A Quasi-2-Dimensional Model for Respiration of the Cornea With Soft Contact Lens Wear

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Purpose: Because neither the human cornea nor a soft contact lens (SCL) is of constant thickness, corneal oxygenation varies locally. To quantify the importance of cornea/SCL thickness variations on oxygen demand, we develop a quasi-2-dimensional (2D) respiration model that accounts for aerobic and anaerobic metabolism and bicarbonate buffering.

Methods: Because metabolism is critical to oxygen demand, we extend the 1-dimensional (1D), 6-layer oxygen metabolic model of Chhabra et al. Lateral diffusion is shown to be negligible. Accordingly, we adopt the 1D reactive-diffusion metabolic model but apply it locally along the cornea/lens extent. This "quasi-2D" approximation permits 2D assessment of oxygen consumption, including the effects of carbon dioxide, glucose, and lactate, bicarbonate, and hydrogen ions. We use both an oxygen deficiency factor and an excess lactate factor to gauge corneal health after accounting for both cornea and contact lens thickness variations.

Results: The quasi-2D respiration model provides quantitative spatial resolution of corneal oxygenation with minimal expenditure of computation time. When only aerobic oxygen loss is included, our quasi-2D approach is in excellent agreement with the fully 2D results of Alvord et al. However, the quasi-2D model predicts 2D concentration profiles of glucose, lactate ions, bicarbonate ions, hydrogen ions, and carbon dioxide, as well as oxygen. Neglect of metabolic reactions and/or thickness variations leads to inaccurate prediction of oxygen demand, especially near the lens periphery.

Conclusions: The quasi-2D respiration model indicates that lateral thickness variations and respiration kinetics are critical for assessing on-eye physiologic performance of an SCL. We find that oxygen deficiency factor and excess lactate factor are useful indices to gauge corneal hypoxia. A user-friendly computer program of the quasi-2D respiration model is available for lens design.

Key Words: two-dimensional model, reactive-diffusion transport, corneal oxygen demand, soft contact lens, metabolism

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nsufficient corneal oxygenation during soft contact lens (SCL) wear is reported to cause physiological complications to the cornea, including hypoesthesia, acidosis, edema, epithelial microcysts, stromal and epithelial thinning, loss of hemidesmosomes and glycosaminoglycans, and increased endothelial polymegathism.¹⁻³ Over the past 4 decades, design requirements of SCLs and the critical corneal oxygen supply to avoid physiological complications have been analyzed extensively.^{4–43} Briefly, Fatt and others created various steady, multilayer, and 1-dimensional (1D) models of reactive oxygen and carbon dioxide diffusion through the cornea.⁸⁻¹² A 1D model assumes a flat cornea/SCL system of constant thickness (ie, rectangular slabs). Harvitt and Bonanno¹³ maintained the 1D framework but advanced the transport model by introducing 5 layers in the system: endothelium (En), stroma (St), epithelium (Ep), postlens tear film (PoLTF), and SCL. Unfortunately, the oxygen consumption kinetics adopted by Harvitt and Bonanno¹³ led to aphysical negative oxygen concentrations. Brennan⁶ constructed a 1D analytic transport model that avoided unrealistic negative oxygen tensions in the stroma and epithelium. Recently, Chhabra et al⁷ extended previous 1D models by incorporating the coupled metabolic effects of glucose, lactate ion, bicarbonate ion, hydrogen ion, carbon dioxide, and oxygen in the cornea/SCL system. These authors were the first to include the metabolic shift from aerobic to anaerobic glycolysis into Monod-based oxygen consumption rates and to predict the diffusion-reactive transport of lactate ions, hydrogen ions, bicarbonate ions, and glucose in the cornea.⁷ Although the mathematical description is more involved, metabolism was shown to be a critical component of corneal oxygenation previously overlooked.

One-dimensional oxygen transport models are typically used to ease the calculation burden. Unfortunately, the peripheral cornea is approximately 40% thicker than is its center. Hence, thickness variations in the cornea are important.^{4,35} Likewise, SCL thickness depends on lens power and is not constant. Fatt et al⁴⁴ accounted for thickness variations in a soft contact lens by using concentric cylindrical rings of differing heights, in effect creating a quasi-2D description. No consideration was given to thickness variation in the cornea, although its importance was later recognized.³⁵ Recently, Alvord et al⁴ presented a fully 2D finite element model of corneal oxygen transport with contact lens wear. Their results demonstrated the importance of lateral thickness variations. Specifically, 1D models underestimate oxygen demand across the entire cornea but especially near the periphery where the cornea is thick.⁴

No oxygenation model to date considers the coupled roles of metabolic reaction products and lateral thickness

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variations of the cornea and contact lens. A full 2D calculation is computationally intensive. Because the cornea and the contact lens are thin compared with the lateral dimension, however, we find that lateral diffusion is negligible. Hence, similar to Fatt et al,⁴⁴ we represent the cornea/ contact lens system as a series of axisymmetric differential shells. Each shell is treated in 1D. Thus, by solving a series of 1D problems for shells of differing thickness, 2D effects are correctly captured with minimal computation effort. This approach is coined quasi-2D or pseudo-2D modeling and is used extensively.^{45–54} In the field of fluid mechanics, a quasi-2D model is often coined the lubrication approximation.55 Our quasi-2D respiration model efficiently incorporates arbitrary corneal geometries and arbitrary contact lens shape, size, and power. Special cases, such as imperfect eyelid closure during sleep (ie, lagophthalmos $^{56-59}$), are readily treated. Because only 1D analysis is required, the quasi-2D model readily amalgamates the analytic model of Brennan⁶ and the nonlinear Monod kinetics of aerobic and anaerobic glycolysis, and the pH buffering of Chhabra et al.⁷ To assess the extent and severity of corneal hypoxia quantitatively, we calculate both an oxygen deficiency factor (ODF) of Chhabra et al⁷ and the excess lactate factor (ELF).

MATERIALS AND METHODS

Model Basis

Consider the half space of an axisymmetric cornea covered with a soft contact lens, as shown in Figure 1. The cornea consists of 3 layers, endothelium (En), stroma (St), and epithelium (Ep), and is bounded by the anterior chamber (AC) and the covering contact lens, itself composed of the



FIGURE 1. Six-layer cornea/SCL geometry with a -3.00-D lens (Acuvue Advance). Starting from the lower left to upper right are the endothelium (En), stroma (St), epithelium (Ep), PoLTF, SCL, and PrLTF. The endothelium and the 2 tear films are not apparent because of the scale of the drawing. For illustration, ten 1D ring elements are shown. The particular cross-hatched ring is shown in perspective in Figure 2.

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PoLTF, SCL, and prelens tear film (PrLTF). Because fluid convection through the cornea/SCL is negligible,^{60–62} reactive diffusion governs transport in the cornea. In spherical coordinates, steady conservation of species demands that

$$D_i \left[\frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial C_i}{\partial r} \right) + \frac{1}{r^2 \sin \theta} \frac{\partial}{\partial \theta} \left(\sin \theta \frac{\partial C_i}{\partial \theta} \right) \right] - Q_i = 0, \quad (1)$$

where r is the radial coordinate, θ is the polar angle, C_i is the molar concentration of species *i* expressed per unit volume of hydrated tissue, D_i is the effective diffusivity of species i in the pertinent layer of the cornea/lens, and Q_i is the consumption rate of species *i* per unit hydrated tissue volume for each corneal layer.⁷ Equation 1 holds separately in each cornea/ SCL layer. The first term in the bracket of Equation 1 accounts for diffusion normal to the surface of the cornea/ SCL (r direction), whereas the second term in the bracket describes lateral diffusion parallel to the cornea/SCL (θ direction). Full solution of Equation 1 is challenging because of the highly coupled and nonlinear enzymatic reaction kinetics for the relevant set of metabolic species in the various corneal layers.⁷ Notice in Figure 1, however, that the thicknesses of the cornea and SCL are much less than their corresponding lateral dimensions. Let S denote the arc length from the lens/ cornea center to the periphery, and let δ be a nominal cornea thickness. Typically, S = 7.5 mm and $\delta = 0.5$ mm. The magnitude of the second term in the bracket of Equation 1 relative to the first term scales as $(\delta/S)^2 = 4 \times 10^{-3}$. This means that more than 99% of diffusion flux occurs normal to the cornea/ lens surfaces with essentially no lateral diffusion. For a typical SCL where $\delta = 0.1$ mm, an even larger portion of diffusive flux occurs only in the radial direction. Consequently, lateral diffusion may be neglected in Equation 1 independent of the particular diffusing species.

By constructing a 2D finite difference model of oxygen diffusion through a hydrogel lens, Fatt et al⁴⁴ confirmed that lateral diffusion is insignificant. Likewise, Lin⁶³ incorporated lateral diffusion of oxygen in a finite difference model of the cornea and SCL and found no spreading of oxygen from thin to thick portions. Even more convincing evidence comes from the recent 2D finite element model of Alvord et al.⁴ After rigorously accounting for lateral transport, radial diffusion was established as the only significant source of oxygen to the central cornea.⁴ Holden et al⁶⁴ experimentally investigated cornea swelling response to a low-oxygen-transmissible contact lens containing a large central aperture (ie, a "donut" lens). If the species responsible for swelling, such as lactate ion and oxygen, diffused laterally, an average small swelling should have been observed. However, these researchers found no swelling in the central exposed area of the cornea but found significant local swelling in those regions covered by the lens.⁶⁴

We conclude that θ -direction diffusion in Equation 1 is negligible, giving:

$$D_i \left[\frac{1}{r^2} \frac{\partial}{\partial r} \left(r^2 \frac{\partial C_i}{\partial r} \right) \right] - Q_i = 0.$$
 (2)

Unfortunately, direct application of Equation 2 does not account for thickness variations. As illustrated by the dashed

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lines in Figure 1, we therefore subdivide the axisymmetric cornea/SCL system into a series of concentric truncated spherical-sector rings, each of which obeys Equation 2 locally. Although Figure 1 illustrates 10 differential rings, enough rings are pieced together to resolve continuous 2D species concentration profiles in the radial and lateral directions, typically around 40. Figure 2 sketches one local ring element, constructed by revolving the cross-hashed region in Figure 1 about the vertical (axisymmetric) axis. The above scaling argument suggests further that local flat cylindrical rings also provide a reasonable approximation for thickness variations. As discussed in Appendix A (see Document, Supplemental Digital Content 1, http://links.lww.com/ICO/A34), however, the front surface of the cornea has approximately 20% more tissue volume than does the back surface, indicating higher metabolism near the anterior surface. We retain the radial-spherical coordinate to describe diffusion normal to the cornea/SCL.

Accordingly, radial dashed lines in Figure 1 converge or "focus" from the anterior corneal surface to the posterior surface. Diffusion funnels into a smaller area. Density of flux lines increases from the anterior to the posterior surface by approximately 20%. We account rigorously for both funneling and cornea cell density by adopting the spherical geometry in Equation 2. There is no loss in computational efficiency compared with rectangular coordinates.

Following Chhabra et al,⁷ we write Equation 2 for oxygen, carbon dioxide, glucose, and lactate, hydrogen, and bicarbonate ions. Both aerobic and anaerobic respiration kinetics are considered along with bicarbonate buffering and acidosis. All Monod reaction kinetics, physical parameters, and boundary conditions are identical to those of Chhabra et al.⁷ We, thus, adopt the 1D metabolic model of Chhabra et al⁷ extended to spherical–radial coordinates. A series of 1D-coupled ordinary differential equations is solved for different axisymmetric ring elements representing differing cornea and contact lens thicknesses. Serial collection of the local 1D profiles then produces a 2D contour plot. In this way, we create 2D profiles from more simple 1D calculations.



FIGURE 2. One illustrative concentric truncated sphericalsector ring corresponding to the local cross-hatched subdivision in Figure 1 of the axisymmetric cornea/SCL system. The direction of anterior oxygen flux is illustrated. Individual rings are pieced together to resolve continuous 2D species concentration profiles in the radial and lateral directions.

Construction of Quasi-2D Contours

We report results in terms of species concentration as a function of vertical distance $(y = r\cos\theta)$ and projected lateral distance $(x = r\sin\theta)$. Species concentrations at each x, y are tabulated in matrix form from the local 1D simulations. Isoconcentration contours are then created in MATLAB (The MathWorks, Inc, Natick, MA⁶⁵). Appendix B explains the method in more detail (see **Document, Supplemental Digital Content 1**, http://links.lww.com/ICO/A34).

The specific 2D cornea/contact lens system considered is shown in Figure 1. Our cornea/contact lens system is similar in geometry to that of Alvord et al⁴ but was created by representing the interfaces of the 6 layers (En, St, Ep, PoLTF, SCL, and PrLTF) as equation-based fits to thickness data. We assume that the endothelium (1.5 μ m), epithelium (50 μ m), PoLTF (3 μ m), and PrLTF (3 μ m) thicknesses are constant. The stromal thickness, however, increases uniformly from the center toward its periphery. Lateral thickness variations of the stroma and contact lens [-3.00-diopter (D) Acuvue Advance;]Johnson & Johnson Vision Care, Jacksonville, FL] are from Alvord et al.⁴ Specifically, the lens center is 80 μ m thick; its thickness initially increases from the lens center outward toward the limbus. After the lens reaches a maximum thickness at a projected lateral distance of 6.18 mm from the center, it thins toward the periphery. Harmonic mean thickness is 120 μ m, calculated following Pearson⁶⁶ and Sammons.⁶⁷ Appendix C gives more geometric detail (see Document, Supplemental Digital Content 1, http://links.lww.com/ICO/A34). Unless otherwise stated, all calculations correspond to the shape of -3.00-D Acuvue Advance lens.

Thickness variations of the other layers, namely, the endothelium, epithelium, PoLTF, and PrLTF, if present, can easily be incorporated into the model with negligible increase in computation time. Likewise, any contact lens shape, size, power, and material can readily be considered, as can any corneal shape. In Appendix C (see **Document, Supplemental Digital Content 1**, http://links.lww.com/ICO/A34), we demonstrate fitting of a positive-power contact lens (+3.00-D Acuvue Advance).

Comparison With 2D Model

Because the fully 2D simulations of Alvord et al⁴ are available, we compare our quasi-2D methodology with their results. Since Alvord et al⁴ treated only reactive diffusion of oxygen, we removed all other metabolic species from the quasi-2D benchmark calculation. We further adopted the specific Monod kinetic expression of Alvord et al⁴ for oxygen consumption and used all of their physical parameters and boundary conditions. The quasi-2D approach permits no lateral transport and, therefore, cannot reflect diffusion of oxygen from the limbal blood vessels into the cornea at the periphery. Accordingly, we calculate a worst case scenario where oxygen deprivation is highest at the cornea/sclera periphery because the cornea is the thickest at that location.

A 2D contour map of the relative error between the 2D and quasi-2D models is presented in Figure 3 for open-eye SCL wear with Dk = 100 Barrer and harmonic mean thickness, $L_{\rm H} = 120 \ \mu$ m. Color contours display regions of

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FIGURE 3. Contour plot of oxygen tension relative error for the quasi-2D oxygen-only model compared with the 2D oxygen-only model of Alvord et al⁴ with a -3.00-D Acuvue Advance SCL with Dk = 100 Barrer and $L_{\rm H} = 120$ µm. Dark blue indicates small deviation between the 2 models, whereas dark red indicates larger relative errors.

constant relative error throughout the cornea. Color versions of all countour figures are available in the appendix D (see Document, Supplemental Digital Content 1, http://links.lww.com/ICO/A34). Dark red regions indicate high relative error, whereas dark blue regions indicate little or no error. We find a low relative error in Figure 3 throughout the cornea (less than 1%) except near the limbus, where a small dark red spot indicates approximately 15% error. The largest error in the quasi-2D approach is expected in this location because oxygen lateral diffusion from the limbus is not accounted for. Although the percentage error is noticeable here, absolute deviation of the calculated oxygen tension is small. At the periphery, where oxygen tension is low in the 2D model $(\sim 4 \text{ mm Hg})$, the quasi-2D model predicts an oxygen tension of 3.35 mm Hg, a small absolute difference of 0.65 mm Hg. Computation time for the finite element model of Alvord et al⁴ was 20 seconds for one particular contact lens using 19,319 elements and 39,900 degrees of freedom. The quasi-2D model requires approximately 6 seconds to solve for 660 elements in each of twenty-six 1D simulations. Incorporation of metabolic species in a fully 2D finite element model most assuredly requires considerably more computation effort with minimal gain in precision compared with the quasi-2D approach.

Metabolism and Buffering

By comparing our metabolic model with a model that considers only oxygen consumption, we assess the importance of aerobic and anaerobic glycolysis, acidosis, and bicarbonate ion buffering. Closed-eye oxygen profiles are shown in Figure 4 at the central cornea from the metabolic model (solid line) and from the "oxygen-only" model (dashed line), each for an SCL with Dk = 75 Barrer and harmonic mean thickness, $L_{\rm H} = 120 \ \mu m$, giving an average lens oxygen transmissibility of $Dk/L_{\rm H} = 62.5$ hBarrer/cm. All else being





FIGURE 4. Closed-eye, central oxygen 1D profile (solid line) from the respiration metabolic model with an SCL of Dk = 75 Barrer ($Dk/L_{\rm H} = 62.5$ hBarrer/cm). The dashed line is for the same lens and location but from the oxygen-only model, neglecting glucose metabolism, acidosis, and bicarbonate-ion buffering.

equal, neglect of glucose metabolism, acidosis, and buffering results in a significant overestimate of corneal oxygenation. This result supports the conclusion that metabolism plays a critical role.⁷ Accordingly, both metabolism and lateral thickness variation are necessary to provide a quantitative assessment of corneal oxygen needs.

RESULTS

Quasi-2D Contours

Oxygen tension contours are shown in Figures 5A and B for open and closed eye, respectively, without SCL wear (calculated by setting $Dk = 10^4$ Barrer). Forty-two local 1D simulations were used with 660 elements in each requiring a total of 30 seconds to construct the 2D profiles for all 6 metabolites. Dark red regions indicate high oxygen tension, whereas dark blue regions indicate low oxygen tension. Tension color scales differ for each figure. Even without SCL wear, Figure 5B reveals that during sleep there is a central stromal swath with tensions less than 5 mm Hg that broadens toward the periphery.

Corresponding open- and closed-eye oxygen tension contours are shown in Figure 6 for a -3.00-D SCL with Dk =30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm). The contour plots reveal that an SCL of this oxygen permeability induces a significant barrier toward corneal oxygenation. In particular, we find larger central dark-blue regions compared with Figure 5 extending inward from corneal periphery (~6-mm lateral distance) during contact lens wear. By comparing Figures 6A and B, the closed eye exhibits considerably less oxygen availability throughout the cornea. For the closed eye in Figure 6B, oxygen tensions decline sharply from the anterior surface of the SCL into the cornea. A decline in oxygen tension is also seen in Figure 6B from the AC/En interface. During eye closure, oxygen transports into the cornea from both the

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A, Open eye. B, Closed eye.

AC and the palpebral conjunctiva. Figure 6B further reveals that precorneal oxygen tensions vary along the lateral dimension (23 vs. 7 mm Hg at center and periphery, respectively). This verifies the assertion that contact lens thickness variations must be included when gauging corneal oxygenation.^{23,30,35} As pointed out by Alvord et al,⁴ 1D models that focus on the center of the cornea underestimate oxygen demand. In particular, the dark blue pocket at the peripheral cornea in Figure 6 suffers the highest oxygen deprivation for both open and closed eye. One-dimensional models assess corneal oxygenation without considering regions of highest oxygen demand.

Two-dimensional glucose contours are shown in Figures 7A and B (open eye and closed eye, respectively) again for a -3.00-D SCL with Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm). Color scales here reflect concentrations in millimolar; they are not the same in each figure. Chhabra et al⁷ argued that glucose, lactate-ion, bicarbonate-ion, and hydrogen-ion concentrations are negligible in the PoLTF, SCL, and PrLTF. Therefore, our 2D contours omit these 3 layers for these particular species. Chhabra et al⁷ also concluded that



FIGURE 6. Oxygen tension contours with a -3.00-D SCL of Dk = 30 Barrer ($Dk/L_{H} = 25$ hBarrer/cm). A, Open eye. B, Closed eye. Dark blue indicates low oxygen tension. The black line at the Ep/PoLTF interface demarks the anterior corneal surface.

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3

Projected lateral distance (mm)

only the AC supplies glucose to the cornea. Our 2D profiles reflect this result by the dark red-to-blue color transition from the AC/En interface into the cornea. We find the lowest concentration of glucose toward the periphery where the cornea is thicker. Because the peripheral cornea is not well oxygenated (Fig. 6), cells here must breakdown glucose anaerobically. However, anaerobic glycolysis produces 2 ATP molecules per glucose molecule consumed compared with the 36 ATP molecules provided through aerobic metabolism.⁷ To meet cell energy requirements, the less-oxygenated corneal periphery consumes more glucose than is consumed at the central cornea. The periphery, thus, has a lower glucose concentration. For the same reason, Figures 7A and B reveal that the closed eye has less glucose available throughout. Because the closed eye is less oxygenated with higher rates of anaerobic glycolysis, more glucose is consumed.

Open- and closed-eye lactate-ion contours are shown in Figures 8A and B, respectively, for a -3.00-D SCL with

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FIGURE 7. Glucose concentration contours with a -3.00-D SCL of Dk = 30 Barrer ($Dk/L_H = 25$ hBarrer/cm). A, Open eye. B, Closed eye. Dark blue reflects low concentration.

Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm). These contours are almost the exact opposite of those in Figure 7: high levels of lactate are now seen at the anterior peripheral surface of the cornea compared with low levels of glucose. Increased anaerobic glycolysis occurs in this region because the cornea is thick and, thus, less oxygenated (Fig. 6). As anticipated, lactate-ion concentrations are everywhere higher in the closed eye relative to those in the open eye.

There is apparent discrepancy between the lactate-ion profiles in Figure 8 with experimental data on corneal swelling. Because lactate ions are reputed to be a primary cause of corneal edema,⁶⁸ Figure 8 suggests that the peripheral cornea exhibits the highest swelling. Yet, experimental data show that the central cornea swells more than does the peripheral.^{24,69–74} A proposed explanation is that lateral transport of lactate (and/or oxygen) spreads edema from the periphery toward the center.^{24,35,69,75} This reasoning belies the quasi-2D model in which lateral transport is neglected. The studies of Holden et al⁶⁴ on corneal swelling using a donut-shaped



FIGURE 8. Lactate-ion concentration contours with a -3.00-D SCL of Dk = 30 Barrer ($Dk/L_H = 25$ hBarrer/cm). A, Open eye. B, Closed eye. Dark blue indicates low concentration.

4 Projected lateral distance (mm)

3

contact lens, however, refute significant lactate-ion lateral transport. Further, high central swelling relative to the periphery is measured even when the cornea is exposed uniformly to a hypotonic tear solution.71,76 Thus, lactate-ion lateral transport to the central cornea is not the cause of lower peripheral swelling. Apparently, the origin is mechanical restraint from the tight network of collagen fibers at the limbus.71,76,77 Anatomical "limbal clamping" and structural continuity with the sclera resist swelling at the cornea-sclera interface.71,76,77 Therefore, high lactate-ion concentrations can exist at the peripheral cornea as shown in Figure 8 and yet be consistent with experiment showing low peripheral swelling. We assert that our scaling argument demanding negligible lateral diffusion remains valid.

Corresponding open- and closed-eye bicarbonate-ion contours are shown in Figures 9A and B for a -3.00-D SCL with Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm). As seen by the dark blue patches, bicarbonate-ion concentrations near the peripheral anterior surface are low and the more so for closed eye. Increased anaerobic glycolysis in this region generates

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FIGURE 9. Bicarbonate-ion concentration contours with a -3.00-D SCL of Dk = 30 Barrer ($Dk/L_{H} = 25$ hBarrer/cm). A, Open eye. B, Closed eye. Dark blue indicates low concentration.

excess hydrogen ions that consume bicarbonate through buffering.⁷ For the same reason, bicarbonate-ion concentrations are everywhere lower in the closed eye.

Open- and closed-eye carbon dioxide contours are shown in Figures 10A and B, respectively, for a -3.00-D SCL with Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm). Carbon dioxide is produced from aerobic respiration and from buffering of hydrogen ions by bicarbonate; it then diffuses outward from the corneal interior.⁷ Accordingly, higher carbon dioxide tensions are seen along the middle of the cornea and contrasting lower tensions along the AC and SCL surfaces. Because hydrogen ions are the result of anaerobic glycolysis, carbon dioxide production is linked to both aerobic and anaerobic glycolysis. Closed eye produces relatively more carbon dioxide in Figure 10B than does the open eye in Figure 10A, especially near the limbus. Also, from Figures 6 and 10, there is strong correlation between low oxygen supply and high carbon dioxide tensions. Both effects are explained by



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FIGURE 10. Carbon dioxide tension contours with a -3.00-D SCL of Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm). A, Open eye. B, Closed eye. Dark blue indicates low tension.

the shift of metabolism toward anaerobic glycolysis because of poor oxygen supply. Models that do not incorporate metabolic respiration cannot capture these phenomena.

Open- and closed-eye pH contours for a -3.00-D SCL with Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm) are shown in Figures 11A and B, respectively. Compared with the open eye, acidosis is significant during closed eye because cells rely heavily on anaerobic glycolysis, resulting in high hydrogenion production.⁷ As expected, acidity is highest near the anterior limbus where oxygenation is low and lactate production is high. Predicted pH values along the anterior corneal surface during open eye are higher than those measured.⁷⁸ One possible reason is that the model does not account for buffering by other species, such as proteins and/or polyelectrolytes.^{61,79}

SCL Oxygen Permeabilities

For the -3.00-D Acuvue Advance SCL shape with $L_{\rm H} = 120 \ \mu m$ shown in Figure 1, we calculated quasi-2D profiles for a range of *Dk* values from 10 Barrer, characteristic of HEMA,

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FIGURE 11. pH contours with a -3.00-D SCL of Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm). A, Open eye. B, Closed eye. Dark blue reflects low pH.

to over 10^4 Barrer (no lens). Only quantitative changes were observed. At lower *Dk*, the model predicts less oxygen, more lactate ions, less glucose, larger pH gradients, fewer bicarbonate ions, and more carbon dioxide supply throughout the cornea. We also calculated the quasi-2D profiles for a +3.00-D Acuvue Advance SCL shape that is thick in the center, declines toward the midperiphery, exhibits a maximum in thickness, and finally thins at the limbus (see **Figure C2 of Appendix C in Supplemental Digital Content 1**, http://links.lww.com/ICO/A34). This particular positive-power lens exhibited low central oxygenation and high mid-peripheral (~4 mm) oxygenation, an outcome that is different from the minus-power lens. Our quasi-2D calculation allows assessment of respiration profiles of 6 metabolic species for any lens power or lens shape and, hence, is a valuable design tool.

Lagophthalmos

Computational efficiency of our quasi-2D technique permits evaluation of useful scenarios, for example, incomplete

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eyelid closure during sleep. During physiologic lagophthalmos, part of the cornea is exposed to the atmosphere rather than to the palpebral conjunctiva and, accordingly, receives more oxygen (155 vs. 61.5 mm Hg).^{56–59} Our quasi-2D model evaluates corneal oxygenation for this case simply by altering the local 1D simulations in the affected region. The resulting oxygen contour is shown in Figure 12 for a -3.00-D SCL of Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm) and 80% eyelid closure. Basically, corneal oxygenation falls from that of open eye to that of closed eye under the lid. We anticipate lateral mixing directly at the junction of the partially closed lid and the SCL. Outside this immediate vicinity there is negligible error.

Precorneal Oxygenation

Although precorneal oxygen tension and/or flux at a particular cross-section has been modeled,^{6,10,11,38} our quasi-2D model readily predicts the effect of thickness variations on these quantities. Figure 13 shows the calculated anterior cornea oxygen tension (evaluated at the Ep/PoLTF interface in our quasi-2D model) as a function of projected lateral distance (solid line) for an SCL (-9.00-D Acuvue 2)with Dk = 28 Barrer and $L_{\rm H} = 140 \ \mu m$. Although the central cornea may be sufficiently oxygenated, there is a rapid decline toward the periphery. Oxygen tension then rises sharply near the cornea-sclera interface because the lens thins at the edges, allowing more oxygen to reach the cornea. Previous 1D models evaluated only the central precorneal oxygen tension to assess corneal oxygen demand. This procedure leads to a significant overestimate of corneal oxygenation, even during open-eve SCL wear. Based on a 1D model at the central cornea, oxygenation may seem sufficient. However, for a minus-power lens, our quasi-2D model establishes considerable reduction in oxygenation near the lens periphery. Figure 13 verifies that the entire extent of the cornea must be considered when assessing physiological performance of an SCL.



FIGURE 12. Open-eye oxygen tension contours for 80% eyelid closure with a -3.00-D SCL of Dk = 30 Barrer ($Dk/L_{\rm H} = 25$ hBarrer/cm). The anterior surface exposed to air receives a high supply of oxygen (155 mm Hg), whereas oxygen supply is limited underneath the eyelid (61.5 mm Hg).

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FIGURE 13. Lateral variation of postlens tear-film oxygen tension in open eye for a -9.00-D Acuvue 2 SCL of Dk = 28 Barrer and $L_{\rm H} = 140 \ \mu m \ (Dk/L_{\rm H} = 20 \ hBarrer/cm)$. Filled circles with standard deviation error bars correspond to the data of Bonanno (personal communication). Solid line is from the quasi-2D model.

Recently, Bonanno (personal communication) irreversibly coated a phosphorescent dye [bovine serum albumin-Pd meso-tetra (4-carboxyphenyl) porphine complex] on the posterior surface of a -9.00-D Acuvue 2 lens and measured the open-eye tear oxygen tension across the lens midline using phosphorescence quenching. Filled circles in Figure 13 correspond to the experimental data of Bonnano (personal communication). With no adjustable parameters other than lens shape and a subject-specific epithelium maximum oxygen consumption rate, agreement is reasonable between model prediction (solid line) and experimental data (filled circles). At the corneal center, however, the model predicts higher oxygen tension, outside the estimated limits of experimental repeatability. Because of fast phosphorescence decay times,^{7,20,80} high oxygen tensions are difficult to measure quantitatively. Also, exact location of the lens center is difficult to determine in the quenching experiments (Bonanno, personal communication).

Oxygen flux at the anterior cornea is another widely used gauge of corneal oxygenation.^{35–39} In a 2D spherical system, local precorneal oxygen flux is given by Fick's law, $J_o = -Dk(\partial P_o/\partial r)$, where $\partial P_o/\partial r$ is the magnitude of the radial gradient of oxygen tension evaluated at the PoLTF/Ep. In the quasi-2D approach, this expression simplifies to $J_o = -(Dk/L)\Delta P_o$, where L is the local SCL thickness and ΔP_o is the oxygen tension difference from the anterior to posterior side of the lens.

The oxygen tension profile for the minus-power lens in Figure 13 suggests that oxygen flux first increases toward the periphery and then rapidly declines near the limbus where the SCL thins at the peripheral edge. Figure 14 shows anterior corneal oxygen flux as a function of projected lateral distance



FIGURE 14. Lateral variation of postlens tear-film oxygen flux for -3.00-D Acuvue Advance SCL of Dk = 75 Barrer and $L_{\rm H} = 120$ μ m ($Dk/L_{\rm H} = 62.5$ hBarrer/cm). A, Open eye. B, Closed eye.

for a -3.00-D Acuvue Advance lens of Dk = 75 Barrer ($Dk/L_{\rm H} = 62.5$ hBarrer/cm). Here, the opposite trend is seen: oxygen flux first declines followed by an increase near the lens periphery.

To understand the flux behavior in Figure 14, we first considered a cornea that thickens toward the limbus and covered by an SCL of constant thickness. The oxygen-tension driving force increased slightly toward the periphery, whereas the oxygen flux increased significantly. Because the cornea thickens near the limbus, more cells (in the stroma) are available to consume oxygen. Accordingly, oxygen demand is larger near the periphery. To meet this increased demand, oxygen flux rises.

In Figure 14, where both lens and corneal thickness vary, oxygen flux diminishes toward the periphery, opposite of what is predicted from the increase in driving force. For a minus-power SCL, the lens thickens toward the periphery, resulting in lower precorneal oxygen tensions and higher driving forces. However, increased lens thickness decreases

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oxygen flux. Local lens thickness and oxygen driving force thus compete to determine oxygen flux. Flux declines toward the periphery because lens thickness increases relatively more than does the driving force (ΔP_o) . Figures 14A and B show a minimum at a projected lateral distance of approximately 6.2 mm corresponding to the thickest portion of the lens. Although this region has the largest ΔP_{0} between the posterior and anterior lens surfaces, oxygen flux is repressed by lens thickening. Beyond the minimum, oxygen flux increases sharply near the limbus because of lens thinning. When analyzing flux using Fick's law, one must consider not only the driving force (ΔP_0) but also the transmissibility to transport (Dk/L). In Figure 14, lens thickness overpowers the driving force and controls the flux. We note in Figure 14A that lateral flux variation across the cornea is small during open eve (maximum change less than 10%). Imprecision of existing measurement techniques is a likely reason that lateral variations in oxygen flux are not experimentally confirmed.⁸¹

Lateral variation of precorneal oxygen flux further accentuates the importance of a 2D calculation. For closed eye (Fig. 14B), oxygen flux at the center is more than 20% of that at the peripheral cornea. Because SCL thickness variations and oxygen driving force compete, a 2D assessment is essential to predict lateral variation of oxygen flux. A 1D estimate of precorneal oxygenation is insufficient because lens transmissibility varies laterally and because corneal oxygen demand is not constant across the entire extent of the cornea.

As mentioned in the introduction, many gauges have been applied to assess critical oxygen demand of the human cornea³³: oxygen transmissibility,^{23,27-32} equivalent oxygen percentage,^{16,17,21,22} critical oxygen requirement,^{33,34} biological oxygen apparent transmissibility (BOAT),^{29,35} precorneal oxygen flux,^{35–39} and total corneal oxygen consumption.⁵ Based solely on Figure 13, one may misinterpret PoLTF oxygen tension as a reliable metric to gauge corneal oxygenation. However, PoLTF oxygen tension simply establishes 1 factor (driving force) in Fick's law and neglects changes in lens resistance. Oxygen flux, which incorporates both driving force and lens transmissibility, is a more meaningful metric of corneal oxygenation. In addition to precorneal oxygen tension and flux, we briefly discuss 2 additional gauges: ODF and ELF.

Oxygen Deficiency Factor

Chhabra et al⁷ introduced ODF as a local measure of the severity of corneal oxygen deprivation. This index has the advantage of sensitivity to regions of high oxygen deprivation.⁷ Because Chhabra et al⁷ defined ODF only for a 1D system, this index must be redefined to account for lateral thickness variations. We first establish a critical oxygen tension in the cornea such that any tension less than this value results in unwanted cell damage. Following Brennan et al,⁸² we argue that a cell suffering oxygen deprivation is damaged irrespective of where it is located in the cornea. We establish this value as the minimum oxygen tension of the periphery for the no-SCL closed-eye case (ODF is defined only for closed eye). We then quantify the number of cells and their magnitude of hypoxia below the minimum oxygen limit. In a 2D model, this simplifies to calculating the volume of hypoxic region divided

by the maximum volume under the hypoxic threshold corresponding to an SCL of Dk = 0, or ODF = V/V_{max} . V is the hypoxic corneal volume for a finite-oxygen transmissibility lens lying below the minimum threshold oxygen tension and above the oxygen tension profile, and V_{max} is the maximum possible hypoxic volume for a zero-Dk SCL (ie, complete anterior corneal oxygen blockage). In our quasi-2D model, hypoxic volumes were found numerically by meshing the cornea into small elements. From 3 or 4 neighboring oxygen tensions, we calculated the average tension and the mesh area. Incremental volume was defined as the mesh area multiplied by the average oxygen tension. Incremental hypoxic volumes were added to obtain the total hypoxic volume.

A solid line in Figure 15 shows ODF as a function of $Dk/L_{\rm H}$ calculated using the quasi-2D model. In this calculation, we used the -3.00-D Acuvue Advance lens with $L_{\rm H} = 120 \ \mu {\rm m}$ (Fig. 1) but varied the oxygen permeability from Dk = 0 to 300 Barrer. Different lenses may result in minor quantitative differences. The trend in Figure 15 is similar to that of the 1D ODF calculations of Chhabra et al⁷: ODF = 100% at Dk = 0 and falls monotonically to zero at very high transmissibilities (not shown in the scale of Figure 15). At $Dk/L_{\rm H} = 150$ hBarrer/cm, the quasi-2D curve (solid line) predicts ODF of less than 5%. Further increases in $Dk/L_{\rm H}$ give only small improvements in corneal oxygenation.

The dashed line in Figure 15 shows ODF calculated for an equivalent 1D system where the cornea and the SCL are each replaced by a constant harmonic mean thickness. The 1D harmonic mean calculation indicates considerably less oxygenation than that predicted by the more realistic quasi-2D model (solid line). For $Dk/L_{\rm H} = 25$ hBarrer/cm, there is a significant lateral variation of oxygen tension, approximately 15 mm Hg at the anterior corneal surface in Figure 6B. A 1D model averages hypoxic volumes over the entire SCL. For



FIGURE 15. ODF as a function of SCL oxygen transmissibility for the -3.00-D Acuvue Advance SCL in Figure 1 reported as the harmonic mean lens thickness. Solid and dashed lines are from the quasi-2D and equivalent 1D models, respectively.

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a hypoxic threshold based on a 1D harmonic-mean lens thickness, it overestimates the amount of hypoxia, especially for lenses for which there is a large variation in oxygen tension. Conversely, for a hypoxic threshold based on a 1D center lens thickness, ODF is underestimated. A 2D model is necessary to capture hypoxia quantitatively.

Excess Lactate Factor

Lactate ions produced by anaerobic glycolysis^{7,61} are suggested to be a primary cause of corneal swelling.⁶⁸ We, therefore, define ELF as an alternative index of corneal cell damage. Calculation of ELF is similar to that of ODF. We first establish the local "safe" value of lactate-ion concentration as the maximum for the peripheral cornea, closed-eye no-SCL case. Again, ELF is defined only for closed eye. Following the procedure for calculating ODF, all cells with lactate-ion concentrations above this maximum value are counted and weighted by their magnitudes above the maximum threshold, or ELF = V/V_{max} . Here V is the critical volume above the maximum threshold lactate-ion concentration for a finite-oxygen-permeability lens and below the lactateion concentration profile, and V_{max} is the maximum possible volume for a zero-Dk SCL.

Solid and dashed lines in Figure 16 show ELF as a function of $Dk/L_{\rm H}$ calculated using the quasi-2D model and the equivalent harmonic mean 1D system, respectively. As in Figure 15, we used the -3.00-D Acuvue Advance lens of Figure 1 but varied the oxygen permeability. ELF follows the same trend with lens oxygen transmissibility as does ODF. At low $Dk/L_{\rm H}$, ODF drops off more quickly than does ELF, indicating the sensitivity of ODF to regions of oxygen deprivation. At $Dk/L_{\rm H} = 150$ hBarrer/cm, ELF is approximately 10%. If $Dk/L_{\rm H}$ is increased further, there is again minimal

decline in ELF. As opposed to those for ODF, the equivalent 1D (dashed line) and quasi-2D (solid line) ELF profiles are similar. Lateral variation of lactate-ion concentration in the cornea is small (only ~5 mM for $Dk/L_{\rm H}$ = 25 hBarrer/cm) as shown in Figure 8B. Hence, for the particular SCL considered, the quasi-2D prediction (solid line) does not deviate substantially from the equivalent 1D assessment (dashed line).

Direct prediction of corneal swelling requires understanding of water flow into the cornea,⁶¹ so neither ODF nor ELF index alone establishes a unique critical SCL transmissibility to avoid edema. Nevertheless, ODF and ELF are physically based indices that allow quantitative comparison of physiological performance between 2 SCLs.

DISCUSSION

One-dimensional models of corneal oxygenation with SCL wear are not accurate throughout the entire extent of the cornea.⁴ Cornea and contact lens thickness variations play important roles. Figure 17 shows open-eye 1D oxygen profiles at the central and peripheral cornea, in addition to that of the equivalent harmonic mean 1D system (harmonic mean corneal and SCL thicknesses). Clearly, cornea and lens thickness variations have a significant effect on oxygen availability. Although the equivalent harmonic mean cornea/SCL system is more accurate than is the central profile, 23,83 1D harmonic mean thicknesses still do not successfully predict corneal oxygenation throughout. For example, ODF for the equivalent 1D system in Figure 15 overestimates oxygen deficiency for all SCL transmissibilities. Huang et al³⁸ argue that SCL thickness variations are no longer important, given the high oxygen permeabilities of current SCLs. However, as illustrated in the no-lens profile of Figure 5A, corneal thickness variations remain important. Only 2D models



FIGURE 16. ELF as a function of SCL oxygen transmissibility for the -3.00-D Acuvue Advance SCL in Figure 1 reported as the harmonic mean lens thickness. Solid and dashed lines are from the quasi-2D and equivalent 1D models, respectively.

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FIGURE 17. Open-eye oxygen profiles at the central (light solid line) and peripheral (dark solid line) cornea for a -3.00-D (Acuvue Advance) SCL of Dk = 75 Barrer and $L_{\rm H} = 120 \,\mu m (Dk/L_{\rm H} = 62.5 \,\text{hBarrer/cm})$, in addition to an equivalent 1D system using harmonic mean thicknesses of the cornea and SCL (dashed line).

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incorporating thickness variations can predict species concentration profiles throughout the cornea.

The proposed quasi-2D model joins together a series of simple 1D calculations. Computational efficiency is a major advantage. Unlike the fully 2D model of Alvord et al,⁴ extension to many metabolites is straightforward. Following Chhabra et al,⁷ we considered the coupled effects of glucose, carbon dioxide, and lactate, hydrogen, and bicarbonate ions, in addition to oxygen. Incorporation of even more complex descriptions of the cornea/SCL system⁶¹ is possible with minimal increase in computation time. The quasi-2D model is available in graphic user interface format on request.

We varied stromal and SCL thicknesses to assess peripheral corneal oxygenation, yet many anatomical and biochemical differences are known to exist between the central and peripheral cornea. Other variables may change toward the peripheral cornea, such as posterior corneal oxygen tension⁸⁴ and collagen fiber spacing.⁸⁵ The largest error in the quasi-2D model arises near the cornea/sclera periphery where oxygenation from the limbal blood supply is not accounted for. Fortunately, absolute error is small. Oxygen from limbal blood vessels has no significant effect beyond the immediate vicinity of the cornea–sclera interface.⁴ Overall corneal oxygenation is driven principally by normally oriented diffusion.^{4,84}

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