin.[5,21] The United States European Study Group consensus criteria were used for diagnosis of Sjögren's syndrome (SS).[22]

Principle of TSAS on the RT-7000

TSAS software had been designed for the Tomey Topographic Modeling System (TMS-2N; Tomey Corporation), but it was never released commercially. We explored a newer version of the TSAS that was developed for the Tomey RT-7000 Auto Refractor-Keratometer. In this version, 15 mire rings from a lighted cone are projected onto the corneal surface. To minimize the interference of lids and lashes, only the 11 central rings are analyzed. The software captures images of the reflected rings each second for up to 10 consecutive seconds. In this study, we examined the right eye for 6 seconds. Data points for analysis consist of the intersections of 256 lines radiating from the center with the 11 reflected rings, yielding a total of 2816 points. Each line of points is converted into a wave pattern based on the light

intensity of the reflected points at that second. Waves at time 0 are set as the standard. The instrument's software uses these waves to calculate parameters that include ring breakup sum (RBU sum), ring breakup time (RBUT), and ring breakup value (RBU value). Detailed explanations of these parameters are provided in Figures 1 and 2.

RBU Value and RBU Sum

An RBU value is the change in ring brightness level of the data points compared with those of the previous second. The sum of the RBU value at any given second and those of the previous seconds is defined as the RBU sum at that second. The RBU sum corresponds to the area of tear film breakup. An eye with an RBU sum of 700, for example, has 10 times the area of tear film breakup as does an eye with a sum of 70.

Ring Breakup Time

The time in seconds after the last blink when the RBU sum exceeds a specified threshold value[20] is considered the RBUT. Based on preclinical testing, the manufacturer found an RBUT less than or equal to 5 seconds to be suggestive of dry eye.

Statistical Analysis

The Pearson χ^2 test was applied to analyze sex differences between the groups. A Shapiro-Wilk test was performed to determine whether data were normally distributed. If a distribution could not be normalized by logarithmic transformation, the Kruskal-Wallis test was used. Normally distributed continuous parameters were analyzed between the groups (control and three DTS groups) by one-way ANOVA and Welch ANOVA tests. Tukey and Tamhane multiple-comparison tests were also applied to the homogenous and nonhomogenous parameters, respectively. Spearman's correlation test was performed to analyze the association between the study parameters. The change over time between the groups was analyzed by using repeated-measures ANOVA. The right eye values were used for comparison of clinical parameters and the RBU parameters. $P \leq 0.05$ was considered statistically significant (SPSS 15.0 for Windows evaluation version; LEAD Technologies Inc., Chicago, IL, was used for all analyses).

RESULTS

The demographic data and clinical parameters for control subjects and DTS patients are presented in Table 2. Etiologic subclassification of DTS patients is provided in Table 3. For statistical analysis, data from patients who met the DTS 3 and 4 severity criteria were combined to form one group, DTS 3/4. Thus, a total of four groups were compared: control and DTS 1, 2, and 3/4. Even though the mean age of the control subjects was slightly younger than that of the DTS patients, the difference did not reach statistical significance. There was also no significant difference in the distribution of the sexes between the control and three DTS subgroups.

Clinical Parameters

Compared with the control group, the symptom severity scores were significantly greater in all the DTS groups combined ($P \leq 0.001$); however, there were no significant differences in symptom severity scores between the three DTS groups ($P = 0.897$ for DTS 1 vs. DTS 2, $P = 1.00$ for DTS 1 vs. DTS 3/4, $P = 0.870$ for DTS 2 vs. DTS 3/4). The Schirmer I values were lower in each DTS group than in the control group, although the difference reached statistical significance only in DTS 3/4 ($P = 0.002$). There was a statistically significant difference in the SRI in the four groups ($P < 0.001$). In post hoc analysis, the control ($P < 0.001$), DTS 1 ($P = 0.016$), and DTS 2 ($P = 0.030$) groups all had significantly lower SRIs than the DTS 3/4 group. The fluorescein TBUTs were statistically significant between the groups, except for DTS 2 versus DTS

TABLE 1. Severity Grading Criteria for DTS

Parameters	Control	DTS1	DTS2	DTS3	DTS4
Symptom severity score*	≤20	>20	>20	>20	>20
Tear breakup time (seconds)	>7	≤7	≤7	≤7	≤7
Conjunctival staining score	0	≤3	≥3	≥3	≥3
Corneal staining score	0	≤2	≤8	>8†	≥12

* Symptom severity score was measured by OSDI questionnaire.
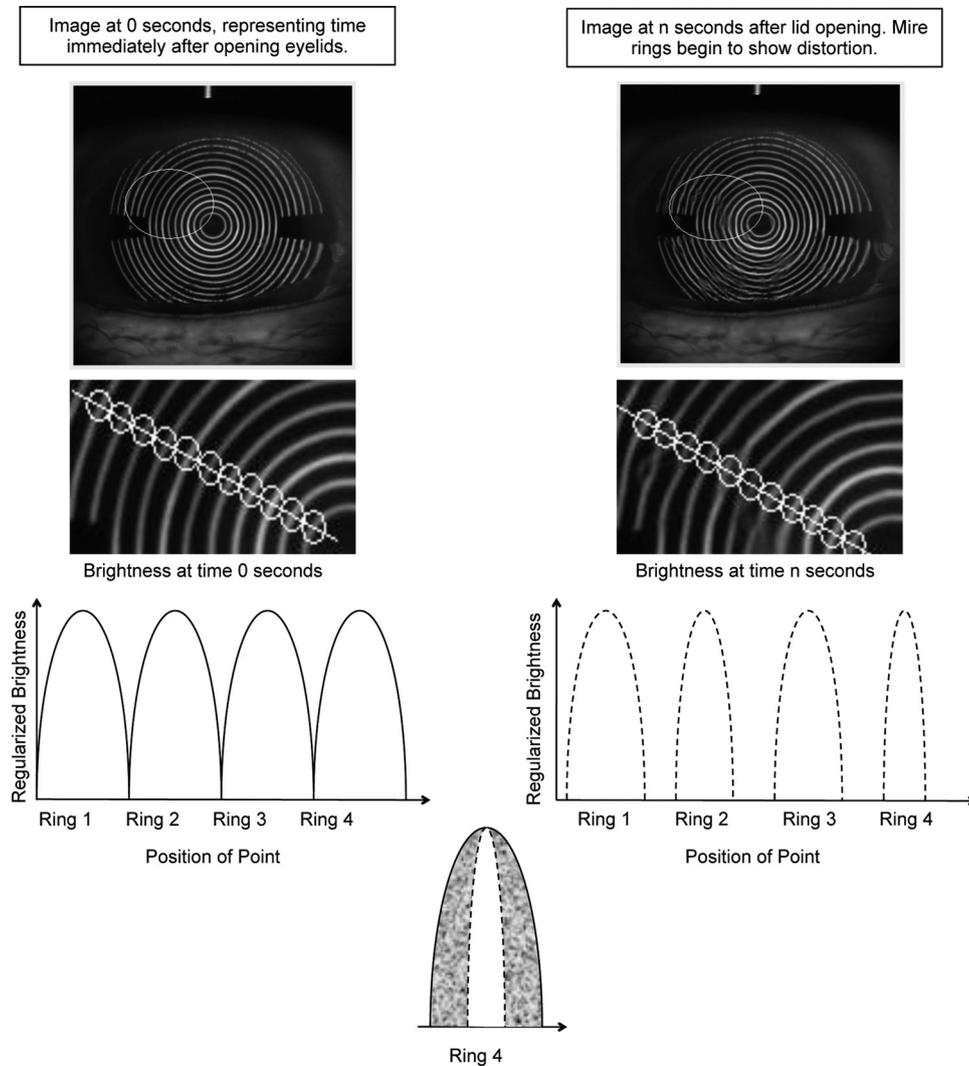† Including central cornea or filaments.

FIGURE 1. There are 256 points evenly distributed on each of the 11 central mire rings. These points are radially connected by lines to make 256 lines. Each line of points is converted into a wave based on the light intensity of the reflected points at that second. The waves are also regularized, or normalized, to account for peripheral rings not reflecting as brightly as central ones due to a greater distance from the light source. The difference of the area under the curves of each point at *n* seconds and 0 seconds is calculated (example: the *shaded area* between the *solid* and *dashed lines* of ring 4). When the difference reaches a designated threshold, the point is considered to be a breakup point. Peripheral breakup points are weighted more heavily to compensate for a lower density of points. The total breakup points in the 11 central rings, after being weighted, is the RBU sum for *n* seconds. The time at which the RBU sum exceeds 20.0 is the RBUT. An RBUT of less than 5.0 seconds is suggestive of dry eye.

3/4 ($P > 0.05$). Corneal fluorescein staining scores were significantly greater in the DTS groups than in the control group (all $P < 0.05$). Conjunctival staining scores were significantly greater in the DTS 2 and 3/4 groups than in the control and DTS 1 groups. Detailed statistical comparisons of the groups are provided in the legend to Table 2.

TSAS Analysis

The RBUT results are presented in Table 2. The RBUT values in the DTS groups were all significantly lower than in the control group, with the lowest values found in DTS 3/4. RBUT was significantly shorter in DTS 3/4 than in DTS 1.

The RBU sums over time in the asymptomatic control group and the three DTS groups are presented in Figure 3. The changes in RBU sum from second 1 to second 6 in the DTS groups combined or between the individual groups was found to be statistically significant ($P < 0.001$).

When the cutoff point was 5.0 seconds for RBUT, as the manufacturer recommended, the sensitivity and specificity of the current TSAS method were 82.0% and 60.0%, respectively. Moreover, the positive predictive value was 0.79, and the negative predictive value was 0.65. Sensitivity and specificity ratios were reanalyzed using RBUT cutoff points ranging from 2.5 to 5.0 seconds (Table 4). The optimum sensitivity (82.2%) and specificity (88.0%) were obtained when the cutoff point was lowered to 3.0 seconds.

DISCUSSION

We evaluated a recently released noninvasive TSAS in patients with DTS. We found that, similar to conventional fluorescein TBUT, RBUT measured with the TSAS became progressively shorter with worsening severity. Furthermore, the RBU sum showed a greater increase over the 6-second evaluation time in the DTS patients than in the control group, and the rate of increase was greater with worsening disease severity. A cutoff point for RBUT of 3.0 seconds was found to have optimum sensitivity and specificity of 82.2% and 88.0%, respectively.

In response to the increasing prevalence of dry eye and increasing recognition of its impact on quality of life, numerous technological advancements have been made in studying disease pathogenesis, diagnosis, and treatment. Development of a noninvasive diagnostic method to measure tear stability and to identify eyes with tear dysfunction with high specificity and sensitivity has been a major goal.

In research studies and clinical practice, the use of corneal topographic systems for identifying tear dysfunction has gradually increased. For example, several studies[15,17,23,24] have documented corneal surface irregularity detected by computerized videokeratoscopy (CVK) indices in patients with DTS. These studies established that indices such as SRI, surface asymmetry index (SAI), potential visual acuity index (PVA), and
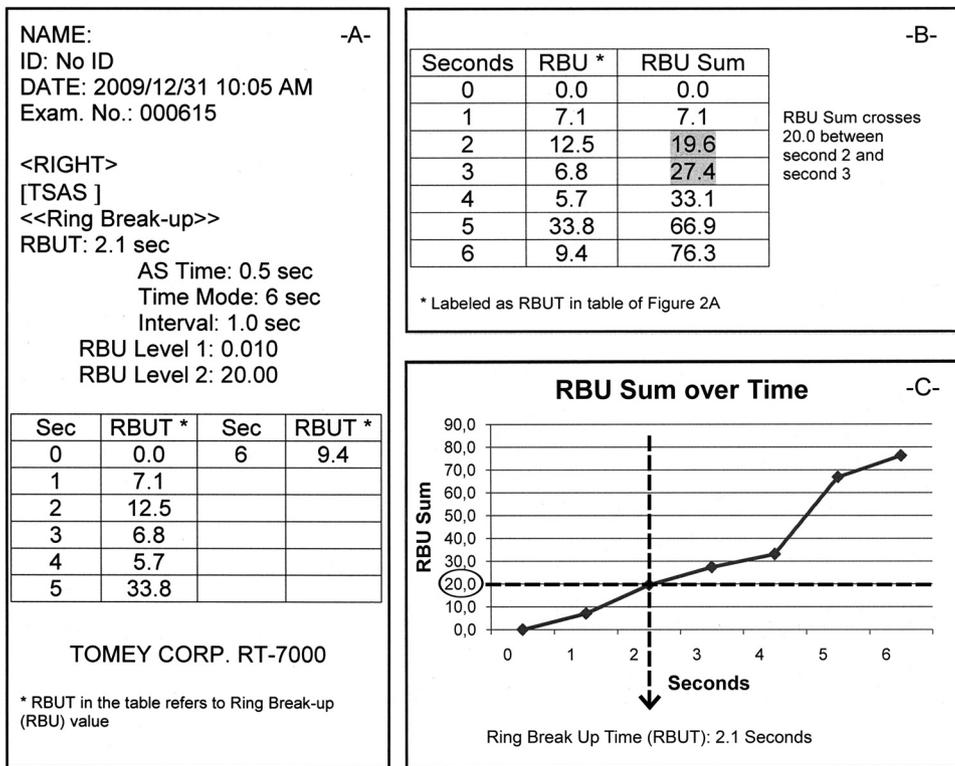
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[TSAS]
<<Ring Break-up>>
RBUT: 2.1 sec
       AS Time: 0.5 sec
       Time Mode: 6 sec
       Interval: 1.0 sec
       RBU Level 1: 0.010
       RBU Level 2: 20.00

Sec	RBUT *	Sec	RBUT *
0	0.0	6	9.4
1	7.1		
2	12.5		
3	6.8		
4	5.7		
5	33.8		

TOMEY CORP. RT-7000

* RBUT in the table refers to Ring Break-up (RBU) value

-B-

Seconds	RBU *	RBU Sum
0	0.0	0.0
1	7.1	7.1
2	12.5	19.6
3	6.8	27.4
4	5.7	33.1
5	33.8	66.9
6	9.4	76.3

RBU Sum crosses 20.0 between second 2 and second 3

* Labeled as RBUT in table of Figure 2A

RBU Sum over Time   **-C-**

Ring Break Up Time (RBUT): 2.1 Seconds

FIGURE 2. RBU values represent the changes in RBU sum between consecutive seconds. For example, at second 2, the value 12.5 on the printout (**A**) indicates an increase of 12.5 RBU from second 1; thus, the RBU sum at second 2 is 7.1 + 12.5 = 19.6. At second 3, the value 6.8 means an increase of 6.8 RBU, and so the RBU sum at second 3 is 7.1 + 12.5 + 6.8 = 27.4 (**B**). The time at which the RBU sum crosses the threshold of 20.0 is the RBUT, at 2.1 seconds in this example (**C**). An RBUT less than 5.0 seconds, as in this case, suggests dry eye.

irregular astigmatism index (IAI) of the Tomey TMS-2N had good sensitivity and specificity for predicting the presence of tear dysfunction identified by corneal fluorescein staining.[15] Other studies have reported that increases in SRI were correlated with decreased functional visual acuity and contrast sensitivity.[25–27]

Several noninvasive techniques for assessing precorneal TBUT without the use of fluorescein have been reported. Indeed, instruments such as the grid xeroscope and tearscope (Keeler) are capable of noninvasive measurement of TBUT. However, identifying tear breakup still requires subjective assessment with these instruments.[11]

Over the past 5 years, several studies have reported the use of CVK systems to assess tear film stability.[11,18,28,29] Kojima et al.[11] described the TSAS software for the TMS-2N, which was programmed to capture Placido ring images sequentially for 10 seconds. In this system, disruption of tear film stability was identified as a change in corneal power. Change of more than 0.5 D in corneal power was designated an area of breakup. Two parameters were established to evaluate the tear film stability (1) tear breakup time (TMS-BUT) and (2) tear breakup area (TMS-BUA). The system provided a summary of the individual breakup points in a single display.[18]

TABLE 2. Demographic and Clinical Features of DTS Patients and Control Subjects

Parameters	Control (*n* = 25) A	DTS 1 (*n* = 23) B	DTS 2 (*n* = 11) C	DTS 3/4 (*n* = 11) D	*P**
Age	48.20 ± 16.55	52.48 ± 16.14	59.36 ± 19.54	55.36 ± 14.14	0.282
Sex (M/F), %	56/44	21.7/78.3	36.4/63.6	36.4/63.6	0.112
OSDI scores	10.40 ± 4.65	35.65 ± 11.95	31.27 ± 11.45	35.73 ± 7.11	<0.001
TBUT	9.12 ± 0.97	5.91 ± 3.10	3.10 ± 1.52	2.91 ± 1.22	<0.001
Conjunctival SS	0 ± 0	0.09 ± 0.29	1.73 ± 2.19	2.36 ± 3.32	0.001
Corneal SS	0 ± 0	0.77 ± 0.97	3.73 ± 1.35	9.36 ± 4.00	<0.001
Schirmer 1	22.63 ± 9.66	14.68 ± 10.72	12.67 ± 8.17	8.50 ± 8.76	0.002
SRI	0.13 ± 0.14	0.42 ± 0.38	0.37 ± 0.34	1.04 ± 0.66	<0.001
RBUT	4.91 ± 1.62	2.40 ± 2.47	1.24 ± 1.75	0.36 ± 0.45	<0.001

Conjunctival SS, conjunctival staining score; corneal SS: corneal staining score.
  * *P* values, among A, B, C, and D groups.
  Age: One-way ANOVA, Sex: Chi-square, OSDI scores: Welch ANOVA, TBUT: Kruskal-Wallis H, Corneal and Conjunctival SS: Kruskal-Wallis H, Schirmer 1: One-way ANOVA (after logarithmic transformation), SRI: One-way ANOVA (after logarithmic transformation), RBUT: Welch ANOVA (after logarithmic transformation), Post hoc *P* values:
     OSDI: $P < 0.001$ (A-B), $P = 0.001$ (A-C), $P < 0.001$ (A-D), $P = 0.897$ (B-C), $P = 1.00$ (B-D), $P = 0.870$ (C-D).
     TBUT: $P < 0.05$ (A-B), $P < 0.05$ (A-C), $P < 0.05$ (A-D), $P < 0.05$ (B-C), $P < 0.05$ (B-D), $P > 0.05$ (C-D).
     Conjunctival SS: $P > 0.05$ (A-B), $P < 0.05$ (A-C), $P < 0.05$ (A-D), $P > 0.05$ (B-C), $P > 0.05$ (B-D), $P > 0.05$ (C-D).
     Corneal SS: $P < 0.05$ (A-B), $P < 0.05$ (A-C), $P < 0.05$ (A-, $P < 0.05$ (B-C), $P < 0.05$ (B-D), $P < 0.05$ (C-D).
     Schirmer 1: $P = 0.076$ (A-B), $P = 0.078$ (A-C), $P = 0.002$ (A-D), $P = 0.967$ (B-C), $P = 0.217$ (B-D), $P = 0.576$ (C-D).
     SRI: $P = 0.082$ (A-B), $P = 0.229$ (A-C), $P < 0.001$ (A-D), $P = 0.997$ (B-C), $P = 0.016$ (B-D), $P = 0.030$ (C-D).
     RBUT: $P = 0.001$ (A-B), $P = 0.003$ (A-C), $P < 0.001$ (A-D), $P = 0.700$ (B-C), $P = 0.004$ (B-D), $P = 0.522$ (C-D).

TABLE 3. Etiologic Subclassification of DTS Patients

Etiology	All DTS (n = 45)	DTS 1 (n = 23)	DTS 2 (n = 11)	DTS 3/4 (n = 11)
MGD	27 (60.0)	15 (65.2)	7 (63.6)	5 (45.5)
SS	5 (11.1)	—	1 (9.1)	4 (36.4)
Non-SS ATD	13 (28.9)	8 (34.8)	3 (27.3)	2 (18.2)

MGD, meibomian gland disease; SS, Sjögren's syndrome; Non-SS ATD, non-Sjögren's syndrome aqueous tear deficiency.

Kojima et al.[11] evaluated the effectiveness of the TSAS for the TMS-2N before and after the insertion of punctal plugs in patients with tear dysfunction and in control subjects. In eyes with DTS, both tear stability regularity and asymmetry indices (TSRI and TSAI) derived from SRI and SAI were found to be greater than in control subjects. The authors concluded that TSAS is effective in objectively assessing the tear stability in patients with DTS.

In two studies, Goto et al.[18,29] documented that TMS-BUT and TMS-BUA had similar specificity to conventional fluorescein TBUT, but videokeratoscopic indices had significantly higher sensitivity in identifying tear film stability. They reported TMS breakup time to be shorter than breakup identified by biomicroscopy.[29] Moreover, they suggested that TSAS for the TMS-2N can be used as a new sensitive method for diagnosing tear dysfunction before and after LASIK.[18,29]

In the present study, a newer version of the TSAS developed for the Tomey RT-7000 Auto Refractor-Keratometer was evaluated. This system projects mire rings onto the cornea and captures images of the mires every second for up to 10 seconds. In our study, we examined the right eye for 6 seconds. The instrument's software evaluates ring brightness to generate parameters that include RBU value, RBU sum, and RBUT. A detailed explanation of the methods used to calculate these indices is provided in the Materials and Methods section and in Figures 1 and 2. The manufacturer suggests that an RBUT less than or equal to 5 seconds is suggestive of dry eye.

Several key differences in the two versions of TSAS software should be highlighted. The TSAS for TMS-2N calculates breakup by changes in corneal power as measured by corneal
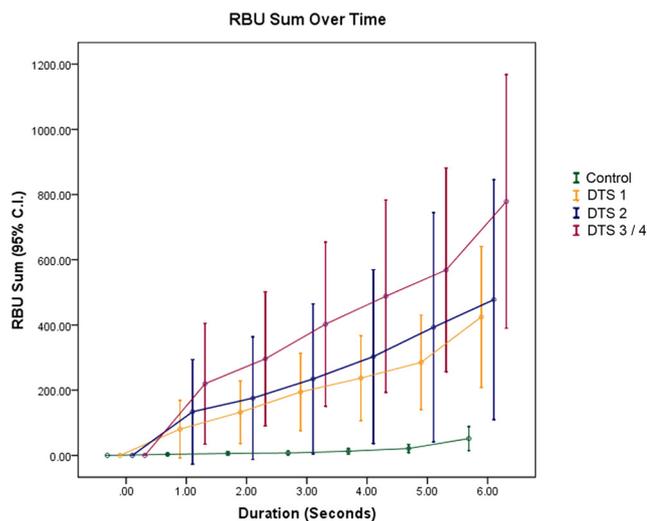
TABLE 4. Sensitivity and Specificity Ratios for TSAS at Different Cutoff Points

Cutoff Point for RBUT (s)	Sensitivity (%)	Specificity (%)
≤5.0	82.0 %	60.0 %
≤4.5	82.2 %	76.0 %
≤4.0	82.2 %	76.0 %
≤3.5	82.2 %	80.0 %
≤3.0	**82.2%**	**88.0%**
≤2.5	80.0 %	88.0 %

The maximal cutoff point for sensitivity and specificity is in bold.

topography, whereas the TSAS for the RT-7000 calculates tear breakup based on the brightness difference of data points on mire rings. In addition, the TSAS for the RT-7000 includes an autoalignment feature to correct for unstable fixation of the patient's eye over the duration of the test. According to the manufacturer that designed both versions, results of the TSAS of the RT-7000 have been found to be more stable.

Using the new system we found that the RBUT was significantly lower in all the DTS severity groups combined ($P < 0.001$) and in each of the subgroups compared with the asymptomatic control group ($P = 0.001$, $P = 0.003$, and $P < 0.001$, respectively). The RBU sum was significantly higher in the entire DTS group at each time interval from 1 to 6 seconds compared with the control group ($P = 0.001$, at 1 second, and $P < 0.001$ at other intervals).

A distinct difference in the pattern of RBU sum was noted between the control subjects and the DTS groups. While the RBU sum remained relatively constant in the control group, the RBU sum in each of the DTS groups progressively increased over the 6-second evaluation period. Among the DTS groups, the DTS 3/4 group had the highest RBU sum over time, followed by the DTS 2 and 1 groups. These differences in RBU sum noted between the DTS and control subjects and between the DTS severity groups indicate that the TSAS is an objective method of detecting tear film instability, and it may prove to be a useful method of monitoring the efficacy of therapies for DTS.

When we evaluated the sensitivity and specificity of the TSAS model used in the present study, sensitivity was found to be as high as 82.0%, but specificity was 60.0%, when the cutoff RBUT of 5.0 seconds suggested by the manufacturer was used. While this test is useful for identifying DTS patients, it is not as strong at discriminating normal individuals from DTS patients. We therefore investigated other cutoff values for RBUT to eliminate this deficiency. Based on these data, the cutoff point of 3.0 seconds for RBUT seems to have greater sensitivity (82.2%) and specificity (88.0%) ratios compared with the cutoff point of 5.0 seconds. Therefore, an RBUT of less than 3.0 seconds appears to be appropriate for identifying an unstable tear film.

One of the most important disadvantages of this new method is the high variability in the RBU sum. Based on the present data, this variability significantly *increased* with the *level of clinical severity* of DTS and increased in all groups over time. This finding was consistent with our observation of minimal variability of the results in repeated examinations of normal eyes. Fortunately, the change in RBU sum over time between the control group and DTS groups became statistically significant at the first second, revealing that the instrument is an efficient and reliable method for identifying tear instability in patients who report eye irritation. Squinting, flinching, lid movement, and looking away from the target were actions observed to increase the RBU readings and thus decrease the RBUT. To minimize the impact of these factors, the subjects were encouraged to keep their eyes wide open

FIGURE 3. RBU sum over time. Control group values had the lowest RBU sum throughout the 6 seconds. The RBU sum increased each second with increasing severity of DTS. Variability increased with increasing severity of DTS and also increased over time in each DTS group. Bars, 95% CI.

and focused on the target for the duration of the test. It should be noted, however, that doing so for 6 seconds can be a challenge, especially for patients experiencing irritation and photophobia; hence, these movements may contribute to the variability of the measurement.

For some subjects, facial anatomy, notably the brow and nose, necessitated repositioning of the head to allow for proper alignment of the lighted cone. Even with repositioning, a few subjects still could not be tested due to prominent facial features. This is a limitation that the manufacturer may want to address in future devices.

In conclusion, the TSAS system for the RT-7000 provides valuable information regarding tear film stability in patients with tear dysfunction. It appears to be a useful, noninvasive tool for diagnosing and stratifying DTS. It may also help as an objective indicator for monitoring therapies for tear dysfunction.

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