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Factors influencing the measurement of oxygen shortfall of the human cornea: Sequencing of test conditions

Jane M. Chi, Barbara A. Fink *, Richard M. Hill, G. Lynn Mitchell

The Ohio State University, College of Optometry, 338 West Tenth Avenue, Columbus, 43210-1240 OH, USA

Abstract

Purpose: The effects of sequencing of test conditions, in this case contact lens thicknesses, on the measurement of the oxygen shortfall of human corneas were studied.
Methods: Corneal oxygen uptake rates were measured with a Clark-type polarographic electrode on the central, unanesthetized right corneas of 14 human subjects. Measurements were made under the following conditions: (1) the normal open eye; (2) after 5 min of static (without blinking) wear of each of seven rigid gas permeable lenses of seven center thicknesses (0.18, 0.12, 0.16, 0.20, 0.24, 0.28, and 0.32 mm); (3) after 5 min of static wear of a polymethylmethacrylate (PMMA) contact lens. Lens thicknesses were randomly assigned numbers, which were sequenced in seven cycles. Two subjects were assigned to each sequencing cycle, and each subject participated in two identical sessions.
Results: The interaction of order *x* thickness was determined to be insignificant ($F = 0.99$; $p = 0.5101$). The effect of lens order was also insignificant ($F = 0.76$; $p = 0.6239$), indicating that the order of lens placement did not affect the measured corneal oxygen shortfall. Not surprisingly, the analysis indicated a significant effect of lens thickness on corneal oxygen shortfall ($F = 3.94$; $p = 0.0032$).
Conclusions: The sequencing of lenses of various thicknesses on the cornea does not affect the measurement of corneal oxygen shortfall.

Keywords: Contact lens thickness; Corneal oxygen uptake; Rigid gas permeable contact lens

1. Introduction

In order to determine the effects of contact lens thickness and transmissibility on the oxygen supply to the cornea, corneal oxygen uptake measurements can be made immediately following the wear of contact lenses for a short period of time [1,2]. Many factors influence the values that are obtained in these measurements. Procedural factors include: the reservoir of oxygen contained in the polarographic electrode [3–8], the membrane material and thickness [3,9–13], the oxygen tension of the surrounding corneal environment [14], the duration of exposure to reduced oxygen tension [4,15–18], the time between exposure and measurement [3,4,10,19], and use of topical anesthetic [20–22]. Subject factors that influence the measured values of corneal oxygen uptake include, but are not limited to, the following: the influence of contact lens wear on the fellow eye [23], the temperature surrounding the cornea [24–26], lid position [27–29], corneal location [30–35], corneal thickness [3,34–38], and corneal health [39–41].

Contact lens wear results in increased corneal oxygen uptake, particularly if the contact lens has low oxygen transmissibility or if tear exchange is not taking place [42]. The wear of polymethylmethacrylate (PMMA) contact lenses results in an increase in oxygen uptake to about 5–6× that of the normal open eye within about 120 s [4,16]. Corneal oxygen uptake increases less dramatically following the wear of oxygen permeable materials, and at higher contact lens transmissibilities the reduction in corneal oxygen uptake with increasing transmissibility diminishes [1,2]. Several studies have investigated the effects of contact lens materials, designs, hydration, and movement on corneal oxygen uptake [1,2,17,20,31,35,43–59].

Four methods are typically used to record and present the cornea's rapid response to the oxygen levels in its environment: (1) absolute units of mmHg/s, (2) as a ratio

* Corresponding author. Tel.: +1 614 292 0084; fax: +1 614 292 7493.
E-mail address: fink.4@osu.edu (B.A. Fink).

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of corneal response to a test environment and response to air, (3) as a percentage of the cornea's response to hypoxia, such as can occur by exposure to a goggle with 100% nitrogen or by the wear of polymethylmethacrylate contact lenses for 5 min, and (4) as a proportion of the total hypoxic range (air to PMMA) within the scale of 0–100 oxygen shortfall units (osu) [60].

One method of determining the response of the cornea to contact lens transmissibility is to measure corneal oxygen uptake rates immediately following 300 s of lens wear [42–52]. Lenses of the same permeability but different center thicknesses can be used to determine the response of the cornea to that lens material across several transmissibilities [1]. The purpose of the study to be presented here was to determine the effects of sequencing of contact lens thicknesses on the measurement of the oxygen uptake rate of human corneas.

2. Methods

2.1. Subjects

Measurements were made on the right corneas of 14 human subjects, 8 males and 6 females, aged 24–58 years (mean 30 years). None of the subjects were contact lens wearers and all had good ocular health. Flattest keratometry values ranged from 41.25 to 44.37 D (mean 43.25 D), and corneas had 0.12–1.87 D of corneal toricity (mean 1.08 D). All subjects participated in at least three instructional and practice sessions and signed an informed consent form, reviewed and approved by the Institutional Review Board, the Biomedical Sciences Human Subjects Review Committee of The Ohio State University.

2.2. Contact lenses

The contact lens materials that were used were polymethylmethacrylate and Siflufocon A, a fluorosilicone acrylate rigid gas permeable material with a Dk of 33×10^{-11} cm^2/s (ml O_2)/(ml mmHg), a modulus of 1730 MPa, a specific gravity of 1.25, and a silicone content of 7–8%. Both lens materials were manufactured to have overall diameters of 8.8 mm, optic zone diameters of 7.4 mm, axial edge lifts of 0.09 mm, and back vertex powers of −3.00 D. They were fitted "on K" (to match the radius of the flattest keratometer reading for each cornea). They were manufactured in seven center thickness: 0.08, 0.12, 0.16, 0.20, 0.24, 0.28, and 0.32 mm. All lenses were verified to assure that all parameters were within ANSI standards and center thicknesses were within 0.01 mm of the ordered values.

2.3. Procedure

Oxygen uptake rates were measured on the central, non-anesthetized corneas of the right eyes of the 14 subjects. The equipment included a Clark-type polarographic electrode with a 25 μm platinum cathode, fitted with a 12 μm thick polyethylene membrane. Calibration was performed by alternately placing the electrode in saline baths saturated by air (155 mmHg O_2) and nitrogen (0 mmHg O_2), while maintained at 36 °C.

Each subject participated in two measurement sessions. Oxygen uptake rates were measured for: (1) the normal open eye, (2) after 5 min of static (without blinking) wear of each of the seven rigid gas permeable lenses of the seven center thicknesses, and (3) after 5 min of static wear of the PMMA contact lens. Contact lenses were worn statically only, with no blinking permitted, so that corneal oxygenation was provided only through contact lens transmissibility and not through tear exchange with blinking. Subjects held their right upper lids, fixated a target with their eyes in the straight ahead position, and blotted any tears that accumulated in the outer and inner canthi during the 5 min of lens wear. This prevented lens movement due to excessive tearing or eye movement. The first measurement of each session was that of the normal open eye. The second measurement of each session was after 5 min of wear of the PMMA contact lenses. Five minutes with no contact lens wear and normal blinking ensued between lens applications.

The sequencing of the lens thicknesses for each subject was as follows. The lenses were randomly assigned a letter label (e.g., A, B, C, D, E, F, G). The lens code for each of the seven lens thicknesses can be seen in Table 1. Seven cycles

Table 1
Lens code for each of the seven lens thicknesses

Lens code	Lens thickness
A	0.24
B	0.20
C	0.12
D	0.28
E	0.16
F	0.32
G	0.08

Table 2
Lens sequence assignment for each of the 14 subjects

Subject number	Sequence number	Lens sequence
1	1	0.24, 0.20, 0.12, 0.28,0.16, 0.32, 0.08
2	1	0.24, 0.20, 0.12,0.28, 0.16, 0.32, 0.08
3	2	0.20, 0.12, 0.28, 0.16, 0.32, 0.08, 0.24
4	2	0.20, 0.12, 0.28, 0.16, 0.32, 0.08, 0.24
5	3	0.12, 0.28, 0.16, 0.32, 0.08, 0.24, 0.20
6	3	0.12, 0.28, 0.16, 0.32, 0.08, 0.24, 0.20
7	4	0.28, 0.16, 0.32, 0.08, 0.24, 0.20, 0.12
8	4	0.28, 0.16, 0.32, 0.08, 0.24, 0.20, 0.12
9	5	0.16, 0.32, 0.08, 0.24, 0.20, 0.12, 0.28
10	5	0.16, 0.32, 0.08, 0.24, 0.20, 0.12, 0.28
11	6	0.32, 0.08, 0.24, 0.20, 0.12, 0.28, 0.16
12	6	0.32, 0.08, 0.24, 0.20, 0.12, 0.28, 0.16
13	7	0.08, 0.24, 0.20, 0.12, 0.28, 0.16, 0.32
14	7	0.08, 0.24, 0.20, 0.12, 0.28, 0.16, 0.32

lens sequences were determined (e.g., A, B, C, D, E, F, G; B C, D, E, F, G, A; C, D, E, F, G, A, B; D, E, F, G, A, B, C; E, F, G, A, B, C, D; F, B, A, B, C, D, E, F; G, A, B, C, D, E, F). Two subjects were assigned to each sequence. Table 2 shows the lens sequence assignments for each of the 14 subjects. Each subject participated in two identical sessions (with identical lens sequences), and data from the two sessions were averaged. Subjects were randomly assigned to the sequencing. The examiner was masked to the lens thicknesses and sequencing.

A relative scale of 0–100 oxygen shortfall units can be used to rate human corneal responses to lens transmissibility. In this scale, 0 osu represents the oxygen uptake rate of the normal open eye and 100 osu represents the oxygen uptake rate associated with severe hypoxic stress (i.e., after an impermeable, un-pumped polymethylmethacrylate contact lens has been worn until maximum corneal oxygen uptake rates are reached).

$$\text{osu} = \frac{\text{TL} - \text{air}}{\text{PMMA} - \text{air}} \times 100$$

where TL, oxygen uptake rate associated with the test lens; air, oxygen uptake rate associated with the normal, open eye; PMMA, oxygen uptake rate associated with PMMA reference lens.

Past studies in this laboratory have shown that corneal oxygen uptake rates for the normal open eye are about 5 mmHg/s, while those following 5 min of PMMA wear are about 30 mmHg/s, with considerable inter-individual variation [42–52].

3. Statistical analyses

Repeated measures analysis of variance was used to look at the effects on corneal oxygen shortfall of lens thickness, lens order, and the interaction between lens thickness and lens order. For each subject, the average of his or her two sessions (replications) is used to quantify the response at a given lens thickness.

4. Results

Table 3 shows the oxygen response of the cornea, in osu, to seven sequences of seven lens thicknesses. Each value is a mean of two measurements on each of 14 subjects. Fig. 1 displays the mean corneal oxygen shortfall for the 14 subjects. The oxygen shortfall for each lens thickness sequence is displayed at each lens thickness.

The interaction of order *x* thickness was determine to be insignificant, using repeated measures ANOVA ($F = 0.99$; $p = 0.51$). The main effect of order was judged to be insignificant ($F = 0.76$; $p = 0.63$), indicating that the order of lens placement did not affect the osu value. The analysis indicated a significant effect of lens thickness on osu ($F = 3.94$; $p = 0.003$). Post hoc testing with an adjustment for multiple comparisons (Tukey's test, $\alpha = 0.05$) found that osu values obtained with the 0.12, 0.20, and 0.28 mm lenses were significantly higher than those obtained with the 0.08 mm thickness lens.

Two aberrant cell means stood out in an interaction plot used to test the interaction of order *x* thickness, allowing unstructured covariance matrix. In this plot, seven lines of cells means (mean osu for the two subjects at each order-thickness combination) were plotted against the thickness. The lines should be roughly parallel if there is no interaction. Both aberrant cell means involved unusually high oxygen shortfall associated with the 0.12 mm thickness lens. This was caused by the data from two subjects, one with lens sequence 1 and the other with lens sequence 3. Both subjects had relatively low oxygen uptake rates associated with the

Table 3
Mean (S.D.) oxygen response of the cornea, in osu, to seven sequences of seven lens thicknesses

Thickness (mm)	Lens sequence							Overall
	1	2	3	4	5	6	7	
0.08	14.45 (2.95), $n = 2$	10.62 (5.09), $n = 2$	5.05 (3.50), $n = 2$	10.40 (5.56), $n = 2$	12.33 (4.82), $n = 2$	15.41 (2.64), $n = 2$	23.82 (4.31), $n = 2$	13.15 (6.37), $n = 14$
0.12	62.09 (41.81), $n = 2$	22.12 (1.96), $n = 2$	65.85 (60.27), $n = 2$	13.14 (4.61), $n = 2$	36.80 (18.15), $n = 2$	19.69 (1.11), $n = 2$	21.78 (7.42), $n = 2$	34.50 (29.44), $n = 14$
0.16	27.81 (2.77), $n = 2$	26.62 (9.73), $n = 2$	20.56 (6.41), $n = 2$	34.68 (4.77), $n = 2$	27.32 (13.06), $n = 2$	21.46 (3.39), $n = 2$	24.39 (13.98), $n = 2$	26.12 (7.90), $n = 14$
0.20	36.96 (6.31), $n = 2$	42.37 (18.64), $n = 2$	21.88 (13.14), $n = 2$	21.64 (0.98), $n = 2$	26.40 (7.74), $n = 2$	27.86 (5.07), $n = 2$	41.84 (6.40), $n = 2$	31.28 (11.28), $n = 14$
0.24	36.78 (10.25), $n = 2$	17.06 (4.70), $n = 2$	21.62 (8.03), $n = 2$	25.40 (7.29), $n = 2$	33.22 (16.62), $n = 2$	30.87 (2.14), $n = 2$	40.03 (18.42), $n = 2$	29.28 (11.41), $n = 14$
0.28	42.59 (16.93), $n = 2$	42.28 (6.58), $n = 2$	35.32 (1.30), $n = 2$	46.69 (30.45), $n = 2$	28.46 (11.01), $n = 2$	26.29 (1.19), $n = 2$	36.36 (5.37), $n = 2$	36.85 (12.70), $n = 14$
0.32	33.53 (6.21), $n = 2$	25.53 (10.90), $n = 2$	24.53 (6.42), $n = 2$	27.87 (8.86), $n = 2$	33.06 (15.88), $n = 2$	31.80 (5.38), $n = 2$	28.07 (29.07), $n = 2$	29.20 (10.96), $n = 14$
Overall	36.32 (19.13), $n = 14$	26.66 (13.53), $n = 14$	27.83 (25.24), $n = 14$	25.69 (15.20), $n = 14$	28.23 (12.37), $n = 14$	24.77 (6.36), $n = 14$	30.90 (13.46), $n = 14$	28.63 (15.92), $n = 98$

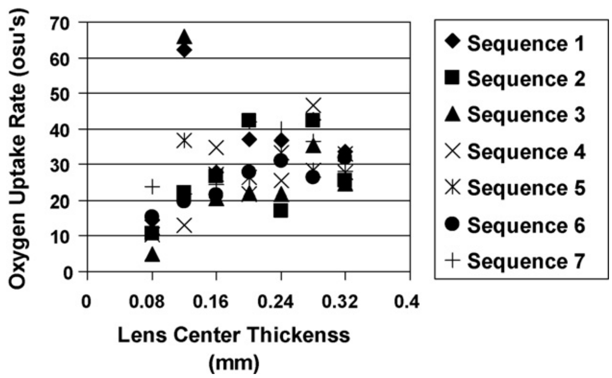

Fig. 1. Mean oxygen shortfall of the human cornea associated with seven thicknesses (0.08–0.32 mm in 0.04 mm steps) of a single rigid gas permeable contact lens material, measured for seven thickness sequences.

wear of the PMMA contact lens in conjunction with relatively high oxygen uptake rates associated with the 0.12 mm lens. The low oxygen uptake rates following PMMA lens wear was most likely due to a delay in polarographic electrode placement following lens removal. Tearing, lens movement, or lens decentration during the 5 min wearing period could also result in reduced measured rates. On the other hand, rapid probe placement following the wear of the 0.12 mm thick lens, or too much pressure between the polarographic electrode and the cornea, could have resulted in unrepresentatively high oxygen uptake rates associated with the 0.12 mm lens.

5. Discussion

In this paper, we looked at the effects of rigid gas permeable contact lens thickness sequencing on corneal oxygen uptake. Data were relativized as a proportion of the cornea's total hypoxic range and expressed in osu. It was determined that the sequencing of lenses of various thicknesses does not affect the measurement of corneal oxygen shortfall. That means that thick lenses are no more likely to affect subsequent measures of corneal oxygen uptake than are thin lenses. This result was expected because a 5-min period of recovery was provided between each period of contact lens wear. Prior studies have shown that, following the wear of PMMA contact lenses, recovery of normal oxygen uptake rates occurs within 60 s of re-exposure to the normal air environment [4,16,61,62]. The lenses used in this study were gas permeable contact lenses, which were associated with corneal oxygen uptake rates that were lower (less changed from baseline) than those associated with the wear of PMMA contact lenses. Past studies have shown that referencing data obtained under test lens conditions to that obtained for the normal open eye reduces differences due to instrument or corneal instabilities [63]. In future studies of the effects of contact lens transmissibility on corneal oxygen uptake, contact lens thicknesses can be used in random order.

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