

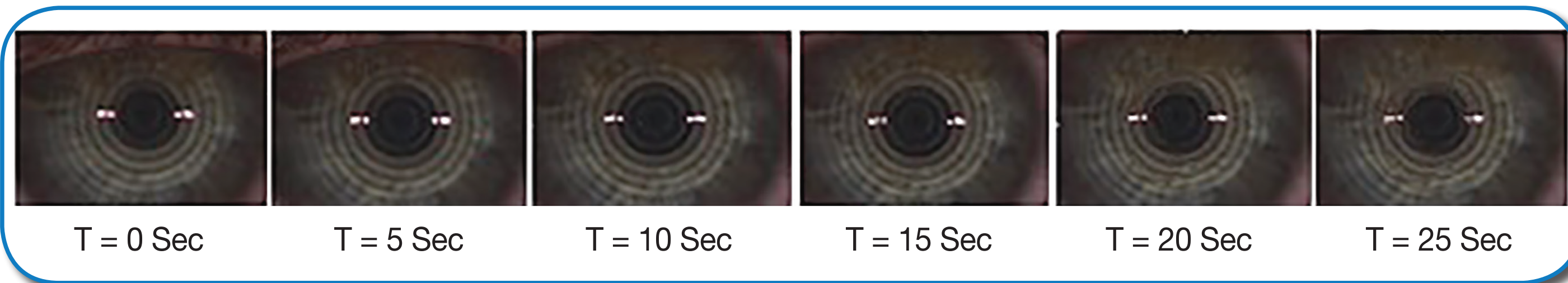
Variability of Pre Ocular and Pre Lens Tear Film Stability Assessed Subjectively and Objectively Using Placido Ring Projection

Authors:
 Cecile Maissa,¹ Sebastian Marx,²
 Julia Wittekind,² Wolfgang Sickenberger³
¹Alcon Vision Care, Fort Worth, TX, USA
²JENVIS Research Institute, Jena, Germany
³Ernst-Abbe-University, Jena, Germany

Introduction

- Contact lens wear is known to be one of the causes of tear film (TF) instability,¹ increased evaporation rate¹⁻³ and dry eye symptoms,^{4,7} leading to decreased ocular comfort towards the end of the day⁸ and reduced wearing time.⁹
 - In cases in which the TF is unable to fully wet the contact lens surface, there is a decrease in TF optical quality, hence visual impairment, an increase in deposition,¹⁰ and reduced comfort are observed.¹¹
 - Further, aging of the TF has been associated with significant changes in the tear lipid layer and a significantly higher TF evaporation in patients older than 45 years.^{12,13} This reduction in TF stability and efficacy is associated with a higher incidence of tear-related problems in an aging population.
- Although several techniques are available, there are no established methods for an objective assessment of the pre-lens TF stability.
- More recently, corneal topographers have been used to assess the pre lens noninvasive tear breakup time (PL NITBUT), enabling the observation of a much larger zone, covering more than the optical zone of a contact lens.
 - Circular mires are projected onto the corneal surface, the reflection on the TF observed and the time (PL NITBUT) recorded at the first sign of mire distortion.¹⁴
 - Although the measurement of the time to first break in the TF is often used as the clinical marker of contact lens on eye wettability, recent findings have shown that this measurement alone is insufficient to characterize fully on-eye contact lens wettability.¹⁵
- The Keratograph 5M (K5 Oculus; OCVLUS Optikgeräte GmbH, Wetzlar, Germany) device can project Placido ring mires onto the lens surface and capture a video of the reflected image (Figure 1). Newly developed software allows simultaneous detection of areas as they destabilize after the blink and when destabilization occurs.
- The objectives of this study were to characterize, using the K5 Oculus, TF stability in subjects wearing nelficon A daily disposable contact lenses for 12 hours and to evaluate inter-subject and day-to-day within-subject variability of TF stability.

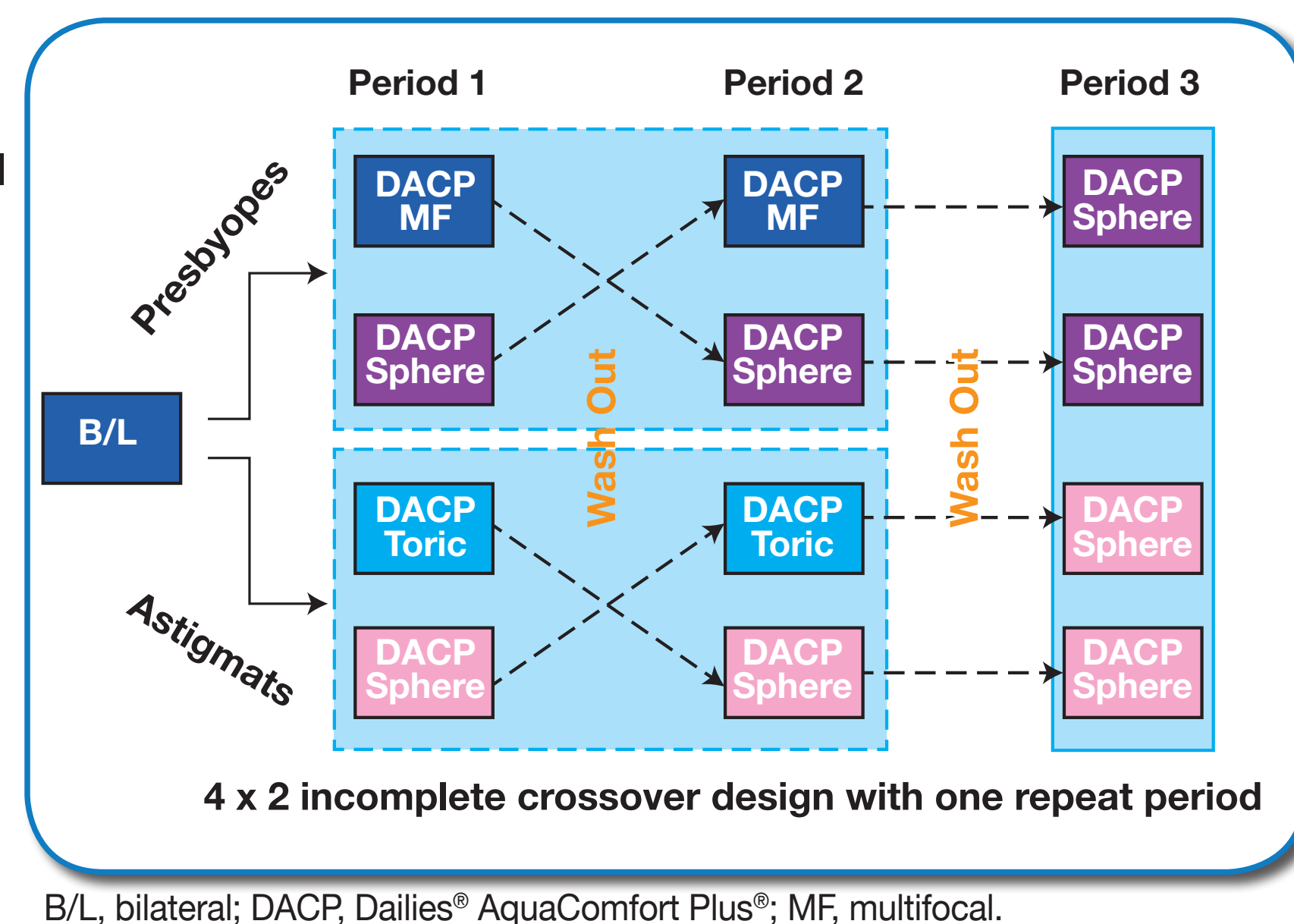
Figure 1. Image of tear film with ring mires projection recorded for 25 seconds post blink



Methods

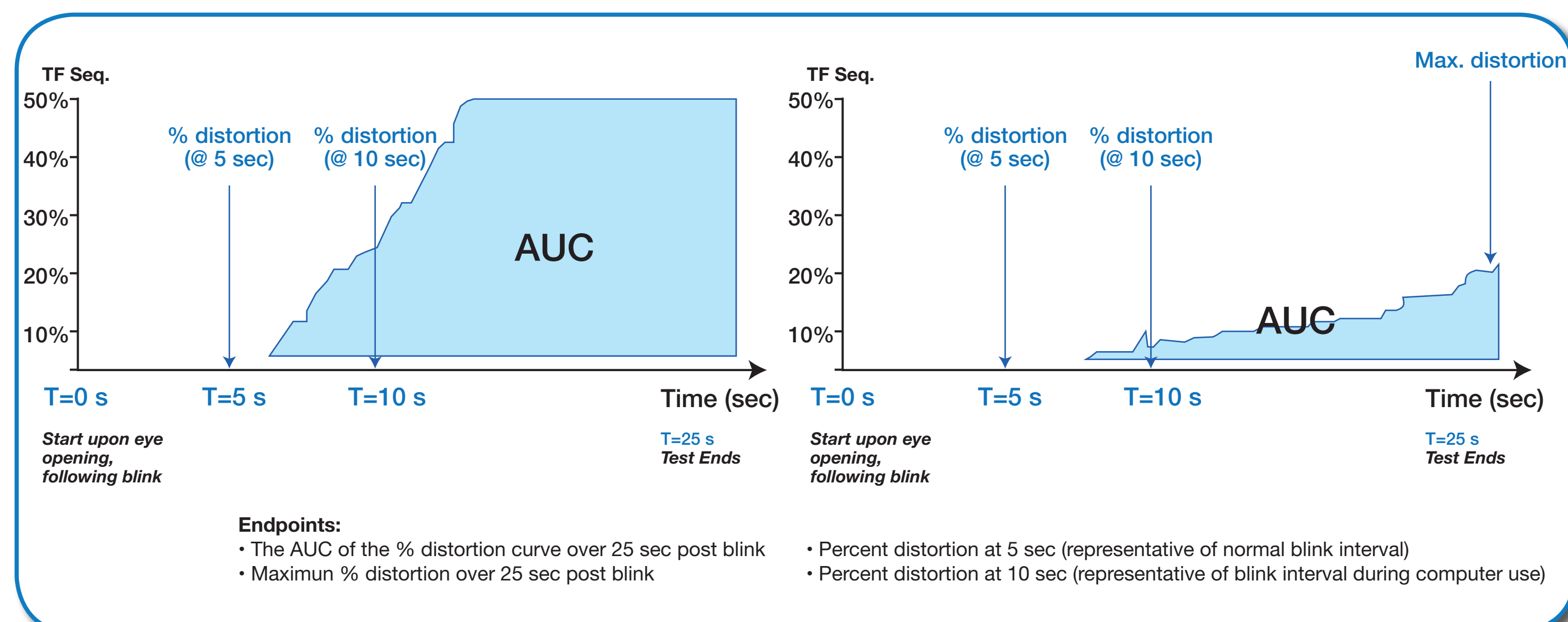
- Prospective randomized bilateral crossover study design (Figure 2).
 - Subjects with presbyopia were assigned to nelficon A (Dailies® Aqua Comfort Plus®; DACP) multifocal lenses, followed by nelficon A sphere lenses, or vice versa.
 - Subjects with astigmatism were assigned to nelficon A toric lenses, followed by nelficon A sphere lenses, or vice versa.
- After a washout period, all subjects were assigned to wear nelficon A sphere lenses to enable retesting to ascertain within-subject variability in measurements during wear of the sphere lenses.
- Subjects were adapted soft contact lens wearers aged ≥18 years, including Presbyopes and Astigmats.
 - Subjects with a noninvasive keratograph breakup time (NIK BUT) value <8 seconds in either eye without lenses at the baseline visit were excluded.
- The subjects wore each lens for a period of 12 hours.
- During each period of wear, TF videos of the ring mires system projected onto the ocular/lens surface using the K5 Oculus-Imaging Live Mode and NIK BUT Mode were recorded for 3 consecutive blinks for 25 seconds post blink¹⁵
 - Before contact lens insertion; pre-ocular tear film (POTF).
 - At 3 different time points post-contact lens insertion (PLTF): 5 min, 8 h, and 12 h.
- The analysis was carried out for 3 consecutive blinks. The videos were assessed subjectively and using the TF-Scan software with investigational overview.
- From the semi-automated analysis of the K5 Oculus NIK BUT videos, the TF was characterized in terms of:
 - The time to first break (NIK BUT to first distortion)
 - The maximum % distortion over 25 sec post blink
 - The area under the curve (AUC) % distortion over 25 sec post blink
 - The distortion % at 5 sec (representative of normal blink interval) post blink
 - The distortion % at 10 sec (representative of blink interval during computer use) post blink

Figure 2. Study design



B/L, bilateral; DACP, Dailies® AquaComfort Plus®; MF, multifocal.

Figure 3. Semi-objective measurements of tear film (TF). Drying up characteristics: right, fast; left, slow.



- Data from the two repeat periods with nelficon A (sphere) was used to characterize the TF over 12 hours of wear and to evaluate its inter-subject and day-to-day within-subject variability.

Table 1. Baseline demographic characteristics

	Presbyopes (N=22)	Astigmats (N=21)	Overall (N=43)
Age, yr			
Mean ± SD	51.7 ± 8.1	25.8 ± 4.5	39.0 ± 14.6
Range	40 to 69	21 to 37	21 to 69
Sex, n (%)			
Male	6 (27.3)	5 (23.8)	11 (25.6)
Female	16 (72.7)	16 (76.2)	32 (74.4)

Subject characteristics

- Subject demographic characteristics are shown in Table 1; overall and for each population group:
 - Astigmats were about half the age of Presbyopes.
 - In both groups, the female to male ratio was ~ 3:1.

Results

Habitual lens characteristics at baseline

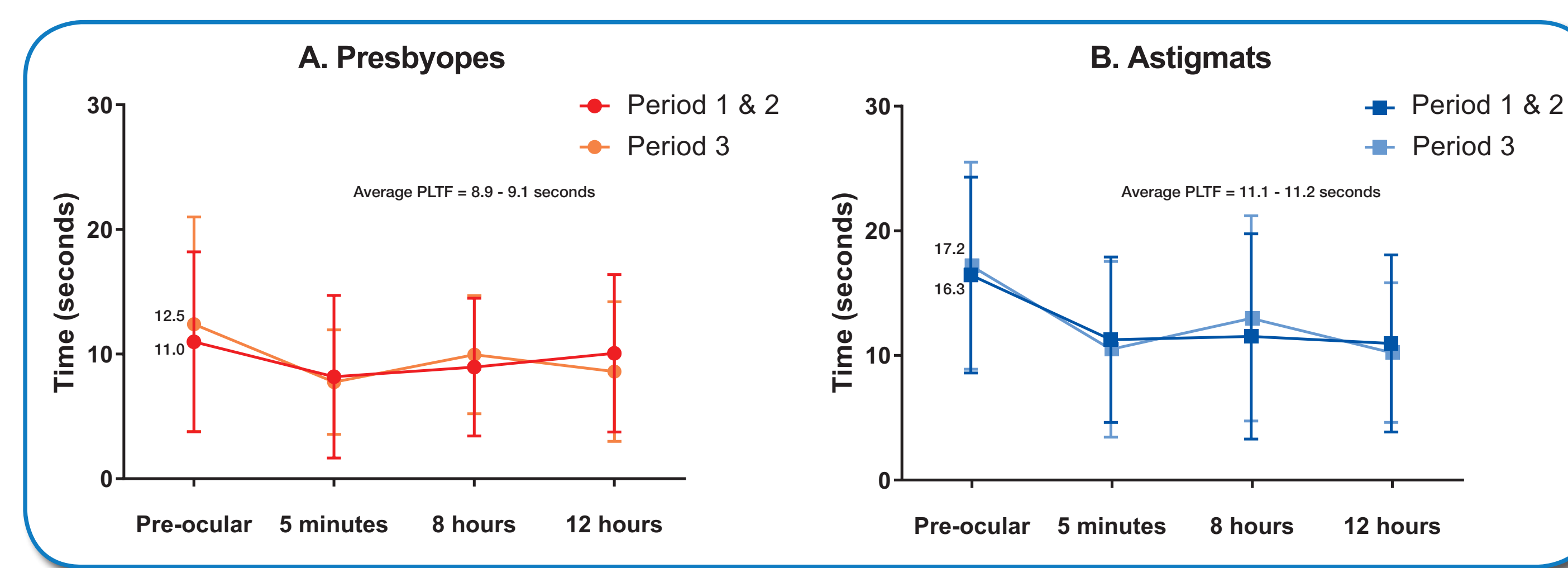
- Among presbyopes, the most common habitual lens type was reusable (14 subjects, 63.6%), and daily lenses were used by 6 subjects (27.3%).
 - Lens material was silicone hydrogel in 14 subjects (63.6%) and non-silicone hydrogel in 6 (27.3%).
- Among astigmats, most subjects (12, 57.1%) habitually used reusable lenses, with 5 (23.8%) using daily lenses.
 - Lens material was silicone hydrogel in 13 subjects (61.9%) and non-silicone hydrogel in 5 (23.8%).

Tear film characteristics

Time to first distortion

- Mean time to first distortion after blink measured semi-objectively was reduced after 5 min, 8 h, and 12 h of nelficon A sphere lens wear compared with pre-contact lens wear in both population groups (Figure 4).
- Median time to first distortion was 18% to ~50% lower in the presence of a contact lens (Table 2) in both population groups.

Figure 4. Time to first distortion in seconds with nelficon A sphere lenses (mean ± SD)

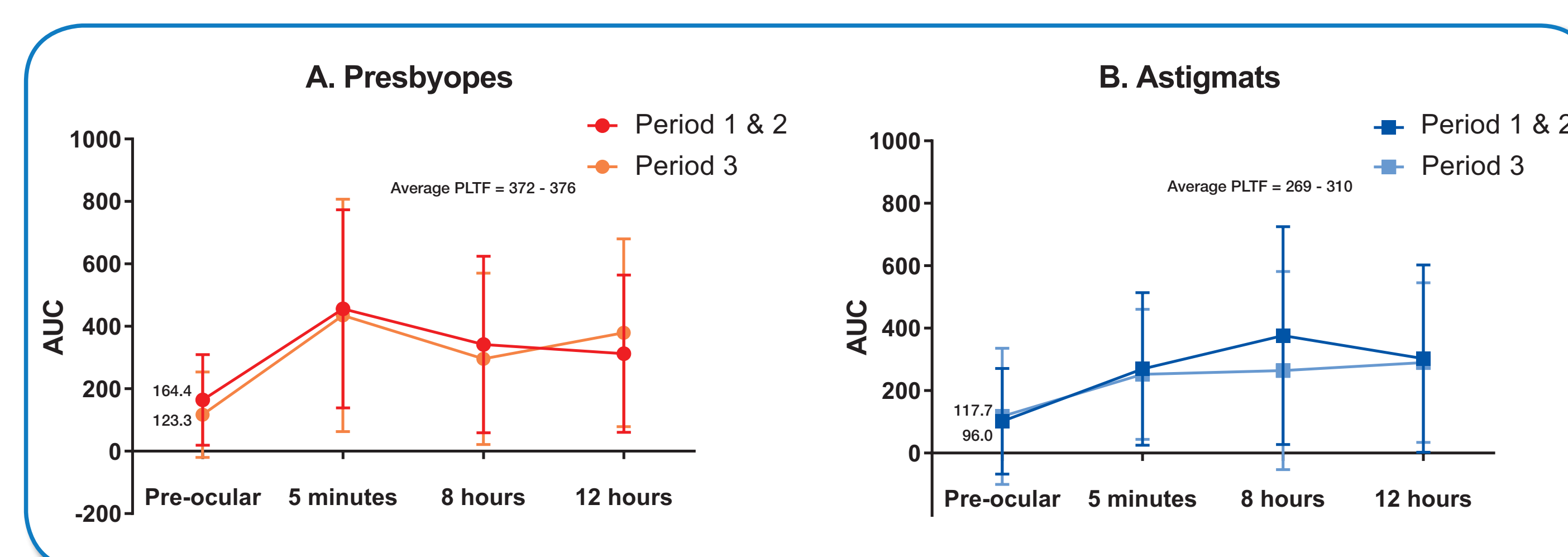


PLTF, post lens tear film

AUC % distortion

- In Presbyopes, the AUC of the % distortion recorded over 25 sec post blink increased from a mean of 123-164 for the POTF to 302-456 for the PLTF after 5 min, 8 hr or 12 hr of wear.
- In Astigmats, the AUC of the % distortion recorded over 25 sec post blink increased from a mean of 96-118 for the POTF to 252-370 for the PLTF after 5 min, 8 hr or 12 hr of wear.

Figure 5. AUC % distortion with nelficon A sphere lenses (mean ± SD)

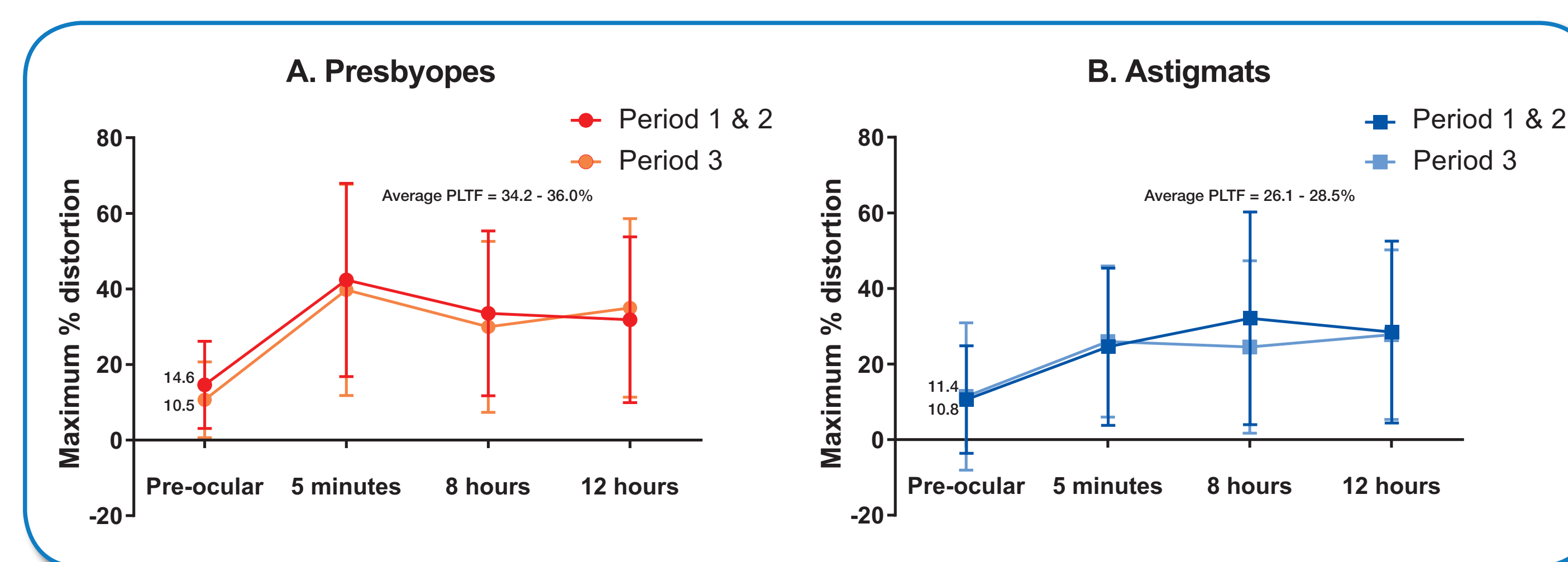


AUC, area under curve; PLTF, post lens tear film

Maximum % distortion

- In Presbyopes, mean maximum % distortion recorded over 25 sec post blink increased from an average of 10%-15% for the POTF to 35%-36% on average for the PLTF (averages over 5 min, 8 hr, and 12 hr of wear) (Figure 6A).
- In Astigmats, mean maximum % distortion recorded over 25 sec post blink increased from an average of ~11% for the POTF to an average of 26%-28% for the PLTF (averages over 5 min, 8 hr, and 12 hr of wear) (Figure 6B).

Figure 6. Maximum % distortion with nelficon A sphere lenses (mean ± SD)

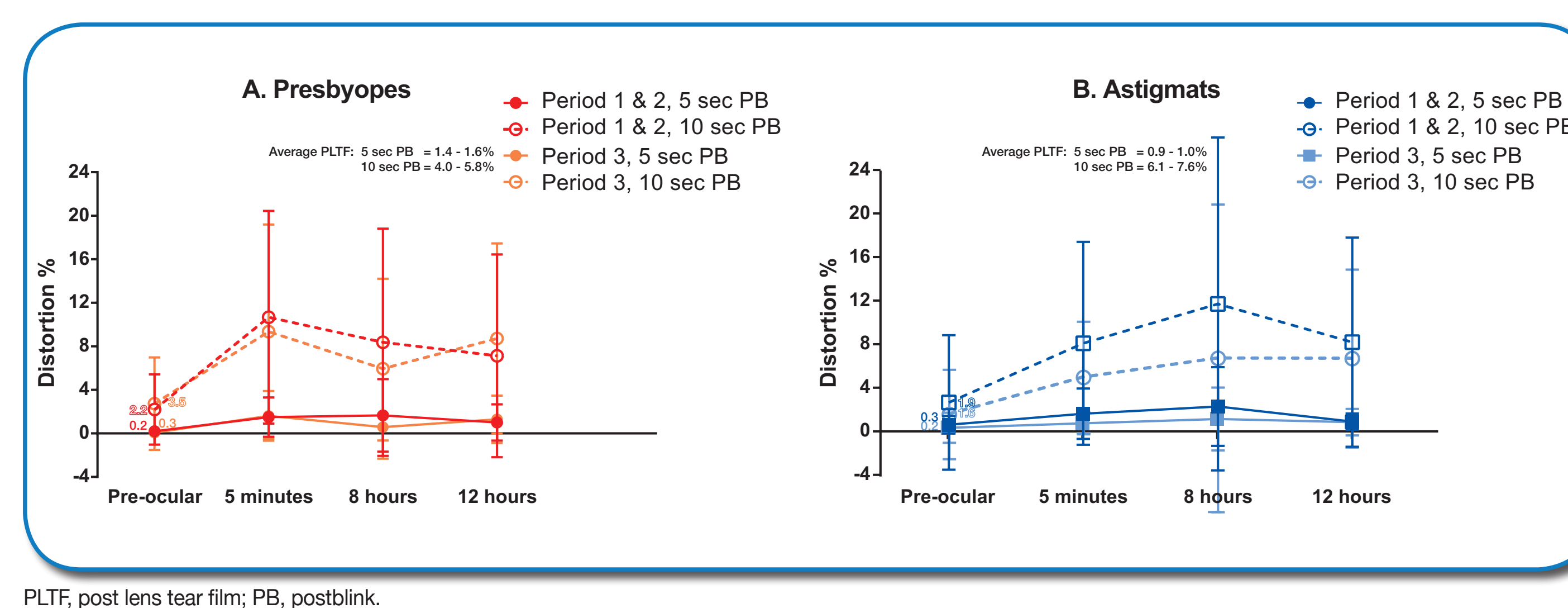


PLTF, post lens tear film

Percent (%) Distortion at 5 and 10 seconds post blink

- Percent (%) distortion at 5 and 10 seconds post-blink for POTF and PLTF measurements are shown in Figure 7A for Presbyopes and in 7B for Astigmats.

Figure 7. Percent (%) distortion at 5 and 10 seconds post blink with nelficon A sphere lenses (mean ± SD)



PLTF, post lens tear film; PB, postblink.

Inter-subject variability

- Among Presbyopes, within each testing condition (POTF, PLTF) the inter-subject variability, expressed as the coefficient of variation (COV), ranged from 47% to 80% for the time to first distortion, from 70% to 111% for AUC % distortion, and 60% to 95% for the maximum % distortion (Table 2).
- Among Astigmats, within each testing condition (POTF, PLTF) COV ranged from 48% to 72% for time to first distortion, from 82% to 185% for AUC % distortion, and from 77% to 170% for the maximum % distortion (Table 2).

Table 2. Inter-subject variability for nelficon A sphere lenses

	Presbyopes				Astigmats			
	Period 1 or 2		Period 3		Period 1 or 2		Period 3	
	Median (Min., Max.)	COV (%)	Median (Min., Max.)	COV (%)	Median (Min., Max.)	COV (%)	Median (Min., Max.)	COV (%)
Time to first distortion (sec)								
Pre-ocular	8.6 (2, 25)	65.8	8.9 (2, 25)	68.7	15.8 (3, 25)	48.1	18.7 (2, 25)	48.4
5 min	5.7 (1, 25)	79.8	6.8 (2, 16)	53.4	9.5 (2, 25)	59.5	7.3 (3, 24)	67.2
8 h	7.2 (2, 24)	61.7	9.2 (3, 18)	47.2	8.3 (2, 25)	72.1	10.8 (2, 25)	63.6
12 h	8.8 (2, 25)	62.7	6.9 (2, 20)	64.3	7.2 (3, 25)	65.6	8.6 (4, 24)	54.8
AUC % distortion								
Pre-ocular	133.2 (0, 392)	88.5	46.9 (0, 430)	111.3	21.3 (0, 705)	176.5	5.0 (0, 732)	185.4
5 min	482.2 (0, 938)	69.6	336.1 (19, 1106)	84.5	172.4 (0, 765)	92.9	274.2 (1, 683)	82.7
8 h	295.9 (1, 957)	82.8	229.2 (8, 1020)	90.9	396.5 (0, 1171)	94.2	177.6 (0, 1297)	120.3
12 h	251.7 (0, 861)	80.6	408.8 (7, 975)	78.1	213.0 (0, 975)	101.2	289.5 (4, 837)	88.1
Maximum % distortion over 25 sec blink								
Pre-ocular	16.7 (0, 32)	79.0	10.4 (0, 28)	95.2	5.5 (0, 51)	132.7	0.5 (0, 60)	170.5
5 min	44.2 (0, 81)	60.4	34.2 (3, 88)	70.5	18.8 (0, 70)	84.2	27.6 (1, 64)	77.1
8 h	34.6 (1, 84)	65.1	30.7 (1, 79)	75.9	32.8 (0, 86)	87.5	25.5 (0, 75)	93.4
12 h	31.3 (0, 70)	69.0	30.9 (1, 73)	67.8	23.4 (0, 85)	84.3	26.0 (1, 65)	80.9

AUC, area-under-the-curve; COV, coefficient of variation

Day-to-day within subject variability

- Day-to-day within-subject variability (mean ± SD for differences between Period 3 and Period 1 and 2 measurements) for time to first distortion, AUC % distortion, and maximum % distortion is shown in Table 3.

Table 3. Mean (±SD) differences for nelficon sphere lenses between Period 3 and Periods 1 & 2 for time to first distortion, AUC % distortion, and maximum % distortion.

	Period 3 – Periods 1 & 2							
	Presbyopes		Astigmats		Presbyopes		Astigmats	
	Time to first distortion, sec	AUC % distortion	Time to first distortion, sec	AUC % distortion	Time to first distortion, sec	AUC % distortion	Time to first distortion, sec	AUC % distortion
Pre-ocular	1.1 ± 11.91	0.9 ± 5.53	Pre-ocular	-30.3 ± 183.78	21.7 ± 183.6	Pre-ocular	-3.3 ± 14.11	0.7 ± 13.62
5 min	-0.3 ± 7.20	-0.7 ± 5.70	5 min	-28.9 ± 362.07	-11.0 ± 181.5	5 min	-3.9 ± 29.18	1.2 ± 15.53
8 h	1.2 ± 5.67	1.0 ± 7.55	8 h	-49.5 ± 279.44	-64.11 ± 351.49	8 h	-4.3 ± 19.02	-4.9 ± 25.48
12 h	-1.1 ± 5.69	-1.0 ± 7.74	12 h	69.6 ± 257.43	14.57 ± 265.5	12 h	3.9 ± 18.24	0.8 ± 20.14

AUC, area-under-the-curve

Conclusions

- In this study, semi-objective (automated analysis with investigator review) measurement of TF characteristics showed significant impact of CL wear on tear film: the time to first distortion was decreased, the AUC for % distortion over time and maximum % distortion were increased during contact lens wear.
 - These results were consistent with subjective break up times found in this study and previously reported data on changes in TF during contact lens wear.
- For both POTF and PLTF, results showed a high variability within both population groups.
- Test – Re test with nelficon A showed a good day-to-day repeatability
- These new endpoints enable improved characterization of TF kinetics during the interblink period in the presence or absence of a contact lens not limited to the time to first distortion/break.

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