The Central and Peripheral Physiological Response of the Cornea to Three Hydrogel Contact Lens Diameters

Thesis

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Abstract

Purpose: The purpose of this study is to compare the physiological response of the cornea to three hydrogel contact lens diameters.

Methods: Fifteen subjects were fitted with three diameters (13.0, 14.0, and 15.0 mm) of Alden Classic hydrogel contact lenses (38% water content, dK 9.0). Lenses had a back vertex power of -3.00 D, center thickness of 0.1 mm, and base curve radius fitted according to guidelines using flat keratometry reading and lens diameter. Corneal oxygen uptake rates were measured at the central and peripheral cornea for the normal open eye and following 5 minutes of contact lens wear under both static (without blinking) and dynamic (with blinking once every 5 seconds) wearing conditions for each lens diameter. Oxygen uptake rates for each lens/condition were averaged between the two measurement sessions and then divided by those of the normal open eye obtained at the same location.

Results: Corneal oxygen uptake rates increased with increasing lens diameter (p=0.006) regardless of location (central or peripheral) or condition (static or dynamic). The mean oxygen uptake relative to air was 4.59 (std=0.8) for the 13mm lens, 4.99 (std=1.4) for the
14mm lens, and 5.03 (std=0.9) for the 15mm lens. For all lens diameters, uptake relative to air was higher under static conditions (mean=5.18, std=1.2) compared to dynamic conditions (mean=4.56, std=0.7, p=0.001). Oxygen uptake relative to air was higher in the periphery (mean=4.95, std=0.9) compared to the central cornea (mean=4.79, std=1.2, p=0.011).

Conclusions: Contact lens diameter does impact oxygenation of the central and peripheral cornea for Alden Classic hydrogel contact lenses.
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Chapter 1: Historical Review

Introduction

Contact lens wear can induce changes in structure and function of the cornea, and many of these changes are related to corneal hypoxia.\(^1\) During contact lens wear, there are two possible mechanisms by which oxygen is provided to the cornea: transmission through the lens material or bulk volume exchange and stirring of tears with the blink. Past studies with rigid contact lenses have shown that lens design can impact the pumping action that takes place during blinking, and contact lens parameters are important in determining the oxygen tension between the cornea and the contact lens.\(^2-5\)

In order to determine how well the cornea is securing oxygen during contact lens wear, a Clark-type polarographic oxygen electrode can be used. Since Hill and Fatt made the first in vivo measurement of oxygen consumption from the atmosphere by the human cornea in 1963, this technique has revealed an increase in epithelial oxygen uptake rate after disruption of the anterior (atmospheric) oxygen supply.\(^6\) This increased oxygen uptake rate is greater if a contact lens is impermeable to oxygen or if it is worn statically (without blinking).\(^7-8\) The measurement of corneal oxygen uptake can be used to indicate a reduction of oxygen reaching its epithelial surface, reflected as an increase in oxygen uptake rate. Differences (reductions) in oxygen uptake rates measured between static
(without blinking) and dynamic (with blinking) conditions provide a measure of tear pump efficiency. Using this technique, the effect of various contact lens designs on the oxygen uptake rate of the cornea can be determined under both static and dynamic conditions.

This study will determine if reduction in hydrogel lens diameter and blinking are effective at providing oxygen to the eye. Not only does tear exchange with the blink enhance corneal oxygenation, but tear exchange could also eliminate debris and metabolic byproducts that can be associated with inflammation, discomfort, and reduction in contact lens wearing time. This study will provide guidelines to fitters of hydrogel contact lenses for enhancing tear exchange, benefiting the many patients who wear hydrogel contact lenses.

**Ocular Structures Involved in Contact Lens Wear**

**The Eyelids**

The eyelids function to spread the pre-corneal tear film, moistening the ocular surface epithelium and providing a smooth optical surface for the refraction of light. The eyelids also assist in the drainage of tears from the ocular surface. They protect the eye by preventing excessive light at the retina and by keeping foreign bodies from the ocular surface.

Palpebral tissues contain both striated muscle from the obicularis oculi and non-striated muscle. Also included are tarsal plates, fibrous tissue, fat, an orbital septum and
conjunctiva. The lids are innervated by the sympathetic system, the facial nerve, the supra and infraorbital nerves, supra and infra troclear nerves, the lacrimal nerve and zygomaticofacial nerve.\textsuperscript{10, 18-19} The orbicularis oculi muscle is located concentrically with the palpebral aperture. It is responsible for lid closure, and it is innervated by the facial nerve. The levator palpebrae superioris is responsible for eyelid elevation. It is innervated by the oculomotor nerve and assisted by Muller’s muscle, which receives sympathetic innervation.\textsuperscript{19}

Within the lids are many types of glands that contribute to tear formation. These include the glands of Karuse, Wolfring, Zeis, Moll, and meibomian glands. The major purposes of many of these glands are to contribute to tear production and maintain the health and optical nature of the eye. The meibomian glands produce the lipid layer for tears, while the glands of Krause and Wolfring, also known as accessory lacrimal glands, produce aqueous. The mucin component of the tears is produced by the bulbar conjunctival goblet cells. Ciliary glands include the sebaceous glands of Zeis and the sweat glands of Moll.\textsuperscript{10, 18-19}

Blinking can be voluntary, reflex, or spontaneous.\textsuperscript{10} Reflex blinking can be due to tactile, optical, or auditory stimuli. Spontaneous blinking is blinking that occurs on a regular basis without an apparent external stimulus. The total blink time is about 258 msec, while the closing phase (82 msec) is about half the time of the opening phase (175 msec).\textsuperscript{11} Blink rate is about 12.55 blinks/minute,\textsuperscript{20} but increases to about 23 blinks/minute in hard contact lens wearers\textsuperscript{21} and to about 20 blinks/minute in soft contact lens wearers.\textsuperscript{22} Blink rate increases with dry eye, windy environments, palpebral aperture
size, and conversation, while it decreases with use of topical anesthesia, use of artificial tears, and reading.\textsuperscript{23-26} Doughty described three types of blinking patterns: irregular (30\%) with a mean blink rate of 7.5 blinks/minute, composed of fairly long interblink intervals interspersed with two or more rapidly repeated blinks; J-type (38\%), with a mean blink rate of 10.7 blinks/minute with short interblink intervals interspersed with a few longer intervals; and normal (33\%), with a mean blink rate of 12.43 blinks/minute and a Gaussian distribution of interblink intervals.\textsuperscript{26}

For RGP lenses, eyelids play a significant role in the positioning and movement of contact lenses.\textsuperscript{27-28} Lid geometry is a major factor in determining the overall diameter of rigid contact lenses. The vertical dimension of the palpebral aperture is about 8-11 mm, and the upper eyelid typically crosses the cornea at the 10:00 and 2:00 positions.\textsuperscript{10,19} Prior to the invention of gas permeable rigid contact lens materials, tear exchange with the blink was critical to corneal oxygenation.\textsuperscript{28} Even with gas permeable materials, tear exchange is still important in the clearance of debris and metabolic byproducts from between the contact lens and the cornea and in the prevention of inflammatory reactions.\textsuperscript{1,27,29-31} In order to enhance tear exchange, it is recommended that small lenses should be fitted if the upper lid is high, if the lower lid is high, or if there is small palpebral aperture. If the upper lid is near or above the upper limbus or the force of the upper lid is not great enough to hold up the lens, it will tend to sag downwards and ride near the lower limbus due to the weight of the lens. This can cause visual problems, discomfort, and lack of tear exchange. If the lower lid is high, it will push the lens upward, particularly upon downward gaze. The lens will be held stationary in this position, with
little tear exchange. Small palpebral apertures with tight lids require a small diameter contact lens to enable lens movement. Large lenses should be fitted if the upper lid is low. A small lens would either be pulled up excessively by the force of the lid, or the upper lid would bump the edge of the lens, resulting in lid discomfort. The upper lid could also push the lens down so that it positions below the center of the cornea. Discomfort and poor tear exchange would result. Lid movement with blinking is a significant factor as the lids interact with the contact lens and the tears creating a tear pump which is used to replenish and circulate the pre- and post-lens tear film. As new tears are introduced to the surface of the cornea essential nutrients are provided and waste products are removed. Soft contact lenses are less reliant on the contribution of the lid to lens created tear pump for corneal oxygenation.

The Tears

The tear film is spread by the eyelids over the rough ocular surface to form a uniform surface for refraction of light. It serves a protective role by flushing debris from the ocular surface, and there is a reflex increase in tear flow with trigeminal nerve stimulation. The tears contain antimicrobial substances, such as lysozyme, lactoferrin, and secregory IgA, and the mucin components help to trap particulate matter. The tears protect the surface of the eye from external environment by responding to constant, varying challenges and maintaining appropriate osmolality, pH, and temperature. The palpebral conjunctival and corneal surface are lubricated by the tears so that they slide over each other during blinking.
In the past, the tear fluid was considered to be a complicated three-layered structure, consisting of a superficial lipid layer, a central aqueous layer, and a mucin layer located adjacent to the ocular surface. The aqueous component, produced by the main and accessory lacrimal glands, makes up the bulk of the tear film, and it is now thought to be mixed with mucins produced by the goblet cells. The tear film is about 3-7 um thick, and the volume is about 6-8 ul.\textsuperscript{19,32-33} Unstimulated tear flow is about 1.2 ul/minute,\textsuperscript{34} and morning tear flow is 15% higher than that of the afternoon.\textsuperscript{35}

**The Cornea**

There are three tunics of the eye, one of which is the corneal scleral tunic. The corneal portion of this tunic makes up the anterior one-sixth portion while the sclera contributes the posterior five-sixths of the tunic. The cornea is the main refractive component of the eye while at the same time it provides a barrier between the intraocular components and the external environment. A unique feature of the cornea is its transparency. It is the highly organized nature of the cornea’s components coupled with its physiology that allows for its transparency.

The cornea can be divided into 5 main regions or layers named from anterior to posterior: epithelium, Bowman’s layer, stroma, Descemet’s membrane, and endothelium. The epithelial layer of the cornea is composed of squamous non-keratinized epithelial tissue, contains 4-7 sub-layers of cells and is about 50 to 60 micrometers thick.\textsuperscript{36} The most superficial layer is covered by microplicae and microvilli, which are projections from the surface of the eye that offer support and increase the ability of the tears to
adhere to the corneal surface. The anterior, most superficial cells are interconnected by zonular occludens that create a seal preventing the flow of material between cells. Beneath the posterior-most layer of epithelial cells are 3-5 layers of wing cells that are connected intercellularly by desmosomes and gap junctions, allowing for intercellular communication. Deep to the wing cells is the most posterior sub-layer of the anterior epithelium, the mitotically active basal cell layer. This single cell layer has about 10-15 percent of its cells dividing daily to replenish the more superficial epithelial cells. The posterior face of the basal layer is anchored to the underlying Bowman’s membrane by hemidesmosomes.¹⁹,³⁷

Bowman’s membrane is composed of an acellular anterior condensation of corneal stroma and averages 8-14 microns in thickness.¹⁹,³⁸-³⁹ With electron microscopy, it is shown to have a lattice of fibrils which are mainly composed of collagen. It is devoid of cells, except for the Schwann cells surrounding the peripheral nerves. The collagen fibrils are interwoven densely to form a felt-like sheet, and the diameter of the collagen fibrils is 20-25 nm and run in various directions.³⁸-⁴⁰ The turnover or replacement of these fibers is relatively low throughout life. This layer is not renewed following trauma.⁴¹ The perimeter of Bowman’s membrane is an anatomical landmark that marks the anterior junction between the cornea and the limbus.³⁸-⁴⁰

A honeycomb pattern on the anterior surface reflects the contour of the base of the epithelium and the attachment of anchoring fibrils to the basal laminae at the hemidesmosomes. The fibrils of Bowman’s layer are composed primarily of collagen types I, III, and V, while type VII collagen is associated with anchoring fibrils from the
epithelium. It is thought that the corneal epithelium synthesizes a greater ratio of type V/type I collagen that the stromal fibroblasts, and it is the higher amount of type V collagen that accounts for thinner collagen fibrils of Bowman’s layer when compared to those of the stroma. Basal epithelial cells adhere to their basement membrane and underlying stoma through a series of anchoring structures, including the hemidesmosome, anchoring fibrils, and anchoring plaques. A complex anchoring fibril network is present in the region of the corneal stroma just beneath the epithelial basement membrane. Type VII collagen fibrils insert into type VII anchoring plaques.

The posterior surface is not defined clearly because the collagen fibrils are intermingled with those of the stroma. The purpose of a study by Mathew, Bergmanson, and Doughty was to define better the ultrastructure of the interface between Bowman’s layer and the stroma with high resolution imaging. Transmission electron microscopy revealed at least three different types of fibrillar arrangements between Bowman’s layer and the anterior stroma. The first type were described as terminating anterior stromal lamellae embedding into an electron-dense material (electron-dense formations, EDFs) within the stomal matrix. The second types consisted of anterior stromal lamellae inserting into Bowman’s layer, while the third type consisted of fibrils extending from Bowman’s layer into the stroma.

Eye rubbing, flattening of the cornea, and low intraocular pressure produce a groove pattern of the anterior corneal mosaic. The structural basis for the normal anterior corneal mosaic pattern is the arrangement of the collagen lamellae attaching to the posterior surface of Bowman’s layer. The mosaic is not seen in patients with Bowman’s
layer dystrophies. When observed with the confocal microscope, pressure on the cornea results in the formation of ridges that protrude from Bowman’s layer into the epithelial basal and wing cell layers, as well as superficial stromal striae. Fibrillar material, called K-structures, correspond to the regions where the stromal collagen merge into Bowman’s layer, resulting in the formation of these ridges and striae. The K-structures form a netlike pattern and are the structural basis for the anterior corneal mosaic formation.45-47

Bowman’s layer functions as the foundation for the corneal epithelium. Because the collagen fibers are denser and they have a lower water content than the stroma, it is thought that Bowman’s layer might lend stability to the eyeball. Therefore, destruction of Bowman’s layer has the potential to result in changes in refractive error due to corneal changes brought about under the influence of intraocular pressure.48 In addition, Bowman’s layer is steeper than the anterior corneal surface and can affect the optical performance of the eye.49 Bowman’s layer also serves to prevent close contact between epithelial and stromal cells to reduce stromal cell activation and inappropriate extracellular matrix assembly.50 During wound healing, on the other hand, diffusible cytokines are permitted to be modulators in bidirectional communication between epithelial and stromal compartments.51

Posterior to Bowman’s membrane is the thickest layer of the cornea, the stroma, which measures on average to be about 500 microns thick and has a water content of 78%.40 The stroma is a highly organized structure composed of laminar sheets of collagen that run parallel to the corneal surface. The type I collagen fibrils making up the lamella are arranged and spaced in an optically conducive pattern that allows for optimal
light transmittance. The lamellar sheets are separated by keratocytes and are surrounded by a proteoglycan matrix. There are 2.4 million keratocytes in the human cornea, with a 70% greater density in the peripheral cornea than centrally and 30% lower density in the posterior cornea than the anterior. The keratocytes synthesize the collagen and proteoglycan matrix initially and then maintain it afterwards. They communicate through gap junctions in lateral and anterior-posterior directions, and the corkscrew organization throughout the stromal suggests that they form completely closed sheets of communicating cells.

The anterior stromal arrangement differs from that of the posterior stroma as the anterior collagen fibers as the anterior fibers are less densely packed than the posterior. The posterior fibers also lie in a more regular arrangement. The lamellae vary in width from about 0.5 to 250 um, and they vary in thickness from about 0.2 to 2.5 um. The lamellae in the anterior region have a flat, tape-like shape with 0.5 – 30 um width and 0.2 – 1.2 um thickness, and they run in random directions, with branching and intertwining. The lamellae in the posterior region resemble broad sheets that are about 100 – 200 um wide and 1 – 2.5 um thick, and they run parallel to the corneal surface.

The ground substance that surrounds the fibers contains glycosaminoglycans (GAGs). GAGs play a significant role in corneal hydration and thus corneal thickness. Sixty-five percent of the corneal GAG is keratan sulfate, whereas 30% is chondroitin/dermatan sulfate. The two major chondroitin/dermatan sulfate proteoglycans in the cornea are decorin and biglycan, while the major keratan sulfate core proteins are
lumican, keratocan, mimecan, and fibromoduline. Also found within the cornea stroma are lymphocytes, macrophages and rarely polymorphonuclear leukocytes.\textsuperscript{19, 36-37}

Descemet’s membrane is the basement membrane of the corneal endothelium, and it is located between the stroma and the endothelium.\textsuperscript{36} This membrane thickens throughout life, being about 3 to 4 microns at birth and progressing to 10 to 12 micrometers by age 60.\textsuperscript{59} Descemet’s adds elastic-like support to the cornea’s structure. This membrane is interlocked with the stroma anteriorly by collagen loops and posteriorly adheres to the endothelium by way of hemidesmosomes.\textsuperscript{39} Type VIII collagen is synthesized and is the most abundant collagen in Descemet’s membrane during fetal life, while Type IV collagen is present in the projections penetrating Descemet’s membrane matrix at regular intervals and is synthesized by the corneal endothelium after birth.\textsuperscript{60} The anterior fetal collagen displays a banded appearance. Descemet’s peripheral edge creates Schwalbe’s line, an interior landmark of the cornea. In contrast to Bowman’s layer, Descemet’s layer can be resynthesized by the endothelium following trauma.\textsuperscript{19, 43}

The endothelium of the cornea is a single layer of hexagonal cells situated just posterior to Descemet’s and is the innermost layer of the cornea. The endothelial cells are described as having both barrier and pump functions to control corneal hydration. The barrier is not complete and is provided by macular occludens and macular adherens in the anterior two-thirds of the lateral cell membranes, with macular occludens and gap junctions in the posterior one-third and marginal fold of the lateral cell membranes.\textsuperscript{40} Junctional adhesion molecule-A (JAM-A) is a tight junction-associated adhesion protein
and found in the corneal endothelium, contributing to the barrier function.\textsuperscript{61} The leakiness of the endothelial barrier is a source of nutrients to the cornea.\textsuperscript{62-64} Inhibiting the endothelial barrier results in swelling at 127 um/hour, while inhibiting the pump system results in swelling at 33 um/hour.\textsuperscript{65} The ion transport systems regulate the ion concentration and pH in the aqueous humor and the corneal tissues.\textsuperscript{62} The function of these pumps is critical to the prevention of corneal edema which can disrupt the highly organized and transparent nature of the stroma leading to decreased light transmittance.\textsuperscript{63} The density of the corneal endothelium is about 4000 cells/mm\textsuperscript{2} at birth. There are about 2500 cells/mm\textsuperscript{2} in mammalian adults, with 3650 cells/mm\textsuperscript{2} in the peripheral corneal endothelium. It is thought that a cell density of at least 400 to 700 cells/mm\textsuperscript{2} is needed for normal function and to prevent corneal edema.\textsuperscript{66-68} Variation in cell size, or polymegathism, is also associated with a reduction in endothelial function. A coefficient of variation, or standard deviation divided by the mean cell size, of less than 0.25 indicates a normal degree of cells size variation.\textsuperscript{69-71} The coefficient of variation increases with corneal surgery, keratoconus, diabetes, and contact lens wear.\textsuperscript{63-64, 72}

\textbf{Anatomy and Physiology of the Central vs. Peripheral Cornea}

The cornea has an average central thickness of 0.52mm and increases to an average thickness of 0.67 in the periphery.\textsuperscript{19, 40} The central cornea is more densely innervated than the peripheral cornea, containing 5-6 times more nerve fibers. The increased organization and well-aligned organelles of the central cornea allow the collagen and nerve fibers to be more densely packed.\textsuperscript{36, 73} The peripheral cornea has a
transition zone where the corneal fibers transition into the irregular fibers of the sclera. The peripheral cornea’s epithelium is more tightly adherent to the underlying basal membrane. The peripheral cornea is also located closer to the limbal blood and lymph vessels; from such the peripheral cornea derives its nutrients and immune defense. The central cornea receives most of its nourishment from tear film and aqueous. The endothelium within the periphery of the cornea demonstrates mitogenic activity, whereas central corneal endothelial cells are non-mitogenic.

The peripheral cornea differs from the central cornea not only anatomically but also physiologically. There is a greater concentration of epithelial stem cells in the periphery of the cornea. Furthermore, the peripheral epithelial cells have a greater proliferative ability and higher mitotic rate. When there is injury to central corneal epithelium, peripheral epithelial cells produce daughter cells that then migrate centrally by pseudopod movement. Epithelial cells tend to shed more frequently in the center of the cornea. While MUC 1 and MUC 16 membrane associated mucins are found in equal proportion comparing the central and peripheral cornea, MUC 4 mucins are found at much higher levels in the periphery. A study by Morgan et al evaluated the minimum Dk/t of a contact lens to prevent corneal swelling. He showed the central cornea to needs a Dk/t of 19.8 to prevent swelling and the periphery needed a Dk/t of 32.6 to prevent swelling for the normal open eye. Due to the immune mediator supply at the periphery of the cornea, corneal infiltrates, which are collections of white blood cells, are more common at that location. These infiltrates tend to be sterile while central infiltrates are thought more commonly to be infectious. The peripheral cornea is more
subject to melts, Mooren’s ulcer, autoimmune diseases, and pellucid marginal
degeneration.\textsuperscript{82} These differences lead to different treatment approaches to central and
peripheral corneal pathologies.\textsuperscript{73}

**Control of Corneal Thickness and Hydration**

The corneal stoma is made up of collagen fibers surrounded by an extracellular
matrix that contains hydrophilic glycosaminoglycans (GAGs). These GAGs create an
imbibition pressure drawing water into the cornea. To counter this force, the corneal
endothelium is replete with ion transport systems providing it with the ability to control
corneal hydration.\textsuperscript{62,83} The basolateral surface of the corneal endothelium has many
sodium-dependant bicarbonate transporters. These transporters remove bicarbonate from
the stroma into the endothelial cells, in a ratio of one sodium molecule for two
bicarbonate molecules. Inside the endothelial cells, cytosolic carbonic anhydrase
converts the bicarbonate into carbon dioxide and water. At the apical membrane,
membrane-bound carbonic anhydrase converts the carbon dioxide to bicarbonate for
eflux into the anterior chamber.\textsuperscript{84} Sodium-hydrogen exchangers and chloride-
bicarbonate exchangers on the basolateral membranes of the endothelial cells are
responsible for pH regulation and sodium chloride uptake into the cells, while sodium-
potassium-ATP-ase brings two potassium molecules into the cells for every three sodium
molecules that are brought out of the cells and into the stroma.\textsuperscript{85-87} Sodium-potassium-
two chloride cotransport brings all three of these molecules into the corneal endothelial
cells and is involved in cell volume regulation.\textsuperscript{88} The net transport of sodium, chloride,
and bicarbonate from the stroma to the aqueous humor provides the osmotic gradient for fluid movement across the endothelium. This takes place through aquaporin I water channels.\textsuperscript{89-90}

A reduction in oxygen supply to the anterior surface of the cornea does not significantly alter the oxygen tension at the endothelium. The endothelium receives all of its metabolic needs—including glucose, amino acids, and oxygen—from the aqueous humor.\textsuperscript{64} Disruption in anterior (epithelial) oxygen supply, however, can result in corneal swelling and changes in cellular structure and function throughout the cornea, including the endothelium.\textsuperscript{1} Increased production of lactate ions by hypoxic epithelial cells results in excess lactate in the stroma to act osmotically to counterbalance the effect of pumped bicarbonate ions from the stroma to the aqueous humor. Accumulation of carbon dioxide results in increased production of hydrogen and bicarbonate ions through carbonic anhydrase, further lowering pH.\textsuperscript{91} Reduction in pH decreases the ion transport function of the endothelium.\textsuperscript{92} This stimulates activity in the sodium-hydrogen exchanger and sodium-bicarbonate co-transporter to attempt to regulate pH while bringing additional sodium into the endothelial cells. This osmotic draw brings water into the endothelial cells, causing endothelial edema or bleb formation.\textsuperscript{62, 93}

In contrast to the endothelium, the epithelium plays a minor role in corneal hydration as it has high resistance to ion conductance intra or paracellularly.\textsuperscript{64} The epithelium of the cornea plays a more significant role as a barrier bound by tight junctions. There are ion transporters in the epithelial cell membrane which are responsible for moving chloride ions from the corneal stroma toward the tears. Sodium-
potassium-ATPase moves sodium out of the epithelial cells and builds up its concentration in the stroma. Sodium-potassium-chloride co-transporters move sodium along its concentration gradient into the epithelial cells, along with potassium and chloride ions.\textsuperscript{94-95} Chloride ions diffuse into the tears through channels in the apical cell membrane.\textsuperscript{96} This chloride transport can be stimulated by catecholamines via cyclic AMP. This sets up osmotic pressure differences that transfer water to the tears from the cornel epithelium through aquaporin V water transport channels.\textsuperscript{97}

Corneal metabolism of glucose is a series of chemical processes by which energy is obtained to provide for the normal function of the cornea, maintaining its transparency through the ion transport systems of the epithelium and endothelium. Glucose is supplied to both the epithelium and the endothelium by the aqueous. The limbal blood vessels and tears play minor roles in the nutrition of the cornea. Oxygen is needed for the most efficient metabolism of glucose through Kreb’s cycle and oxidative phosphorylation, which generate 38 molecules of ATP for each molecule of glucose.\textsuperscript{98} In the absence of oxygen, on the other hand, there is a net gain of only two molecules of ATP through glycolysis, and lactic acid is produced.\textsuperscript{37, 99-100}

Oxygen is supplied to the corneal endothelium by the aqueous. The epithelium receives its oxygen from the atmosphere, under open eye conditions, and from the superior palpebral conjunctiva, under closed eye conditions.\textsuperscript{101} The tears provide 155 mmHg of oxygen, while the aqueous provides about 55 mmHg of oxygen.\textsuperscript{100, 102-105} Contact lenses reduce the amount of oxygen available to the cornea, and it is essential that both rigid and soft contact lenses allow adequate amounts of oxygen to reach the
corneal surface to prevent hypoxia and resultant complications. Various models have been developed to predict the distribution of oxygen in the cornea under open-eye, closed-eye, and contact lens wearing conditions. These models incorporate the geometry and transmissibility of the cornea-contact lens system components, the oxygen consumption rates of the layers of the cornea, and the oxygen tension at the aqueous and tear (pre-lens) boundaries.\(^98, 106-109\)

**Corneal Pathophysiology with Contact Lens Wear**

When considering various modalities of vision correction, it is important to review the adverse side effects that may result from them. Contact lens use can result in various forms of corneal pathology that may be from hypoxia, hypercapnia (carbon dioxide accumulation), allergic, mechanical, toxic or osmotic in origin.\(^1\)

**Hypoxia and Hypercapnia**

Epithelial Metabolic Rate Reduction

With contact lens manufacturing it is important to consider the Dk (inherent permeability of the material to oxygen) and the Dk/t or transmissibility, with “t” being the central thickness point of the contact lens. Dk/t is usually reported based on -3.0D contact lens thickness. Hypoxia has been shown to stimulate anaerobic glycolysis to supplement the production of ATP. Reduced amounts of ATP can lead to a metabolic rate decrease, delay in epithelial cell turnover, epithelial thinning, oxygen flux reduction, epithelial microcysts, and increased epithelial fragility.\(^110\)
A reduction in the metabolic rate of the cornea will lead to decreased mitotic rates of corneal epithelium.\textsuperscript{111} To maintain a steady corneal thickness the sloughing rate of epithelial cells must be reduced. Larger cells, potentially due to reduced epithelial sloughing have been reported.\textsuperscript{112} In a study of extended wear contact lens patients it was shown that epithelial thinning can result.\textsuperscript{113} Contact lenses have also been shown to reduce corneal oxygen flux.\textsuperscript{113-114}

Epithelial microcysts have also been shown to occur with contact lens wear and are thought to be due to decreased epithelial metabolism and cell growth.\textsuperscript{115} Microcysts tend to appear after 6-8 weeks of daily or extended wear contact lenses. They take three months to clear after cessation of hydrogel extended lens wear, with the highest number seen seven days after removal of extended wear contact lenses.\textsuperscript{116} Increased epithelial fragility has also been documented with contact lens wear in diabetic patients.\textsuperscript{117} Following contact lens wear, there is a reduction in the thickness of all epithelial cell layers and the development of abnormally shaped basal cells. There is a decrease in hemidesmosome synthesis and reduced epithelial adhesion.

Compromised Junctional Integrity

Multiple studies have shown that wear of contact lenses with low Dk/t can lead to loosening of tight junctions and increased separation between neighboring corneal epithelial cells.\textsuperscript{118-119} Historically it was thought that the decrease in the barrier function of the epithelium puts a person more at risk for microbial keratitis, decreased glycogen stores, corneal abrasions and punctate staining. Epithelial abrasions are associated with
contact lens wear and the associated loosening of the corneal epithelium. Less significant corneal injury than an abrasion is superficial punctate keratopathy which is also associated with contact lens use. Superficial punctate keratopathy is thought to be the premature shedding of epithelial cells or damage to groups of cells. Extended wear lenses has been shown to produce punctate staining is as many as 86% of cases. This type of staining may be the result of hypoxia or toxicity to solutions.

Microbial keratitis is the most significant corneal complication associated with contact lens use. It is thought that hypoxia and compromised epithelial cell junctions lead to risk of infection. Infection with RGP lens wear does not occur as frequently as with soft lenses. Infectious keratitis is associated with ulcer formation that penetrates to the stroma, with concomitant edema, infiltrates, and aqueous flare. Of all strains of bacteria, Pseudomonas aeruginosa is the most common infectious pathogen when cultured. Epithelial damage caused by contact lenses of low transmissibility results in exposure of the wing cell layer of the corneal epithelium and binding by the Pseudomonas organisms. Epithelial defects associated with contact lens wear due to hypoxic, mechanical or osmotic stress puts patients at increased risk for infection. Furthermore, the increase contact time of an infectious organism with the corneal surface increases the likelihood of adherence and penetration. A contact lens may also reduce the eyes natural defense that comes from blinking, immune proteins in the tears, and tear flow.
Epithelial Glycogen Depletion

Epithelial glycogen depletion is also associated with contact lens use. Glycogen is a natural component of human epithelium. This glycogen is converted to glucose through metabolic processes. A reduction in epithelial glycogen is a sign of increased anaerobic corneal activity and is associated with corneal edema. Mechanical trauma associated with contact lens wear may also contribute reduced glycogen stores. The cornea has the ability to return to normal glycogen levels after 8 hours of exposure to normal atmospheric oxygen concentrations.128

Stromal Lactate Accumulation

When the cornea experiences hypoxia, it begins to create ATP through the Embden-Meyerhof anaerobic pathway.129-130 One of the end products of this pathway is lactate. Lactate is not able to diffuse out of the cell resulting in lactate accumulation within the cornea.101 This accumulation leads to decreased corneal pH and corneal edema. The stromal edema associated with hypoxia is due to an increase in stromal osmotic pressure.

Edema can also be caused by hypotonic tear film. Corneal thickening due to contact lens wear on an unadapted eye ranges typically from 1.5%-5% with daily wear lenses (Dk/t from 18x10^{-9} to 7x10^{-9}(cm ml O_2)/(sec ml mm Hg)).131 Extended wear of hydrogel lenses shows overnight edema of 10%-12%.131-132 Within the first week of extended wear lenses this degree of thickening can be expected.133-134 The edema associated with PMMA contact lens wear has been shown to significantly increase central
Edema associated with hydrogel lens wear can also create posterior stromal striae, and, in cases of swelling greater than 10% edema, posterior stromal folds have also been noted. However, corneal striae are not typically seen in hydrogel lens users on a daily wear schedule, and the number of striae are slowly reduced during the first few weeks of wear. This is consistent with the decrease in corneal edema associated with long term contact lens wear.

Stromal hypoxia and hypercapnia induce stromal acidosis, which can also lead to the endothelial compromise. Contact lens wear on an unadapted cornea can lead to endothelial edema, also known as an endothelial bleb, within minutes of contact lens application. After several hours of wear the edema remits. This response to lens wear appears to increase with the decrease in the oxygen transmissibility of the lens. There is no such effect in silicone contact lenses. Endothelial polymegethism, however, has been shown in almost all contact lens wearers and is also thought to be due to stromal acidosis. The direct mechanism involved however is still unclear. It has been shown, however, that the amount of endothelial polymegethism is a sign of endothelial health.

Other conditions associated with contact lens wear and the resulting hypoxia and hypercapnia are corneal hypoesthesia, superficial vascularization, deep stromal vascularization, and stromal thinning during long term lens wear.
Other Causes of Corneal Pathophysiology with Contact Lens Wear

Corneal pathophysiology can also be associated with the following: allergy and toxicity, mechanical effects of the contact lens, and osmotic effects.\textsuperscript{1} Allergic and toxic responses to contact lens material, solutions or a build-up of proteins on contact lenses are also causes of corneal inflammation and subsequent complications due to contact lens use. Associated inflammation can cause limbal vessel hyperemia, peripheral corneal infiltrates and keratic precipitates.\textsuperscript{116,147} Solution toxicity can cause punctate staining and epithelial pseudodendrites. Mechanical effects and osmotic changes associated with contact lens wear and resulting corneal desiccation can also be contributors to corneal compromise.\textsuperscript{148-150}

The Contact Lens

Lens Materials

Hydrogel contact lenses are made of hydrophilic polymers. The monomers that make up these polymers include: hydroxyethylmethacrylate (HEMA), the primary monomer from which the first commercial soft contact lenses were made; ethylene glycol dimethacrylate (EDDMA), that contains two methacrylate groups in one molecule and is used as a crosslinking agent to increase dimensional stability of the polymer; methacrylic acid, used to increase water content in the hydrogel; methyl methacrylate (MMA), used to lower water content or improve the stiffness and strength of some soft contact lenses; vinyl pyrrolidone, used to increase water content; styrene, a hydrophobic and water
insoluble monomer used to increased the index of refraction and lower the water content; isobutyl methacrylate and pentyl methacrylate, hydrophobic monomers that decreases water content and increases lens modulus and finally divinylbenzene, which is used as a crosslinking agent.\textsuperscript{151}

The Food and Drug Administration has classified hydrogel materials into four groups for solution approval purposes.\textsuperscript{152} Groups 1 and 2 are nonionic polymers for less than 50\% water content and greater than 50\% water content, respectively. Group 1 is the most soilage and chemical resistant category out of the four groups. Groups 3 and 4 are ionic polymers of less than 50\% water content and greater than 50\% water content, respectively. Group 4 represents the most easily protein deposited and chemical reactive of the four groups.\textsuperscript{153}

Hydrogel contact lenses depend on the water in the lens matrix to dissolve oxygen and allow it to pass through the lens to the cornea during contact lens wear.\textsuperscript{154-155} Oxygen transmissibility, or Dk/t, of a contact lens is determined by three components: “D,” the diffusion coefficient or rate that oxygen molecules move through the contact lens; “k,” the gas solubility in the material that determines how many oxygen molecules will be in the material and water content of the lens; and “t,” the thickness of the material. Increasing the diffusion coefficient or gas solubility will increase oxygen transmissibility, while increasing lens thickness results in a reduction in transmissibility.\textsuperscript{156} The average thickness of a contact lens will vary with lens power.\textsuperscript{157-160} “Dk” is the permeability of the lens material and is a measure of how fast oxygen is passing through the material. The Dk of a hydrogel contact lens can be predicted from its water content:
Log(10)Dk = 0.01785 (WC%) + 0.176. WC% is the water content in percent.¹⁶¹

Dehydration of hydrogel materials can reduce oxygen transmissibility.¹⁶² Lens hydration and transmissibility are impacted by both environmental conditions, such as humidity, temperature, and airflow rates, and subject factors, such as blink rate and tear characteristics.¹⁶²-¹⁶⁴

**Oxygen Tension under a Contact Lens**

Past RGP studies have shown that contact lens material and design can influence the corneal oxygen uptake rates measured after static wear of contact lenses. Contact lenses fitted to parallel the corneal curvature result in the greatest central corneal oxygen debt after short periods of static lens wear, compared to steeper and flatter fits. Steeper lenses provide for a volume of tears between the contact lens and central cornea, whereas flatter lenses might result in slight movement or decentering that could provide oxygenated tears from the annulus of tears in the lens periphery.⁵ Three separate studies, using the PMMA material, have demonstrated the influence of lens diameter on the corneal oxygen uptake rates measured after the static wear of contact lenses. In one study, overall diameter varied from 8.2 to 9.4 mm in 0.3-mm steps. Optic zone diameter was 1.4 mm smaller than the overall diameter, so as to maintain a constant peripheral curve width. The increase in sagittal depth resulted in steeper fitting lenses, increased tear pooling, and reduction in post-exposure corneal oxygen uptake rates.³ In the second study, the optic zone diameter was held constant at 7.4 mm, whereas overall diameter varied from 8.2 to 10.0 mm in 0.3 mm steps. Post-exposure corneal oxygen uptake rates
were not significantly different among these designs, because the volume of tears over
the central cornea remained constant.\textsuperscript{165} In the third study, a constant tear layer thickness
was maintained as overall and optic zone diameters varied (from 7.6 to 10.6 mm for
overall diameter, with optic zone diameter being 1.4 mm smaller) by varying the base
curve radius. The two smallest lenses were associated with significantly lower oxygen
uptake rates than those obtained with the two largest lenses, indicating that central
corneal oxygen demand can increase as more of the cornea is covered.\textsuperscript{166} Other studies
have shown that changes in axial edge lift\textsuperscript{4} and contact lens power,\textsuperscript{167} while keeping all
other parameters constant, do not affect corneal oxygenation under the static wear of non-
gas-permeable contact lenses.

On the other hand, several studies have demonstrated that increasing the oxygen
transmissibility of contact lenses will result in reduction in post-exposure corneal oxygen
uptake rates.\textsuperscript{168-171} Lens material also influences the oxygen supply to the cornea.
Increasing material permeability (Dk) or decreasing lens thickness (t) will increase lens
transmissibility (Dk/t) and oxygen supply to the cornea. While lenses of the same
calculated Dk/t values, but of different Dk and t combinations should evoke the same
corneal oxygen uptake response, it has been shown that this does not happen. It has been
reported that, when a gas permeable hydrophilic contact lens is sandwiched between the
cornea and an impermeable PMMA lens, the oxygen dissolved in the hydrogel lens
serves as a reservoir of oxygen to the cornea during periods of oxygen deprivation.\textsuperscript{172}
The cornea can draw dissolved oxygen from the contact lens for a few minutes, until the
oxygen supply in the lens is exhausted. It is possible to detect this reservoir effect in both
hydrogel and rigid gas permeable lenses. Thick, high Dk rigid gas permeable lenses result in less change in corneal oxygen uptake (compared to the non-lens-wearing eye) than did thin, lower Dk lenses of the same Dk/t.\textsuperscript{173}

**Corneal Oxygenation and Tear Exchange with Rigid Contact Lenses**

Past studies have also quantified the effects of lens materials and designs on both corneal oxygen uptake under dynamic wearing conditions and tear pump efficiency (difference values in oxygen uptake rates between static and dynamic conditions). Contact lenses fitted so that the base curve radius parallels the corneal curvature provide for better tear exchange and larger difference values than do steeper or flatter fitting lenses.\textsuperscript{5,174} Lenses with small overall diameters, regardless of changes in optic zone diameter or tear layer thickness, provide for better tear exchange and larger difference values than do larger lenses.\textsuperscript{3,165-166} Axial edge lifts of 0.13 mm or greater are associated with significantly larger difference values than are axial edge lifts of 0.09 mm or less.\textsuperscript{4} For single cut rigid contact lenses, plus powered lenses are associated with lower difference values than are minus powered lenses.\textsuperscript{167} Tear exchange has been found to be most sensitive to changes in base curve radius, followed by overall diameter change (66.9\% as effective) and axial edge lift changes (64.6\% as effective). Design equivalencies that produced identical tear exchange to 0.05 mm flattening of the base curve toward alignment were 0.07 mm steepening of the base curve toward alignment, 0.35 mm decrease in overall diameter, or 0.037 mm increase in axial edge lift.\textsuperscript{175}
Tear exchange with rigid contact lenses has been measured to be about 9.8%. This depends on lens design, cornea-to-contact lens base curve fitting relationship, and contact lens overall diameter. Flame photometry was used by Cuklanz and Hill to calculate the fraction of tears exchanged per blink for a PMMA contact lens. They measured the concentration of sodium ions placed in the contact lens before insertion of the lens, the concentration of sodium ions in a similar tear volume outside the contact lens, and the concentration of sodium ions in a tear reservoir from the contact lens after a predetermined number of blinks. These measurements determined tear exchange to be 10-15% per blink. Dillehay used freezing point depression nanoliter osmometry to calculate tear exchange. She found a range of 5.59% to 22.88% for rigid contact lenses fitted to parallel the flattest corneal meridian (“on K”). She determined that steeper base curves were associated with reduced tear exchange, while flatter base curve increased tear exchange. Jochum used the same methods to investigate the effects of rigid contact lens diameter on tear exchange, while holding the base curve radius constant. She discovered that smaller diameter lenses allowed for more tear exchange than did larger lenses. Large palpebral apertures were also associated with greater tear exchange.

**Tear Exchange with Hydrogel Contact Lenses**

Past studies have shown that blinking has little effect on the percent of oxygen beneath hydrogel contact lenses. It has been estimated that blinking with hydrogel contact lenses provides only 1-2% tear exchange. Polse found less tear exchange with
hydrogel contact lenses than with rigid contact lenses. He used fluorophotometry with three different hydrogel materials to determine an average fractional tear volume replenishment rate of 0.011. He concluded that the amount of oxygen delivered to the cornea by tear pumping is relatively small for hydrogel lenses and that oxygen received to the cornea covered by such lenses principally comes from diffusion through the material. Soft contact lenses exhibit minimal tear exchange due to their large diameter, close apposition to the cornea, and relative lack of movement.

In a study by Wagner, Polse, and Mandell, altering the cornea-to-contact lens base curve fitting relationship did not reduce corneal edema even though lens movement was altered. On the other hand, Parrish and Larke found that flat-fitting hydrogel lenses resulted in lower corneal oxygen uptake rates, or lower oxygen debt, than steeper lenses when worn under dynamic (with blinking) conditions. They concluded that the lower oxygen uptake rates associated with the flatter lenses were the result of tear pumping, or tear exchange, with the blink. Conversely, Smith found no significant difference in corneal oxygen uptake between static and dynamic conditions following the wear of two soft contact lens materials, and Florkey et al found that blinking resulted in no reduction in corneal oxygen uptake with piggyback systems.

Efron and Fitzgerald simultaneously measured central and peripheral corneal oxygen uptake rates following the wear of non-uniform-thickness (−6.00 D) hydrogel contact lenses under both static and dynamic conditions. While oxygen uptake rates were higher for the peripheral cornea, the corneal oxygen uptake was not affected by blinking at either location, indicating that tear exchange plays an insignificant in corneal
oxygenation during hydrogel contact lens wear. Efron and Carney measured corneal oxygen uptake following the wear of both rigid and soft gas permeable contact lens worn under both static (without blinking) and dynamic (with blinking) wearing conditions. Blinking resulted in a significant reduction in corneal oxygen uptake for the rigid contact lenses but not for the soft contact lenses.\textsuperscript{178}

McNamara et al quantified tear mixing by placing fluorescein isothiocyanate-dextran on the posterior surface of hydrogel contact lenses with diameters of 12.0, 12.5, 13.0, and 13.5 mm. They had twenty-three subjects wear the four different hydrogel contact lens diameters and evaluated the changes in fluorescence intensity in the postlens tear film. Tear mixing was assessed as the percentage decrease in fluorescence intensity per blink. In addition, lens movement was videotaped and lens comfort was graded. The mixing under the 12.0 mm lens was 0.59\% per blink greater than with the 13.5 mm lens (p=0.0024). Lens diameter also influenced lens comfort. After adjusting for the effects of comfort, the relationship between diameter and tear exchange was weakened, although the mean rate under the 12.0 mm lens was still 0.43\% per blink greater than with the 13.5 mm lens (p=0.0468). They concluded that smaller diameter soft lenses provide substantially better tear mixing than larger lenses, but, compared to the tear exchange obtained with rigid contact lenses, the tear exchange is modest. Even the small lenses provided only 1.24\% tear mixing per blink.\textsuperscript{186}

Stehulak evaluated and compared the performance of four silicone hydrogel contact lenses: Vistakon Acuvue® Advance® (galyfilcon A with Hydraclear), Bausch & Lomb PureVision® (balafilcon), Ciba Vision Night & Day® (lotrafilcon A), and Ciba
Vision O2 Optix® (lotrafilcon B). The lenses were evaluated under both static and
dynamic wearing conditions by measuring corneal oxygen uptake. He found no
significant effect of lens material (p=0.072) on tear exchange, measured as the difference
between static and dynamic condition data. However, corneal oxygen uptake associated
with the static wear of the silicone hydrogel contact lenses was significantly higher than
that associated with the dynamic wear of the same lenses (p=0.0006). He concluded that
the additional oxygen supplied via tear exchange resulted in lower oxygen uptake
following dynamic conditions. He also concluded that the fact that a significant
difference was found with silicone hydrogel lenses indicates that they provided better tear
exchange than hydrogel lenses. A possible reason for this is that the modulus of
elasticity, an indication of the stiffness of the materials, is greater for the silicone
hydrogel materials than for the hydrogel materials. A stiffer lens might be expected to
behave like a rigid lens, standing away from the corneal surface, rather than conforming
to it.\textsuperscript{187}

In addition, it has been shown that significantly larger differences between static
and dynamic condition data are seen for materials of lower Dk than with materials of
higher Dk, with lenses of moderate to high transmissibilities resulting in difference
values that are not significantly different from each other.\textsuperscript{170} Within a particular material,
these differences in oxygen shortfall between static and dynamic wearing conditions
serve as an index of tear pump efficiency. Across materials, however, these differences
reflect differences in lens transmissibility. After exposure to low levels of oxygen, such
as the cornea experiences beneath lenses of low transmissibility, there is a much more
marked increase in corneal oxygen uptake compared to readings after exposure to moderate levels of oxygen.\textsuperscript{7} The relationship between oxygen uptake and lens transmissibility at high transmissibilities is such that a large increase in transmissibility is necessary to result in a significant reduction in oxygen uptake.\textsuperscript{168-170, 187} Increases in oxygen tension through tear exchange will, therefore, result in a more pronounced difference between static and dynamic condition data for materials of low permeability. When comparing materials, differences in oxygen shortfall between static and dynamic conditions reflect different corneal oxygen dynamics rather than actual differences in tear exchange. For lenses of high transmissibility, the tear pump plays only a minor role in corneal oxygenation and no statistically significant differences have been noted in the oxygen shortfall between static and dynamic wear for high Dk rigid gas permeable materials.\textsuperscript{168} In addition, lid closure during blinking reduces the oxygen available for transmission through lenses of high transmissibility; therefore, oxygen uptake rates can actually be higher following dynamic wear of the lenses than following static wear of the lenses.\textsuperscript{168} Benjamin and Hill showed that even brief periods of lid closure, such as occurs during blinking, can result in increase in corneal oxygen uptake rates for the normal open eye without a lens.\textsuperscript{8}

When hydrogel contact lenses are worn, measurable and significant lens dehydration takes place due to evaporation.\textsuperscript{163, 188} Because the oxygen permeability of hydrogel materials is dependent on water content and is limited by the solubility of oxygen in water, lens dehydration is associated with a reduction in oxygen transmissibility of the lenses, resulting in increased corneal oxygen uptake rates.
following contact lens wear. If the degree of lens dehydration is not equal for static and dynamic wearing conditions, then tear exchange determined as the difference between static and dynamic condition data might be over or under-estimated.
Chapter 2: Objectives

The purpose of this study is to compare the physiological response of the cornea to three hydrogel contact lens diameters. Measurement of corneal oxygen uptake will be used as the physiological indicator of corneal oxygenation, with lower oxygen uptake rates being associated with more oxygenation. The contact lenses will be worn under both static (without blinking) and dynamic (with blinking once every 5 seconds) conditions. A comparison of the oxygen uptake rates obtained under static and dynamic conditions will evaluate how well lens design provides for tear exchange with the blink. Measurements will be made for both the central and peripheral cornea to determine if blinking increases oxygenation at both locations. The specific objectives of this study include the following:

1. To determine if there are significant differences in the oxygen uptake rates, relative to air, associated with the central and peripheral cornea.
2. To determine if there are significant differences in the oxygen uptake rates, relative to air, associated with different lens diameters.
3. To determine if there are significant differences in oxygen uptake rates, relative to air, between static and dynamic wearing conditions.
4. To determine if there are significant differences in the difference values between static and dynamic wearing conditions associated with different lens diameters.
Chapter 3: Methods

Introduction

Measurement of corneal oxygen uptake was used as a physiological indicator of corneal oxygenation during contact lens wear, with lower oxygen uptake rates being associated with more oxygenation. The effect of hydrogel contact lens diameter on corneal oxygenation was determined for both central and peripheral corneal locations under both static (without blinking) and dynamic (with blinking once every five seconds) wearing conditions. Therefore, corneal oxygen uptake rates were measured on the right eyes of fifteen subjects at two locations for the normal open eye and at two locations after five minutes of hydrogel contact lens wear. Subjects wore the contact lenses for five minutes because past studies have shown that the maximum rate of oxygen uptake is reached in about three minutes of contact lens wear in the open eye.\textsuperscript{190-191} Recovery of the normal oxygen uptake rate after exposure to environments of oxygen content lower than that of air occurs within sixty seconds of re-exposure to the normal air atmosphere.\textsuperscript{190, 192-195} Five minutes were allotted in this study between lenses. Contact lenses were worn under both static and dynamic conditions. A comparison of the oxygen uptake rates obtained under static and dynamic conditions evaluates how well lens design provides for tear exchange with the blink, with lower oxygen uptake rates being
anticipated under dynamic wearing conditions if tear exchange takes place. Measurements were made for both the central and peripheral cornea to determine if blinking increases oxygenation at either or both locations. Three different contact lens diameters were evaluated: 13.0 mm, 14.0 mm, and 15.0 mm.

Subjects

Human subjects were needed for this study because the purpose of this study is to determine the physiological response of the human ocular surface to three different hydrogel lens diameters and two blinking conditions. Past studies involving measurement of corneal oxygen uptake with various lenses and materials have determined an estimated population standard deviation of seven percent. The standard deviation for this study is unknown, but can be estimated from the past studies as being about seven percent. Using Ott’s equation based on alpha = 0.05, beta = 0.10, and an estimated population standard deviation, fifteen subjects were recruited for this study. Recruitment occurred through e-mail and word-of-mouth. After the study had been explained to the subjects, they signed a “Consent to Participate in Research” form previously approved by The Ohio State University’s Health Science Human Subject Review Committee.

Eligibility criterion included that subjects had to be greater than or equal to eighteen years of age. The ocular dimensions (corneal curvature, toricity) had to be typical or representative of those of the normal population. Subjects had to have good ocular health and could not have worn contact lenses for at least thirty days prior to the
study. Ocular parameters were considered to be typical of those of the normal population if keratometry measurements were between 39.00 D and 48.00 D, corneal toricity was between 0 D and 2.50 D, and palpebral aperture size was between 8.0 mm and 13.0 mm.

Prior to data collection, subjects were be given a vision examination to assess the ocular parameters and health and assure eligibility for the study. The vision examination conducted on the first visit including questions regarding: date of birth, age, systemic or season allergies, systemic health, ocular and systemic medications, and history of contact lens wear. Measurements included: palpebral aperture height, corneal diameter, corneal curvature, visual acuity, refraction and tear break-up time (TBUT) were recorded. Iris color was also documented. Candidates free of corneal disease that had not worn contacts within thirty days of the exam were enrolled in the study for measurement sessions. Right eye keratometry measurements were used to determine the fit for the contact lenses.

Of the fifteen subjects enrolled in the study, seven were females and eight were males. All fifteen subjects were Caucasian. The subject’s age varied from 23-55 years old. Subject profiles can be found in Tables 1-15. The mean keratometry measurement for the flattest corneal meridian of the right eyes was 42.86D and ranged from 40.62D to 45.07D. The mean corneal toricity of the right eyes was 0.62D and ranged from 0.05D to 1.62D. The mean palpebral aperture height of the right eyes was 11mm and ranged from 8mm to 13mm.
**Contact Lenses**

All subjects were fitted with three diameters of one hydrogel contact lens material. This lens was made of polymacon, available from Alden Optical. The lens parameters are listed in Table 16. They have a water content of 38% and a permeability (Dk) of $9.0 \times 10^{-9}$ (cm/sec)(mlO$_2$/ml x mmHg) and a Dk/t of 9.0. This low transmissibility was used so that the effects of tear exchange on corneal oxygenation would not be masked by transmission of oxygen through the lens. Three overall diameters were used: 13.0 mm, 14.0 mm, and 15.0 mm. The back vertex power was -3.00 D, which was considered typical for contact lens wearers. The center thickness of the lenses was 0.10 mm. The lenses were of a simple bicurve design, with an 8.5 mm front optical diameter for all lenses. Because the lenses were -3.00 D in power, lens thickness increased from the center toward the periphery of the lenses. Thickness profiles of the lenses vary somewhat with the diameter and base curve of the lenses; however, the thickest portion of the lens was approximately 1 mm from the lens edge.

The base curve of the contact lenses varied depending on the overall diameter. Alden manufactured lenses for the study that ranged from 6.5 mm to 9.8 mm in 0.1 mm steps. Increasing overall diameter will increase the sagittal depth of the contact lens, necessitating a flattening of the base curve radius to maintain a constant sagittal depth. In addition, the cornea becomes flatter towards the periphery; therefore, a flatter base curve radius is also needed to maintain the cornea-to-contact-lens fitting relationship. Alden Optical provided a table of recommended base curve radii for the three contact lens diameters used. This is shown in Table 17.
Polymethylmethacrylate (PMMA) lenses were also used. This material is not permeable to oxygen so that the maximum oxygen uptake rate of each cornea can be determined. The PMMA contact lenses had the following parameters:

Overall diameter: 8.8 mm
Optic zone diameter: 7.4 mm
Axial edge lift: 0.09 mm
Back vertex power: -3.00 D
Center thickness: 0.12 mm
Base curve radius: fitted “on K”

The PMMA lenses were fitted “on K” or parallel to the flattest meridian of the cornea in order to minimize the tear thickness between the cornea and the contact lens. All lenses were nontoxic to the cornea.

**Equipment**

The equipment used in measuring corneal oxygen uptake rates consisted of a polarographic electrode, a gas analyzer, a chart recorder, a water tank heater and compressed gas cylinders. A Clark-type Radiometer Copenhagen polarographic electrode was used to measure corneal oxygen uptake rates. It was connected to a Radiometer Copenhagen pH/blood gas analyzer. The electrode consisted of a platinum cathode, 25 um in diameter, and a silver anode, 500 um in diameter. They were sealed, side by side, in glass, and the contact end of the probe was flat. The glass probe was
immersed in a Lucite tube filled with a buffered electrolyte solution, to provide an electrolyte layer over the anode and cathode. The electrolyte consisted of disodium hydrogen phosphate dihydrate, potassium dihydrogen phosphate, potassium chloride, and silver chloride. The external source of about -630 mV provided the electrons for reduction of oxygen at the cathode, while oxidation took place at the anode.

A polyethylene membrane was fitted directly over the oxygen probe, held in place with an O-ring, and was used as a small oxygen reservoir. This oxygen reservoir cannot be measured accurately, and it allows for non-steady state diffusion of oxygen from the probe to the cornea. The membrane material, thickness, and solubility of oxygen in the materials can have effects on the oxygen uptake rates obtained. Therefore, data acquired by this method are for comparison to other measurements. Measurements obtained with the contact lenses are divided by those obtained for the normal open eye to factor out membrane influences. These data indicate how much oxygen uptake rates are elevated above those of the normal open eye following contact lens wear.

The reduction of the dissolved oxygen at the cathode sets up an electric current through the electrolyte solution, which is proportional to the oxygen tension in the membrane. As the probed is pressed perpendicularly against the cornea, the oxygen from the probe enters the cornea (diffusion or consumption). The supply of oxygen to the electrode decreases, resulting in a reduction in current and a reduction of oxygen tension being displayed on the gas analyzer.

The data produced by these instruments were recorded on a Fisher Recordall Series 5000 recording chart that was connected to the gas analyzer. Both the gas analyzer
and graph paper demonstrated a reduction in oxygen tension over time as the oxygen probe was pressed to the cornea. Oxygen uptake rates could be measured from the chart paper as the slope of the line generated. The slope was determined between 140 mm Hg and 40 mm Hg, by measuring the horizontal distance between where the line intersected the 140 and 40 mm Hg marks. This part of the line was used because it is most consistent, has been traditionally used by studies in the past, and makes calculations of oxygen uptake rate easy. The calculations of oxygen uptake rate took into consideration that the chart moved at a speed of 10 inches per minute. Steeper slopes indicated greater oxygen uptake rates, and these indicate more severe oxygen deprivation with contact lens wear.

A water bath made by Precision Scientific, Inc. was used to regulate the temperature of the saline where the polarographic electrode rested between measurements. It was maintained at corneal temperature, 36 °C. One hour prior to each data-collecting session, the equipment was turned on so the water bath could be heated to 36 °C and the equipment could be calibrated. To prepare the water bath, distilled water was added to fill it about half full. Two jars of 0.9% saline were used in the calibration procedure. They were partially filled with marbles, to keep them from floating in the water bath, and inserted into the water bath. Both baths, therefore, were maintained at a temperature of 36 °C, because the oxygen sensor is sensitive to changes in temperature. The gas analyzer was calibrated for the 155 mm Hg (air) and 0 mm HG (nitrogen) oxygen positions. All other oxygen tension values that would be measured lie linearly between these two positions, since the oxygen tension is proportional to current output.
The oxygen probe was first placed into the bath bubbled with tubing from a tank of compressed nitrogen. The monitor and chart recorder were both set to zero. The oxygen probe was then immersed into the second bath, which had been bubbled with air from an aquarium pump (Second Nature Whisper 600), establishing the 155 mmHg oxygen tension level on the monitor and chart recorder.

The response of the polarographic electrode system to a change in oxygen tension is not immediate. It depends on cathode diameter, membrane thickness, solubility of oxygen in the membrane material, and inertia in the system. The true drop in oxygen tension with time due to oxygen uptake by the cornea can be obtained by subtracting a time constant. The time constant is defined as the time required for the reservoir oxygen tension to drop from 140 mm Hg to 40 mm Hg when the probe is set first in the air-saturated saline bath and then immediately into the nitrogen-saturated bath. The probe containing the electrode was placed in the jar of saline bubbled with air, and the gas analyzer and chart recorder were calibrated to read 155 mm Hg. The chart recorder was switched on. The electrode was then quickly removed from the first jar and inserted into the jar with nitrogen-bubbled saline. This allowed a time constant to be determined.

Determining the time constant was the final step of the calibration process. The time constant for this project has been defined as the time it takes the pen on the chart recorder to move from the 140 mmHg line to the 40 mmHg line as the information was transferred from the probe to the gas analyzer to the recorded output. It was previously determined that the paper could not advance more than 8 mm as recorded by the chart recorder in the time it took the pen to travel from the 140 mmHg to 40 mmHg line. If
more than 8mm was recorded the probe was disassembled and reconstructed for recalibration. In other words, time constants of less than two seconds were considered satisfactory. The time constant was subtracted from each oxygen uptake measurement.

**Procedure**

Prior to each of the data-gathering sessions, the equipment was stabilized for one hour and calibrated, and the time constant was determined. The electrode tip was scrubbed and rinsed in tap water and electrolyte solution prior to membrane application. A new polyethylene membrane of about 13 microns in thickness was used for each session. The membranes were stretched slightly when placed over the electrode in order to assure that the membrane was thin enough to assure a satisfactory time constant. The membrane was examined to assure there were no folds in the membrane or bubbles trapped between the membrane and the electrode. The temperature of the water bath was checked prior to calibration and throughout each data-gathering session to make sure it remained at corneal temperature.

Oxygen uptake rates were measured at two locations for the normal open eye and at two locations after 5 minutes of contact lens wear for both dynamic and static blinking conditions while wearing the hydrogel contact lenses, as well as for the central cornea after PMMA contact lens wear. The measurements made included the following:

1. Normal open eye, central cornea (minimum response)
2. Normal open eye, periphery (minimum response)
3. PMMA, static, central cornea (maximum response)
4. PMMA, dynamic, central cornea
5. After 5 minutes of 13.0 lens, static, central
6. After 5 minutes of 13.0 lens, dynamic, central
7. After 5 minutes of 13.0 lens, static, peripheral
8. After 5 minutes of 13.0 lens, dynamic, peripheral
9. After 5 minutes of 14.0 lens, static, central
10. After 5 minutes of 14.0 lens, dynamic, central
11. After 5 minutes of 14.0 lens, static, peripheral
12. After 5 minutes of 14.0, dynamic, peripheral
13. After 5 minutes of 15.0 lens, static, central
14. After 5 minutes of 15.0 lens, dynamic, central
15. After 5 minutes of 15.0 lens, static, peripheral
16. After 5 minutes of 15.0 lens, dynamic, peripheral

All measurements were made in a random order as numbers 1-16 were drawn consecutively from a box indicating the measurement to be done. All measurements were performed on the unanesthetized corneas of the right eyes of the subjects. Two oxygen uptake measurements of each session were of the normal open eye, both central and peripheral, before any contact lens was inserted or after five minutes of contact lens wear. These measurements were the longest measurements to make since the oxygen uptake rate is slowest under this condition. For the central measurement, the experimenter held the subject’s lid while the subject fixated straight ahead. The oxygen probe was applied
directly and perpendicularly to the cornea. For the peripheral corneal measurement, a stand containing a fixation point and a light source was placed 29.7 mm in front of the subject’s right cornea. For peripheral measurements the subject was instructed to look at a fixation point located 11.5 mm to the left of the central target and light source positioned 29.7 mm from the patient’s cornea. This nasal peripheral gaze caused the light source to project an image 5 mm from the center of the cornea, just inside the patient’s temporal limbus.

Another measurement of each session was taken after 5 minutes of wear of the PMMA contact lens. This resulted in the greatest degree of corneal hypoxia, because the lens is impermeable to oxygen, fitted so that there was a small reservoir of tears between the cornea and the contact lens, and blinking was not permitted so there was little to no tear exchange.

During static wearing periods, the experimenter placed the contact lens on the subject’s cornea and the experimenter continued to hold the lid away from the contact lens, to prevent interaction between the upper lid and the contact lens. The subject fixated straight ahead during static wearing periods so that eye movement would not cause the lens to move on the eye and result in tear exchange beneath the lens. The contact lens was spritzed with saline solution at the 2 minute and 4 minute mark of the static wearing sessions to prevent contact lens dehydration. The subject used a tissue to blot any excess tears that might accumulate during the five minutes of lens wear so that the contact lens would not move as the result of excessive tearing. The experimenter checked the contact lens position and movement throughout the five minute wearing
periods. With thirty seconds remaining in the wearing period, the experimenter had the subject reach over his own head with his left hand and grip his right upper lid margin, holding the lid securely against the bony orbit. The experimenter then turned on the chart recorder, removed the contact lens with a suction cup, and placed the oxygen probe on the cornea to measure its oxygen uptake rate. The experimenter counted one second between contact lens removal and probe application.

Oxygen uptake rates were made for the contact lens diameter/location/wearing condition in random order as mentioned previously. The static wearing periods with the hydrogel contact lenses was similar to that for the PMMA contact lens, except that the lens was not removed with a suction cup. It was manually slid off the cornea for measurements to be made centrally or peripherally. For the dynamic wearing periods, the experiments again inserted the contact lens, but then released first the lower lid and then the upper lid. The subject was to blink once every five seconds to a tone generation by a computer. The subject was instructed to blink fully but normally, not forcing his/her lids closed during blinks. Between blinks the subject once again kept both lids open and fixated straight ahead. With fifteen seconds remaining, the subject was told he/she had three blinks to go, and the chart recorder was switched on. As soon as the subject had completed the last blink, he/she reached over his head with his left hand and firmly held open the upper lid of the right eye. He either fixated straight ahead or at the peripheral target for central and peripheral measurements, respectively. The lens was slid off the cornea and the oxygen probe applied one second later, as was done for static wearing.
conditions. Five minutes with no lens wear separated the five-minute periods of lens wear allowed oxygen uptake rates to return to baseline levels.190, 193-195

Each subject participated in three sessions. During the first session, subjects were provided with an eye examination and the lenses were fitted. They also practiced having corneal oxygen uptake measurements made. The second and third sessions consisted of the sixteen measurements of oxygen uptake.

Data Analyses

After each measurement session the corneal oxygen uptake rates were computed. To determine this rate a millimeter ruler was used to measure the linear distance between the marks were the pen passed through the 140 mmHg line and the 40 mmHg line. From this measured distance the determined time constant was subtracted.

The chart recorded was set to advance the paper at 10 inches per minute, or 4.167 mm/second or written inversely as 0.24sec/mm. The net distance recorded in millimeters as mentioned in the previous paragraph can converted to a time unit by multiplying the net distance by the paper’s advancement rate. To determine our final oxygen uptake rate the change in partial pressure (140 mm Hg-40 mm Hg) was divided by the computed time as was reported in mmHg/sec. To simplify the above calculation, 416.67 was divided by all net distances measured to give oxygen uptake rates in mmHg/sec.
Statistical Analysis

Population mean oxygen uptake rates were computed along with their standard deviations for 3 contact lens diameters, 2 wearing conditions, and 2 corneal locations. The oxygen uptake rate means were calculated by adding two measurements from each measurement session for each subject for a specific diameter, location and condition. After the two measurements were added, they were divided by 2 giving us a mean oxygen uptake rate data point.

The overall mean for each diameter, condition and location were also given, along with their standard error and 95% confidence intervals. A mixed linear model was used to compare the effect of lens diameter, condition and location on the calculated means. The initial model included checking for a 3-way interaction, and then all possible 2-way interactions with the data. When a significant result was found for lens diameter, a post-hoc comparison of the means between lens diameters was calculated to reveal why a significant value was calculated for diameter. The post-hoc analysis adjusted the p-values obtained for multiple comparisons using the method of Tukey-Kramer.

Difference values between mean relative static condition data and mean relative dynamic condition data for the 13.0, 14.0, 15.0 mm diameter contact lenses, with standard deviations, minimum and maximum values, and 95% confidence limits for the mean were obtained. Similar difference values were also calculated for the central and peripheral cornea. A repeated measures analysis to assess the impact of lens diameter and location on the difference values between the static and dynamic condition data was also completed.
Chapter 4: Results

**Absolute Oxygen Uptake Rate Data**

Tables 18-32 show the absolute oxygen uptake rate data for two sessions for each subject under static and dynamic lens wearing conditions in central and peripheral locations for 13mm, 14mm and 15mm overall diameter Alden Classic hydrogel contact lenses. Uptake rate measurements are given in the units mmHg/sec. Tables 18-32 also include oxygen uptake rate measurements of the normal open eye, prior to contact lens wear or after 5 minutes of no contact lens wear. These measurements are called “normal open eye” measurements. Oxygen uptake rates after the static and dynamic wear of PMMA contact lenses are also recorded with measurements at the central location only.

Table 33 shows the population statistics, including the mean oxygen uptake rates and standard deviations for three contact lens diameters (13.0, 14.0 and 15.0mm), two wearing conditions (static and dynamic), and two corneal locations (central and peripheral). It can be seen that, for both the central and peripheral cornea and for all three lens diameters, oxygen uptake rates obtained under static wearing conditions appear to be higher than those obtained under dynamic wearing conditions.
Oxygen Uptake Rate Relative to Air in Central and Peripheral Locations After Static and Dynamic Wear

Tables 34-36 show the oxygen uptake rate data relative to air for subjects under static and dynamic lens wearing conditions in central and peripheral locations for 13mm, 14mm and 15mm diameter Alden Classic hydrogel contact lenses. In order to calculate the oxygen uptake rate relative to air, each oxygen uptake rate determined following contact lens wear was divided by the oxygen uptake determined for the normal open eye for the same subject, session, and corneal location. Uptake relative to air was calculated at each visit and then the average of the response at both visits was used in these analyses.

Table 37 shows the population statistics including mean oxygen uptake rates and standard deviations for measurements relative to those of the normal open eye for 3 contact lens diameters (13.0, 14.0, and 15.0 mm), 2 wearing conditions (static and dynamic), and 2 corneal locations (central and peripheral). Once again, it appears that the relativized corneal oxygen uptake associated with the dynamic wear of contact lenses is less than that associated with the static wear of contact lenses for all three diameters and for both the central and peripheral cornea.

Data Analysis of Oxygen Uptake Rates

Tables 38 shows the mean, standard error and 95% confidence interval for the relative oxygen uptake rates stratifying based on lens diameter, condition and location. Table 39 shows the results of mixed linear modeling comparing the effect of lens
diameter, condition and location on oxygen uptake relative to open eye. Table 40 contains post-hoc comparisons of mean oxygen uptake relative to air between lens diameters.

Collectively, Tables 38-40 show corneal oxygen uptake rates increased with increasing lens diameter (p=0.006) regardless of location (central or peripheral) or condition (static or dynamic). The mean oxygen update relative to air was 4.59 (std=0.8) for the 13mm lens, 4.99 (std=1.4) for the 14mm lens, and 5.03 (std=0.9) for the 15mm lens. For all lens diameters, uptake relative to air was higher under static conditions (mean=5.18, std=1.2) compared to dynamic conditions (mean=4.56, std=0.7, p=0.001). Oxygen uptake relative to air was higher in the periphery (mean=4.95, std=0.9) compared to the central cornea (mean=4.79, std=1.2, p=0.011).

A repeated measures analysis was used to assess the impact of lens diameter and location on the difference values between mean relative static condition data and mean relative dynamic condition data. There was no difference with respect to lens diameter (p=0.12) or location (p=0.059). The large variability resulted in non-significant p-values. Table 41 shows the difference values between mean relative static condition data and mean relative dynamic condition data for the 13.0, 14.0, and 15.0 mm diameter contact lenses, with standard deviations, minimum and maximum values, and 95% confidence limits for the mean. Table 42 shows the difference values between mean relative static condition data and mean relative dynamic condition data for the central and peripheral cornea, with the standard deviations, minimum and maximum values, and 95% confidence limits for the mean. Table 43 shows the impact of lens diameter and location
on the difference values between mean relative static condition data and mean relative
dynamic condition data.
Chapter 5: Discussion

Use of Oxygen Uptake Relative to that of the Normal Open Eye

When measuring corneal oxygen uptake by fitting a polyethylene membrane directly over the polarographic electrode, the volume of the oxygen reservoir, which is needed in the calculation of corneal oxygen uptake, cannot be measured accurately.\textsuperscript{197} The tear film, electrolyte fluid between the membrane and the probe, and the membrane itself are all part of the oxygen reservoir; all are variable, even during the taking of the measurements.\textsuperscript{198} In addition, there is a non-steady-state diffusion of oxygen from the probe to the cornea. Therefore, it is best to compare oxygen uptake measurements obtained following contact lens wear, rather than evaluate the rates in mmHg/sec.\textsuperscript{198}

Historically, four methods have been used to record the cornea’s response to its oxygen environment. The first is to report the absolute units, mmHg/sec. Another method is to record the ratio of the corneal oxygen uptake under test conditions (e.g., with contact lens wear) to the corneal oxygen uptake for the normal open eye in air. A third method is to report the percentage of the cornea’s response to hypoxia, as with a five-minute exposure to 100% nitrogen or following the wear of a PMMA contact lens. Finally, corneal oxygen uptake may be presented as a proportion of the total hypoxic range (air to PMMA), within the scale of 0-100 oxygen shortfall units (OSUs).\textsuperscript{193}
The repeatability of measurements of corneal oxygen uptake was studied for six human corneas over the course of 3 years. Oxygen uptake rates obtained after PMMA contact lens wear were compared to those obtained for the normal open eye. Significant differences were found between the three measurement periods for the normal open eye data and for the data associated with contact lens wear; however, no significant differences were found for the relativized data (oxygen uptake rates obtained with the contact lens wear divided by those obtained for the normal open eye). Use of the relativized data better reveals differences between subjects and test conditions.

For this discussion, the data relativized to that of the normal open eye will be used. In order to calculate the oxygen uptake rate relative to air, each oxygen uptake rate determined following contact lens wear was divided by the oxygen uptake rate determined for the normal open eye for the same subject, session, and corneal location.

**Oxygen Uptake Rates of the Central and Peripheral Cornea**

Table 37 shows the mean oxygen uptake rates relative to those of the normal open eye for 3 contact lens diameters (13.0, 14.0 and 15.0 mm), 2 wearing conditions (static and dynamic, and 2 corneal locations (central and peripheral). Each mean is the result of 2 measurements on each of the 15 subjects. The standard deviations are also shown. The data associated with the central and peripheral cornea can be compared for each lens diameter and wearing condition.

From Table 37, it appears that, under static conditions, the mean relativized corneal oxygen uptake for the central cornea is lower than that of the peripheral cornea.
for 13.0 mm diameter lens (4.69 versus 4.84), but higher than that of the peripheral cornea for the 14.0 mm diameter lens (5.61 versus 5.32) and for the 15.0 mm diameter lens (5.42 versus 5.22). Under dynamic conditions, the mean relativized corneal oxygen uptake for the central cornea is lower than that of the peripheral cornea for all three lens diameters: 13.0 mm (4.34 versus 4.50), 14.0 mm (4.22 versus 4.83), and 15.0 mm (4.48 versus 4.99). Table 38 demonstrates that, collectively, oxygen uptake relative to air was higher in the periphery (mean=4.95, std=0.9) compared to the central cornea (mean=4.79, std=1.2, p=0.011). As Table 39 shows, there were no significant interactions between corneal location and lens diameter or between corneal location and wearing condition.

Past studies have investigated the effect of corneal location on corneal oxygen uptake and have found conflicting results. Hill measured the respiratory profiles of the rabbit cornea and concluded that the oxygen uptake rate, in mmHg/sec, does not seem to vary along the 180° meridian of the corneal.\textsuperscript{200} Efron and Fitzgerald measured human corneal oxygen uptake rates for the central cornea and at four sites peripheral to the center of the cornea—superior, nasal, inferior, and temporal.\textsuperscript{185} They found no differences in oxygen uptake rate, in mmHg/sec, among the five locations. Fink et al. found no difference in corneal oxygen uptake for these same five corneal sites under either open or closed eye conditions.\textsuperscript{201} Pilskalns measured corneal oxygen uptake rates of 15 subjects with keratoconus at three corneal locations: central cornea, 2.5 mm temporal to central, and 4.5 mm temporal to central.\textsuperscript{202} The mean oxygen uptake rates under normal open eye conditions were not significantly different among the three corneal locations measured.
On the other hand, Szczotka et al found that human, open-eye corneal oxygen uptake rates are significantly greater for the inferior cornea than for the central cornea. Inferior corneal oxygen uptake rates were 1.14x that of the central cornea (p<0.0001).\textsuperscript{203} It was speculated that this was due to thicker layers of respiring corneal epithelial cells in the peripheral cornea. Following 300 seconds of lid closure, the oxygen uptake rate of the inferior cornea was significantly greater than that of the central cornea (p=0.008), with measurements of 1.49x and 1.44x that of the open-eye central cornea for the inferior and central cornea, respectively.\textsuperscript{204} Brunstetter et al. found that the oxygen uptake of the inferior cornea was 1.03x that of the central cornea (p=0.004).\textsuperscript{205}

Because the superior cornea is often covered by the upper eyelid, Benjamin and Hill compared the corneal oxygen uptake rates of the central and superior cornea. They found that the oxygen uptake rates for the superior cornea were 1.48x to 2.41x those of the central (open eye) cornea.\textsuperscript{206} The superior cornea is thicker than the central cornea, but it is thinner than the temporal, inferior, and nasal peripheral cornea.\textsuperscript{207-209}

In the present study, contact lens thickness might account for differences in relativized corneal oxygen uptakes between the central and peripheral cornea. The study lenses had a power of -3.00 D and were thicker in the periphery than in the center of the lens. Although the thickness profiles of the lenses varied somewhat with lens diameter and base curve radius, the thickest portion of the contact lenses was about 1 mm from the lens edge. Increase in lens thickness results in a reduction in lens transmissibility. Therefore, less oxygen diffused through the peripheral portions of the contact lenses than through the central portion, resulting in a lower oxygen tension over the peripheral cornea
than over the central cornea. It would be anticipated that the lower oxygen tension over the peripheral cornea would, therefore, be associated with higher oxygen uptake rates of the peripheral cornea.

**Effect of Lens Diameter**

We evaluated the influence of lens diameter on corneal oxygen uptake by comparing 13mm, 14mm and 15mm diameter lenses. These three diameters were selected because they bracket the current customary soft contact lens diameter options available to clinicians of 13.8 mm and 14.5 mm. The 13mm lens had a mean oxygen uptake rate of 4.59 (SE= 0.78), the 14mm lens’ mean oxygen uptake rate was 4.99 (SE=1.35) and the 15mm lens had an oxygen uptake rate of 5.03 (SE=0.85) including both static and dynamic measurements. Thus, according to Tables 38-40, corneal oxygen uptake rates significantly increase (p=0.006) with increasing lens diameter.

Three previous studies using PMMA material have demonstrated the influence of lens diameter on the corneal oxygen uptake rates measured after the static wear of contact lenses. In one study, where overall diameter was varied from 8.2 to 9.4 mm in 0.3-mm steps, the increase in sagittal depth associated with a larger diameter lens resulted in steeper fitting lenses, increased tear pooling, and a reduction in corneal oxygen uptake rates after lens removal.\(^3\) In a second study, overall diameter was varied from 8.2 to 10.0 mm while the optic zone diameter was held constant at 7.4 mm. They found corneal oxygen uptake rates measured after lens removal were not significantly different between the different diameter lenses. It is thought that the reason for this lack of change is the
volume of tears over the central cornea remained constant despite the change in lens diameter. In the third study, a constant tear layer thickness was maintained as overall diameter and optic zone diameter varied by varying the base curve radius. They found the two smallest lenses, with the smallest being 7.6 mm, to be associated with significantly lower oxygen uptake rates than those obtained with the two largest lenses, with the largest lens being 10.6 mm. This indicated that central corneal oxygen demand increases as more of the cornea is covered.

Our present study, using Alden Classic hydrogel lenses, finds similar results to the previously mentioned PMMA lens studies, finding corneal oxygen uptake rates to significantly increase as more of the cornea is covered. During the static wear of contact lenses, oxygen is supplied to the cornea by passing through the lens and by the tear reservoir between the contact lens and the cornea. Differences in corneal oxygen uptake among the lenses, therefore, can usually be explained in terms of lens transmissibility and fit. Transmissibility was the same for all lenses for the center of the lenses. However, because all lenses were -3.00D, the larger diameter lenses had greater peripheral thickness, greater average thickness, and lower transmissibility at the periphery of the lens. The greatest thickness of the lenses was approximately 1 mm from the edge of the lenses, although this varied somewhat with lens diameter and base curve radius. The cornea-to-contact lens base curve relationship should also have been the same, providing the same volume of tears between the contact lens and the cornea. In contrast to the volume of tears that is increased by increasing sagittal depth of rigid contact lens, whether this is done by increasing lens diameter or reducing lens base curve radius,
hydrogel contact lens materials tend to drape the cornea, regardless of their sagittal depth. Therefore, changes in hydrogel lens fit have less influence on the tear volume between the corneal and the contact lens. This study suggests diameter of hydrogel contact lenses should be considered as new lenses are developed with the goal of making lenses as healthy for patients’ eyes as possible.

Effect of Wearing Condition

In our study, for all lens diameters, uptake relative to air was higher under static conditions (mean=5.18, std=1.2) than under dynamic conditions (mean=4.56, std=0.7, p=0.001). Previous studies have likewise compared wearing condition and had differing results. One study showed that blinking has little effect on the percent of oxygen beneath hydrogel contact lenses. Another study estimated blinking with hydrogel contact lenses only provides 1-2% tear exchange. Smith found no significant difference in corneal oxygen uptake between static and dynamic conditions following the wear of two soft contact lens materials, and Florkey et al found that blinking resulted in no reduction in corneal oxygen uptake with piggyback systems. Efron and Fitzgerald simultaneously measured central and peripheral corneal oxygen uptake rates following the wear of non-uniform-thickness (-6.00 D) hydrogel contact lenses under both static and dynamic conditions. Corneal oxygen uptake was not affected by blinking at either the central or peripheral location, indicating that tear exchange plays an insignificant role in corneal oxygenation during hydrogel contact lens wear. Furthermore, Efron and Carney measured corneal oxygen uptake following the wear of both rigid and soft gas
permeable contact lens worn under both static (without blinking) and dynamic (with blinking) wearing conditions. Blinking resulted in a significant reduction in corneal oxygen uptake for the rigid contact lenses but not for the soft contact lenses.\textsuperscript{178}

It has been shown that significantly larger oxygen uptake rate differences between static and dynamic conditions are seen for materials of lower Dk than with materials of higher Dk, with lenses of moderate to high transmissibility resulting in difference values that are not significantly different from each other.\textsuperscript{170} This may explain why the results from this study vary from some of the previous studies. This study used Alden Classic hydrogel contact lenses what have a lower Dk of $9.0 \times 10^{-9}$ (cm/sec)(mlO$_2$/ml x mmHg) so that the effects of tear exchange on corneal oxygenation would not be masked by transmission of oxygen through the lens.

When hydrogel contact lenses are worn, measurable and significant lens dehydration takes place due to evaporation.\textsuperscript{188, 210} This is associated with a reduction in oxygen transmissibility of the lenses, resulting in increased corneal oxygen uptake rates following contact lens wear.\textsuperscript{189} It is possible that more lens dehydration took place during the static wear of the contact lenses than during the dynamic wear of the lenses. If this were the case, then the differences between the oxygen uptake rates measured under static and dynamic conditions would have been exaggerated.

**Lens Diameter and Tear Exchange**

During contact lens wear, there are two possible mechanisms by which oxygen is provided to the cornea: transmission through the lens material or through the stirring and
recirculation of tears with the blink, also known as the tear pump. Our study compared tear pump efficiency (difference values in oxygen uptake rates between static and dynamic conditions) for all three diameters, (13 mm, 14 mm and 15 mm) in both central and peripheral locations with the Alden Classic hydrogel contact lens. As seen in Tables 41-43, neither diameter (p=0.12) nor location (p=0.06) had a significant impact on tear pump efficiency. The 14 mm lenses had a mean (0.94, std=1.61) greater than the 13 mm (mean= 0.34, std=0.84) and 15 mm (mean= 0.59, std=1.07) lenses. The mean centrally for all lenses was 0.90 (std=1.24) and 0.35 (std=1.17) peripherally.

Past studies with rigid contact lenses have shown that lens design can impact the pumping action that takes place during blinking and that contact lens parameters are important in determining the oxygen tension between the cornea and the contact lens.\(^2\) According to studies using PMMA lenses, three variables that influence tear pump efficiency are diameter, axial edge lifts and base curve radii. Lenses with small overall diameters, regardless of changes in optic zone diameter or tear layer thickness, provide for better tear exchange and larger difference values than larger lenses.\(^3, 165-166\) Axial edge lifts of 0.13mm or greater are associated with significantly larger difference values than axial edge lifts of 0.09mm or less.\(^4\) Lastly, tear exchange has been shown to be most sensitive to changes in base curve radius, with contact lenses fitted to parallel the cornea being associated with better tear exchange than steeper or flatter fits. Tear exchange with rigid contact lenses has been measured to be about 10% per blink.

When comparing hydrogel contact lenses with rigid contact lenses, Polse found less tear exchange with hydrogel contact lenses than with rigid contact lenses.\(^{180}\) He
concluded that the amount of oxygen delivered to the cornea by tear pumping is relatively small for hydrogel lenses and that oxygenation of the cornea covered by a contact lens principally comes from transmission through the material. An additional study evaluated the effect of diameter on tear pump efficiency and concluded that smaller diameter soft lenses provide substantially better tear mixing than larger lenses, but, compared to the tear exchange obtained with rigid contact lenses, the tear exchange is modest. Even the small lenses provided only 1.24% tear mixing per blink.\textsuperscript{186} Again, the present study did not find tear pump efficiency (as measured by difference values in oxygen uptake rates between static and dynamic conditions) to differ significantly with respect to lens diameter or location. This study suggests that developing lenses with a high Dk/t’s should continue.
Chapter 6: Conclusions

The purpose of this study was to compare the physiological response of the cornea to three hydrogel contact lens diameters. Measurements were taken after the contact was worn under both static and dynamic conditions. The comparison of the oxygen uptake rates obtained under static and dynamic conditions evaluated how well lens design provided for tear exchange with the blink. Measurements were made for both the central and peripheral cornea to determine if blinking increased oxygenation at both locations. Our conclusions are listed in the order of our four objectives as follows:

1. Our first objective was to determine if there are significant differences in the oxygen uptake rates, relative to air, associated with the central and peripheral cornea. Significant differences in the oxygen uptake rates were found between the central (mean=4.79) and peripheral (mean=4.95) locations (p=0.011).

2. Our second objective was to determine if there are significant differences in the oxygen uptake rates, relative to air, associated with different lens diameters. Significant differences were found between the lens diameters as
corneal oxygen uptake rates increased with increasing lens diameter (p=0.006). The mean oxygen uptake relative to air was 4.59 (std=0.8) for the 13mm lens, 4.99 (std=1.4) for the 14mm lens, and 5.03 (std=0.9) for the 15mm lens.

3. Our third objective was to determine if there are significant differences in oxygen uptake rates, relative to air, between static and dynamic wearing conditions. For all lens diameters, a significant difference was found as uptake relative to air was higher under static conditions (mean=5.18, std=1.2) compared to dynamic conditions (mean=4.56, std=0.7) p=0.001.

4. Our fourth objective was to determine if there are significant differences in the difference values between static and dynamic wearing conditions associated with different lens diameters. A repeated measures analysis was used to assess the impact of lens diameter on the difference values between mean relative static condition data and mean relative dynamic condition data. The results demonstrated a non-significant difference with respect to lens diameter (p=0.12). This may be due to some large variability in the data.
References


174. Dillehay S. *Tear Exchange under Rigid Contact Lenses as a Function of Base Curve/Cornea Relationship.* Columbus, Ohio: College of Optometry, The Ohio State University; 1986.
177. Jochum KL. The Effect of Varying Overall Diameter on the Tear Exchange under a Rigid Contact Lens. Columbus, Ohio: College of Optometry, The Ohio State University; 1988.


202. Pilskalns B. *Oxygen demands in keratoconus of the central and peripheral cornea associated with the wear of hybrid contact lenses.* Columbus, Ohio: College of Optometry, The Ohio State University; 2005.


Appendix A: Tables

<p>| | |</p>
<table>
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<tr>
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<tr>
<td><strong>Systemic Health Problems</strong></td>
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<tr>
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<td>41.00 @005 ; 41.62 @095</td>
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*Table 1. Subject characteristics for Subject 1*
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<td>Avian birth control</td>
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<td>Keratometry</td>
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<tr>
<td>Left Eye</td>
<td>42.25 @180 ; 42.87 @090</td>
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<td>Left Eye</td>
<td>41.00 @090 ; 41.25 @180</td>
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<td>Toricity</td>
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**Table 3. Subject characteristics for Subject 3**
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<th>Medications</th>
<th>Allergies</th>
<th>Contact Lens History</th>
<th>Refractive Error and VA:</th>
<th>Keratometry</th>
<th>Toricity</th>
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<tr>
<td>4</td>
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<td>Female</td>
<td>Caucasian</td>
<td>No systemic health problems. Pregnant 21 weeks.</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>No contact lens wear for past 35 days. Wore monthly replacement soft contact lenses for 12 years.</td>
<td>Right Eye: -4.75 -0.75 @010 20/15, Left Eye: -4.75 -0.75 @005 20/15</td>
<td>Right Eye: 40.62 @001 ; 41.87 @091, Left Eye: 40.62 @003 ; 41.25 @093</td>
<td>Right Eye: 1.25D WTR, Left Eye: 0.63D WTR</td>
<td>13mm</td>
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<td>5</td>
<td>55</td>
<td>Female</td>
<td>Caucasian</td>
<td>Sarcoidosis diagnosed 2006 by lymph node biopsy</td>
<td>None</td>
<td>Activella, occasional use of Visine</td>
<td>None</td>
<td>Never wore contact lenses</td>
<td>Right Eye: +0.75D 20/20+, Left Eye: plano -0.25x 085 20/15</td>
<td>Right Eye: 44.50 @180 ; 45.00 @090, Left Eye: 45.00 @180 ; 46.00 @090</td>
<td>Right Eye: 0.50D WTR, Left Eye: 1.00D WTR</td>
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Table 4. Subject characteristics for Subject 4

Table 5. Subject characteristics for Subject 5
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<td><strong>Medications</strong></td>
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<tr>
<td><strong>Allergies</strong></td>
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<td><strong>Contact Lens History</strong></td>
<td>Never wore contact lenses</td>
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<tr>
<td>Right Eye</td>
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<td>Left Eye</td>
<td>-1.00 DS 20/20+</td>
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<td>Right Eye</td>
<td>42.75 @003 ; 42.87 @093</td>
</tr>
<tr>
<td>Left Eye</td>
<td>42.75 @175 ; 43.12 @085</td>
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</tr>
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<td>Right Eye</td>
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<tr>
<td>Left Eye</td>
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*Table 6. Subject characteristics for Subject 6*

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<td><strong>Race</strong></td>
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<td><strong>Systemic Health Problems</strong></td>
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<td><strong>Ocular Health Problems</strong></td>
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<td><strong>Medications</strong></td>
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</tr>
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<td><strong>Allergies</strong></td>
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<td>Last wore contact lenses several months ago – monthly replacement lenses</td>
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<td>-5.75 -0.75 x 030 20/15</td>
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<td>Right Eye</td>
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<tr>
<td>Left Eye</td>
<td>45.00 @178 ; 45.62 @088</td>
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<td>Right Eye</td>
<td>1.25D WTR</td>
</tr>
<tr>
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<td>0.62D WTR</td>
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*Table 7. Subject characteristics for Subject 7*
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<td>Medications</td>
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</tr>
<tr>
<td>Allergies</td>
<td>None</td>
</tr>
<tr>
<td>Contact Lens History</td>
<td>Has not worn contact lenses for 3 months; wore soft contact lenses off and on previous 6 months</td>
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| Refractive Error and VA:  
  Right Eye | -1.25 -0.50 x 150 20/15 |
  Left Eye  | -1.25 -0.50 x 015 20/15 |
| Keratometry  
  Right Eye | 43.25 @022 ; 43.62 @112 |
  Left Eye  | 43.75 @008 ; 44.37 @098 |
| Toricity  
  Right Eye | 0.37D WTR |
  Left Eye  | 0.62D WTR |
| Palpebral Aperture Size | 11.5mm |

Table 8. Subject characteristics for Subject 8

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<td>Systemic Health Problems</td>
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<td>Ocular Health Problems</td>
<td>None</td>
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<td>Medications</td>
<td>None</td>
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<tr>
<td>Allergies</td>
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<td>Contact Lens History</td>
<td>Has not worn contact lenses for previous 2 months. Prior to that wore soft contact lenses for 10 years.</td>
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| Refractive Error and VA:  
  Right Eye | -2.25 -1.00 x 095 20/15 |
  Left Eye  | -3.00 -0.75 x 092 20/15 |
| Keratometry  
  Right Eye | 43.37 @100 ; 43.50 @010 |
  Left Eye  | 43.50 @085 ; 43.62 @175 |
| Toricity  
  Right Eye | 0.13D ATR |
  Left Eye  | 0.12D ATR |
| Palpebral Aperture Size | 11.5mm |

Table 9. Subject characteristics for Subject 9
<table>
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<th>Age</th>
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<td>Sex</td>
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</tr>
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<td>Allergies</td>
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### Table 10. Subject characteristics for Subject 10

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<td>Plano</td>
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<td>+0.25</td>
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<tr>
<td>42.25 @178</td>
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<td>44.00 @095</td>
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<td>1.62D WTR</td>
<td>2.00D WTR</td>
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| Palpebral Aperture Size | 8mm OD 10mm OS |

---

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<td>Dry Eye Symptoms</td>
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<td>Medications</td>
<td>Eczema medications</td>
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<td>Allergies</td>
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### Table 11. Subject characteristics for Subject 11

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<th>Left Eye</th>
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<tr>
<td>43.87 @175</td>
<td>44.37 @091</td>
<td></td>
</tr>
<tr>
<td>44.00 @180</td>
<td>44.62 @090</td>
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<th>Toricity</th>
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<th>Left Eye</th>
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<td>0.50D WTR</td>
<td>0.62D WTR</td>
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| Palpebral Aperture Size | 8mm OD 10mm OS |

---
<table>
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<td>Ocular Health Problems</td>
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<tr>
<td>Medications</td>
<td>None</td>
</tr>
<tr>
<td>Allergies</td>
<td>None</td>
</tr>
<tr>
<td>Contact Lens History</td>
<td>Has never worn contact lenses</td>
</tr>
</tbody>
</table>

| Refractive Error and VA: |         |
| Right Eye               | Plano 20/15 |
| Left Eye                | Plano 20/15 |

| Keratometry:            |         |
| Right Eye               | 41.37 @007 ; 42.00 @097 |
| Left Eye                | 41.37 @180 ; 41.62 @090 |

| Toricity:               |         |
| Right Eye               | 0.63D WTR |
| Left Eye                | 0.25D WTR |

| Palpebral Aperture Size | 11.5mm   |

*Table 12. Subject characteristics for Subject 12*

<table>
<thead>
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</thead>
<tbody>
<tr>
<td>Sex</td>
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<tr>
<td>Race</td>
<td>Caucasian</td>
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<tr>
<td>Systemic Health Problems</td>
<td>None</td>
</tr>
<tr>
<td>Ocular Health Problems</td>
<td>None</td>
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<tr>
<td>Medications</td>
<td>None</td>
</tr>
<tr>
<td>Allergies</td>
<td>None</td>
</tr>
<tr>
<td>Contact Lens History</td>
<td>Stopped wearing contact lenses 45 days ago. Previously wore soft contact lenses for 13 years (Acuvue)</td>
</tr>
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| Refractive Error and VA: |         |
| Right Eye               | -3.75DS 20/15 |
| Left Eye                | -3.75DS 20/15 |

| Keratometry:            |         |
| Right Eye               | 43.62 @178 ; 44.75 @088 |
| Left Eye                | 44.00 @180 ; 44.25 @090 |

| Toricity:               |         |
| Right Eye               | 1.13D WTR |
| Left Eye                | 0.25D WTR |

| Palpebral Aperture Size | 9mm      |

*Table 13. Subject characteristics for Subject 13*
<table>
<thead>
<tr>
<th>Age</th>
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</thead>
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<tr>
<td>Systemic Health Problems</td>
<td>None</td>
</tr>
<tr>
<td>Ocular Health Problems</td>
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<td>Medications</td>
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<tr>
<td>Allergies</td>
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<td>Plano -0.25 @165 20/15</td>
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<td>0.62D WTR</td>
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<td>Left Eye</td>
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**Table 14. Subject characteristics for Subject 14**

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<th>29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
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</tr>
<tr>
<td>Race</td>
<td>Caucasian</td>
</tr>
<tr>
<td>Systemic Health Problems</td>
<td>None</td>
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<tr>
<td>Ocular Health Problems</td>
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<td>Medications</td>
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<tr>
<td>Allergies</td>
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</tr>
<tr>
<td>Contact Lens History</td>
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</tr>
<tr>
<td>Refractive Error and VA:</td>
<td></td>
</tr>
<tr>
<td>Right Eye</td>
<td>Plano -0.25 @090 20/15</td>
</tr>
<tr>
<td>Left Eye</td>
<td>-0.50DS 20/15</td>
</tr>
<tr>
<td>Keratometry</td>
<td></td>
</tr>
<tr>
<td>Right Eye</td>
<td>45.07 @092 ; 45.12 @002</td>
</tr>
<tr>
<td>Left Eye</td>
<td>45.37 @093 ; 45.62 @003</td>
</tr>
<tr>
<td>Toricity</td>
<td></td>
</tr>
<tr>
<td>Right Eye</td>
<td>0.05D ATR</td>
</tr>
<tr>
<td>Left Eye</td>
<td>0.25D ATR</td>
</tr>
<tr>
<td>Palpebral Aperture Size</td>
<td>9.5 OD 9.0 OS</td>
</tr>
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**Table 15. Subject characteristics for Subject 15**
<table>
<thead>
<tr>
<th>Lens</th>
<th>Alden Classic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Material</td>
<td>polymacon</td>
</tr>
<tr>
<td>Water Content</td>
<td>38%</td>
</tr>
<tr>
<td>dK</td>
<td>9.0 x 10^{-9} (cm/sec)(mlO2/ml x mmHg)</td>
</tr>
<tr>
<td>Overall Diameter</td>
<td>13.0, 14.0, and 15.0 mm</td>
</tr>
<tr>
<td>Back Vertex Power</td>
<td>-3.00 D.S.</td>
</tr>
<tr>
<td>Center Thickness</td>
<td>0.10 mm</td>
</tr>
<tr>
<td>Base Curve Radii</td>
<td>6.5 – 9.8 mm in 0.1 mm steps</td>
</tr>
</tbody>
</table>

**Table 16. Alden Classic hydrogel contact lens parameters**

<table>
<thead>
<tr>
<th>Flat K-Reading</th>
<th>13.0 mm</th>
<th>14.0 mm</th>
<th>15.0 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>48.00 to 48.87 D</td>
<td>7.7 mm</td>
<td>8.1 mm</td>
<td>8.5 mm</td>
</tr>
<tr>
<td>47.00 to 47.87 D</td>
<td>7.9 mm</td>
<td>8.3 mm</td>
<td>8.7 mm</td>
</tr>
<tr>
<td>46.00 to 46.87 D</td>
<td>8.0 mm</td>
<td>8.4 mm</td>
<td>8.8 mm</td>
</tr>
<tr>
<td>45.00 to 45.87 D</td>
<td>8.1 mm</td>
<td>8.5 mm</td>
<td>8.9 mm</td>
</tr>
<tr>
<td>44.00 to 44.87 D</td>
<td>8.1 mm</td>
<td>8.5 mm</td>
<td>8.9 mm</td>
</tr>
<tr>
<td>43.00 to 43.87 D</td>
<td>8.2 mm</td>
<td>8.6 mm</td>
<td>9.0 mm</td>
</tr>
<tr>
<td>42.00 to 42.87 D</td>
<td>8.2 mm</td>
<td>8.6 mm</td>
<td>9.0 mm</td>
</tr>
<tr>
<td>41.00 to 41.87 D</td>
<td>8.3 mm</td>
<td>8.7 mm</td>
<td>9.1 mm</td>
</tr>
<tr>
<td>40.00 to 40.87 D</td>
<td>8.4 mm</td>
<td>8.8 mm</td>
<td>9.2 mm</td>
</tr>
<tr>
<td>39.00 to 39.87 D</td>
<td>8.5 mm</td>
<td>8.9 mm</td>
<td>9.3 mm</td>
</tr>
</tbody>
</table>

**Table 17. Recommended base curve radii for three Alden Classic hydrogel contact lens diameters (13.0, 14.0, and 15.0 mm)**
Tables 18-32. Corneal Oxygen Uptake Rates (mm Hg/sec) for each subject.

<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Open Eye</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>6.56</td>
<td>6.36</td>
</tr>
<tr>
<td>Session 2</td>
<td>6.17</td>
<td>6.13</td>
</tr>
<tr>
<td><strong>PMMA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Static: 37.88 Dynamic: 41.67</td>
<td></td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 31.09 Dynamic: 31.09</td>
<td></td>
</tr>
<tr>
<td><strong>13.0 mm</strong></td>
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<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>28.25</td>
<td>29.98</td>
</tr>
<tr>
<td>Session 2</td>
<td>20.73</td>
<td>21.87</td>
</tr>
<tr>
<td><strong>14.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>35.46</td>
<td>36.87</td>
</tr>
<tr>
<td>Session 2</td>
<td>22.10</td>
<td>22.52</td>
</tr>
<tr>
<td><strong>15.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>43.40</td>
<td>42.09</td>
</tr>
<tr>
<td>Session 2</td>
<td>27.78</td>
<td>26.12</td>
</tr>
</tbody>
</table>

Table 18. Subject 1’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Open Eye</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>5.71</td>
<td>5.46</td>
</tr>
<tr>
<td>Session 2</td>
<td>6.27</td>
<td>5.82</td>
</tr>
<tr>
<td><strong>PMMA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Static: 31.45 Dynamic: 28.54</td>
<td></td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 38.58 Dynamic: 33.07</td>
<td></td>
</tr>
<tr>
<td><strong>13.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>29.55</td>
<td>26.88</td>
</tr>
<tr>
<td>Session 2</td>
<td>33.33</td>
<td>26.71</td>
</tr>
<tr>
<td><strong>14.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>27.78</td>
<td>22.46</td>
</tr>
<tr>
<td>Session 2</td>
<td>30.19</td>
<td>24.95</td>
</tr>
<tr>
<td><strong>15.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>38.76</td>
<td>27.96</td>
</tr>
<tr>
<td>Session 2</td>
<td>32.30</td>
<td>35.77</td>
</tr>
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</table>

Table 19. Subject 2’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).
<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Normal Open Eye</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>6.86</td>
<td>6.81</td>
</tr>
<tr>
<td>Session 2</td>
<td>6.67</td>
<td>6.61</td>
</tr>
<tr>
<td></td>
<td><strong>PMMA</strong></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Static: 32.18</td>
<td>Dynamic: 37.04</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 31.33</td>
<td>Dynamic: 41.25</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Diameter</th>
<th>Static</th>
<th>Dynamic</th>
<th>Static</th>
<th>Dynamic</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.0 mm</td>
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</tr>
<tr>
<td>Session 1</td>
<td>38.94</td>
<td>26.37</td>
<td>28.15</td>
<td>30.75</td>
</tr>
<tr>
<td>Session 2</td>
<td>28.74</td>
<td>25.96</td>
<td>26.12</td>
<td>28.44</td>
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<tr>
<td>14.0 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>37.37</td>
<td>30.30</td>
<td>32.81</td>
<td>30.19</td>
</tr>
<tr>
<td>Session 2</td>
<td>29.98</td>
<td>27.87</td>
<td>24.44</td>
<td>27.41</td>
</tr>
<tr>
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<tr>
<td>Session 1</td>
<td>53.76</td>
<td>29.98</td>
<td>39.12</td>
<td>32.30</td>
</tr>
<tr>
<td>Session 2</td>
<td>34.58</td>
<td>32.18</td>
<td>28.06</td>
<td>32.55</td>
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</table>

Table 20. Subject 3’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Normal Open Eye</td>
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<tr>
<td>Session 1</td>
<td>7.91</td>
<td>7.34</td>
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<td>Session 2</td>
<td>7.34</td>
<td>5.97</td>
</tr>
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<td><strong>PMMA</strong></td>
<td></td>
</tr>
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<td>Session 1</td>
<td>Static: 42.09</td>
<td>Dynamic: 32.94</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 31.81</td>
<td>Dynamic: 51.76</td>
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</table>

<table>
<thead>
<tr>
<th>Overall Diameter</th>
<th>Static</th>
<th>Dynamic</th>
<th>Static</th>
<th>Dynamic</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.0 mm</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>29.66</td>
<td>27.69</td>
<td>25.18</td>
<td>27.50</td>
</tr>
<tr>
<td>Session 2</td>
<td>25.80</td>
<td>25.03</td>
<td>38.23</td>
<td>35.01</td>
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<tr>
<td>14.0 mm</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>40.85</td>
<td>24.44</td>
<td>24.44</td>
<td>31.93</td>
</tr>
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<td>Session 2</td>
<td>29.24</td>
<td>26.97</td>
<td>38.76</td>
<td>45.79</td>
</tr>
<tr>
<td>15.0 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>54.11</td>
<td>26.71</td>
<td>34.58</td>
<td>17.36</td>
</tr>
<tr>
<td>Session 2</td>
<td>32.94</td>
<td>36.08</td>
<td>44.56</td>
<td>24.95</td>
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</tbody>
</table>

Table 21. Subject 4’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).
## Table 22.
Subject 5’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Open Eye</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>6.93</td>
<td>7.24</td>
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<tr>
<td>Session 2</td>
<td>6.42</td>
<td>5.41</td>
</tr>
<tr>
<td><strong>PMMA</strong></td>
<td></td>
<td></td>
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<tr>
<td>Session 1</td>
<td>Static: 45.29</td>
<td>Dynamic: 33.74</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 36.23</td>
<td>Dynamic: 49.31</td>
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<tr>
<td>13.0 mm</td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>41.67</td>
<td>32.55</td>
</tr>
<tr>
<td>Session 2</td>
<td>31.57</td>
<td>29.76</td>
</tr>
<tr>
<td>14.0 mm</td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>39.31</td>
<td>31.69</td>
</tr>
<tr>
<td>Session 2</td>
<td>35.61</td>
<td>31.21</td>
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<td>Dynamic</td>
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<td>38.05</td>
<td>33.60</td>
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<tr>
<td>Session 2</td>
<td>36.23</td>
<td>35.61</td>
</tr>
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</table>

## Table 23.
Subject 6’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Open Eye</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>6.16</td>
<td>7.82</td>
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<tr>
<td>Session 2</td>
<td>8.98</td>
<td>8.77</td>
</tr>
<tr>
<td><strong>PMMA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Static: 25.80</td>
<td>Dynamic: 29.34</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 35.61</td>
<td>Dynamic: 35.16</td>
</tr>
<tr>
<td>13.0 mm</td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>14.27</td>
<td>29.55</td>
</tr>
<tr>
<td>Session 2</td>
<td>29.24</td>
<td>28.15</td>
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<tr>
<td>14.0 mm</td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>28.34</td>
<td>23.15</td>
</tr>
<tr>
<td>Session 2</td>
<td>30.53</td>
<td>26.80</td>
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<tr>
<td>15.0 mm</td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
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<td>29.04</td>
<td>33.60</td>
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<tr>
<td>Session 2</td>
<td>32.18</td>
<td>27.41</td>
</tr>
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88
<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal Open Eye</strong></td>
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<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>7.77</td>
<td>8.00</td>
</tr>
<tr>
<td>Session 2</td>
<td>7.63</td>
<td>6.22</td>
</tr>
<tr>
<td><strong>PMMA</strong></td>
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<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Static: 35.92</td>
<td>Dynamic: 44.09</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 41.67</td>
<td>Dynamic: 38.23</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Static</th>
<th>Dynamic</th>
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<th>Dynamic</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.0 mm</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>37.20</td>
<td>35.16</td>
<td>41.46</td>
<td>31.45</td>
</tr>
<tr>
<td>Session 2</td>
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<td>37.04</td>
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<td>14.0 mm</td>
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<td>32.43</td>
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<td>37.71</td>
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<td></td>
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<td>15.0 mm</td>
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<tr>
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<td>34.15</td>
<td>30.64</td>
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</tr>
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<td>Session 2</td>
<td>34.87</td>
<td>32.81</td>
<td>45.54</td>
<td>35.31</td>
</tr>
</tbody>
</table>

Table 24. Subject 7's corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal Open Eye</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>6.68</td>
<td>6.37</td>
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<td>Session 2</td>
<td>6.65</td>
<td>7.44</td>
</tr>
<tr>
<td><strong>PMMA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Static: 46.82</td>
<td>Dynamic: 64.60</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 39.12</td>
<td>Dynamic: 30.19</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Static</th>
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<th>Dynamic</th>
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<td>32.05</td>
<td></td>
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<tr>
<td>14.0 mm</td>
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<td>43.18</td>
<td>39.31</td>
<td>40.45</td>
<td>30.19</td>
</tr>
<tr>
<td>15.0 mm</td>
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<td>Session 1</td>
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<td>37.71</td>
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<td>Session 2</td>
<td>32.68</td>
<td>36.39</td>
<td>34.15</td>
<td>37.37</td>
</tr>
</tbody>
</table>

Table 25. Subject 8's corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).
<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>7.82</td>
<td>8.27</td>
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<tr>
<td>Session 2</td>
<td>7.74</td>
<td>7.59</td>
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<tr>
<td><strong>PMMA</strong></td>
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<td></td>
</tr>
<tr>
<td>Session 1</td>
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<td>Dynamic: 26.21</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 33.20</td>
<td>Dynamic: 54.47</td>
</tr>
<tr>
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<td>Static: 26.16</td>
<td>Dynamic: 39.68</td>
</tr>
<tr>
<td>Session 1</td>
<td>38.94</td>
<td>35.92</td>
</tr>
<tr>
<td>Session 2</td>
<td>34.29</td>
<td>19.07</td>
</tr>
<tr>
<td><strong>14.0 mm</strong></td>
<td>Static: 42.52</td>
<td>Dynamic: 31.93</td>
</tr>
<tr>
<td>Session 1</td>
<td>52.74</td>
<td>36.87</td>
</tr>
<tr>
<td>Session 2</td>
<td>32.05</td>
<td>20.83</td>
</tr>
</tbody>
</table>

Table 26. Subject 9's corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th></th>
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<tbody>
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<td></td>
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<td>5.73</td>
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<tr>
<td>Session 2</td>
<td>7.83</td>
<td>9.07</td>
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<td></td>
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<td>Dynamic: 35.16</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 48.45</td>
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</tr>
<tr>
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<td>Static: 27.69</td>
<td>Dynamic: 34.01</td>
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<tr>
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<td>36.87</td>
<td>29.24</td>
</tr>
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<td>Static: 36.55</td>
<td>Dynamic: 42.30</td>
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<td>19.11</td>
</tr>
<tr>
<td>Session 2</td>
<td>42.74</td>
<td>36.23</td>
</tr>
</tbody>
</table>

Table 27. Subject 10’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).
<table>
<thead>
<tr>
<th>Central Cornea</th>
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</tr>
</thead>
<tbody>
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</tr>
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<tr>
<td>Session 2</td>
<td>4.65</td>
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<tr>
<td><strong>PMMA</strong></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
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<tr>
<td>Session 2</td>
<td>Static: 27.60</td>
</tr>
<tr>
<td>13.0 mm</td>
<td>Static</td>
</tr>
<tr>
<td>Session 1</td>
<td>38.58</td>
</tr>
<tr>
<td>Session 2</td>
<td>22.52</td>
</tr>
<tr>
<td>14.0 mm</td>
<td>Static</td>
</tr>
<tr>
<td>Session 1</td>
<td>44.33</td>
</tr>
<tr>
<td>Session 2</td>
<td>25.10</td>
</tr>
<tr>
<td>15.0 mm</td>
<td>Static</td>
</tr>
<tr>
<td>Session 1</td>
<td>34.44</td>
</tr>
<tr>
<td>Session 2</td>
<td>26.04</td>
</tr>
</tbody>
</table>

Table 28. Subject 11’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th>Central Cornea</th>
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<tr>
<td>Session 2</td>
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<td><strong>PMMA</strong></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Static: 41.46</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 33.47</td>
</tr>
<tr>
<td>13.0 mm</td>
<td>Static</td>
</tr>
<tr>
<td>Session 1</td>
<td>31.81</td>
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<tr>
<td>Session 2</td>
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<tr>
<td>14.0 mm</td>
<td>Static</td>
</tr>
<tr>
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<td>Session 2</td>
<td>34.72</td>
</tr>
<tr>
<td>15.0 mm</td>
<td>Static</td>
</tr>
<tr>
<td>Session 1</td>
<td>49.02</td>
</tr>
<tr>
<td>Session 2</td>
<td>24.37</td>
</tr>
</tbody>
</table>

Table 29. Subject 12’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).
<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Open Eye</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>5.74</td>
<td>5.28</td>
</tr>
<tr>
<td>Session 2</td>
<td>6.60</td>
<td>5.97</td>
</tr>
<tr>
<td></td>
<td><strong>PMMA</strong></td>
<td></td>
</tr>
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<td>Dynamic: 32.43</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 27.32</td>
<td>Dynamic: 30.64</td>
</tr>
<tr>
<td><strong>13.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>31.57</td>
<td>24.08</td>
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<tr>
<td>Session 2</td>
<td>32.94</td>
<td>23.88</td>
</tr>
<tr>
<td><strong>14.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>37.54</td>
<td>23.47</td>
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<tr>
<td>Session 2</td>
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<td>24.02</td>
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<td>Dynamic</td>
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<tr>
<td>Session 2</td>
<td>28.34</td>
<td>25.48</td>
</tr>
</tbody>
</table>

Table 30. Subject 13’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal Open Eye</td>
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</tr>
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<td>Session 1</td>
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<td>5.28</td>
</tr>
<tr>
<td>Session 2</td>
<td>5.57</td>
<td>5.58</td>
</tr>
<tr>
<td></td>
<td><strong>PMMA</strong></td>
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</tr>
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<td>Session 1</td>
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<td>Dynamic: 28.64</td>
</tr>
<tr>
<td>Session 2</td>
<td>Static: 29.98</td>
<td>Dynamic: 24.15</td>
</tr>
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<td>Dynamic</td>
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<tr>
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<td>23.74</td>
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<td>25.03</td>
<td>23.95</td>
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<td>Dynamic</td>
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<td>Dynamic</td>
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</tr>
<tr>
<td>Session 2</td>
<td>28.34</td>
<td>22.34</td>
</tr>
</tbody>
</table>

Table 31. Subject 14’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).
### Table 32. Subject 15’s corneal oxygen uptake rates (mm Hg/sec) for 2 sessions, for the central and peripheral cornea of the normal open eye and following both static and dynamic wear of 3 hydrogel contact lens overall diameters (13.0, 14.0, and 15.0 mm) and PMMA contact lens (central cornea only).

<table>
<thead>
<tr>
<th></th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
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<td>6.72</td>
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<tr>
<td>Session 2</td>
<td>6.76</td>
<td>6.01</td>
</tr>
<tr>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Static: 37.88 Dynamic: 37.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Static: 48.17 Dynamic: 30.19</td>
<td></td>
<td></td>
</tr>
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<td><strong>13.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
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<td>25.10</td>
</tr>
<tr>
<td>Session 2</td>
<td>31.09</td>
<td>36.87</td>
</tr>
<tr>
<td><strong>14.0 mm</strong></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Session 1</td>
<td>30.98</td>
<td>27.06</td>
</tr>
<tr>
<td>Session 2</td>
<td>34.87</td>
<td>26.04</td>
</tr>
<tr>
<td><strong>15.0 mm</strong></td>
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<td>Session 1</td>
<td>37.54</td>
<td>23.67</td>
</tr>
<tr>
<td>Session 2</td>
<td>34.44</td>
<td>27.69</td>
</tr>
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</table>

### Table 33. Population mean oxygen uptake rates and standard deviations for 3 contact lens diameters (13.0, 14.0, and 15.0 mm), 2 wearing conditions (static and dynamic), and 2 corneal locations (central and peripheral).

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
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<td>28.67</td>
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<tr>
<td>Standard Deviation</td>
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<td>5.28</td>
</tr>
<tr>
<td><strong>14.0 mm</strong></td>
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<td>Dynamic</td>
</tr>
<tr>
<td>Mean</td>
<td>36.77</td>
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<td>Dynamic</td>
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<td>Mean</td>
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<td>29.64</td>
</tr>
<tr>
<td>Standard Deviation</td>
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<td>6.51</td>
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</table>
Table 34-36. Data relative to air (normal open eye measurements) for both the central and peripheral cornea for 15 subjects for the 13.0 mm, 14mm and 15mm diameter Alde Classic hydrogel contact lens. The values for each cell are the averages of two corneal oxygen uptake measurements.

<table>
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<td>4.49</td>
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<td>3.87</td>
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<td>3.45</td>
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<td>4.69</td>
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<td>Subject 8</td>
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<td>5.04</td>
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<td>4.67</td>
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<td>4.07</td>
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<td>3.91</td>
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<td>4.34</td>
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<tr>
<td>Subject 15</td>
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<td>4.55</td>
</tr>
</tbody>
</table>

Table 34. Oxygen uptake rate measurements relative to air (normal open eye measurements) for both the central and peripheral cornea for 15 subjects for the 13.0 mm diameter Alde Classic hydrogel contact lens.
<table>
<thead>
<tr>
<th>Subject</th>
<th>Central Cornea</th>
<th>Peripheral Cornea</th>
</tr>
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<td>4.26</td>
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</table>

Table 35. Oxygen uptake rate measurements relative to air (normal open eye measurements) for both the central and peripheral cornea for 15 subjects for the 14.0 mm diameter Alden Classic hydrogel contact lens.
<table>
<thead>
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<th>Peripheral Cornea</th>
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<td>5.78</td>
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<td>3.71</td>
</tr>
<tr>
<td>Subject 10</td>
<td>4.74</td>
<td>3.74</td>
</tr>
<tr>
<td>Subject 11</td>
<td>6.27</td>
<td>5.33</td>
</tr>
<tr>
<td>Subject 12</td>
<td>6.02</td>
<td>3.60</td>
</tr>
<tr>
<td>Subject 13</td>
<td>4.67</td>
<td>3.94</td>
</tr>
<tr>
<td>Subject 14</td>
<td>4.94</td>
<td>4.44</td>
</tr>
<tr>
<td>Subject 15</td>
<td>5.28</td>
<td>3.77</td>
</tr>
</tbody>
</table>

Table 36. Oxygen uptake rate measurements relative to air (normal open eye measurements) for both the central and peripheral cornea for 15 subjects for the 15.0 mm diameter Alden Classic hydrogel contact lens.

<table>
<thead>
<tr>
<th>13.0 mm</th>
<th>Central</th>
<th>Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Mean</td>
<td>4.69</td>
<td>4.34</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>0.95</td>
<td>0.44</td>
</tr>
<tr>
<td>14.0 mm</td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Mean</td>
<td>5.61</td>
<td>4.22</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>2.11</td>
<td>0.69</td>
</tr>
<tr>
<td>15.0 mm</td>
<td>Static</td>
<td>Dynamic</td>
</tr>
<tr>
<td>Mean</td>
<td>5.42</td>
<td>4.48</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>0.70</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Table 37. Population mean oxygen uptake rates and standard deviations for measurements relative to those of the normal open eye for 3 contact lens diameters (13.0, 14.0, and 15.0 mm), 2 wearing conditions (static and dynamic), and 2 corneal locations (central and peripheral).
Table 38. Population oxygen uptake rates relative to air (means, standard errors of the mean, and 95% confidence intervals) for 3 contact lens diameters (13.0, 14.0, and 15.0 mm), 2 wearing conditions (static and dynamic), and 2 corneal locations (central and peripheral).

<table>
<thead>
<tr>
<th>Level</th>
<th>Mean</th>
<th>SE</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13mm</td>
<td>4.59</td>
<td>0.78</td>
<td>4.40, 4.79</td>
</tr>
<tr>
<td>14mm</td>
<td>4.99</td>
<td>1.35</td>
<td>4.66, 5.33</td>
</tr>
<tr>
<td>15mm</td>
<td>5.03</td>
<td>0.85</td>
<td>4.82, 5.24</td>
</tr>
<tr>
<td>Condition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynamic</td>
<td>4.56</td>
<td>0.72</td>
<td>4.41, 4.70</td>
</tr>
<tr>
<td>Static</td>
<td>5.18</td>
<td>1.20</td>
<td>4.94, 5.43</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>4.79</td>
<td>1.15</td>
<td>4.56, 5.03</td>
</tr>
<tr>
<td>Peripheral</td>
<td>4.95</td>
<td>0.91</td>
<td>4.76, 5.13</td>
</tr>
</tbody>
</table>

Table 39. Results of mixed linear modeling: mixed linear modeling was used to compare the effect of lens diameter, condition and location on oxygen uptake relative to open eye. Uptake relative to air was calculated at each visit and then the average of the response at both visits was used in the analysis.

<table>
<thead>
<tr>
<th>Effect</th>
<th>DF</th>
<th>F-statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lens diameter x Condition x Location</td>
<td>2, 14</td>
<td>2.94</td>
<td>0.086</td>
</tr>
<tr>
<td>Lens diameter x Location</td>
<td>2, 14</td>
<td>0.67</td>
<td>0.53</td>
</tr>
<tr>
<td>Lens diameter x Condition</td>
<td>2, 14</td>
<td>3.17</td>
<td>0.073</td>
</tr>
<tr>
<td>Condition x Location</td>
<td>1, 14</td>
<td>2.97</td>
<td>0.11</td>
</tr>
<tr>
<td>Lens diameter</td>
<td>2, 14</td>
<td>7.73</td>
<td>0.006</td>
</tr>
<tr>
<td>Condition</td>
<td>1, 14</td>
<td>27.32</td>
<td>0.0001</td>
</tr>
<tr>
<td>Location</td>
<td>1, 14</td>
<td>8.60</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Table 40. Post-hoc comparisons of mean oxygen uptake relative to air between lens diameters

*Adjusted for multiple comparison using method of Tukey-Kramer
<table>
<thead>
<tr>
<th>Lens</th>
<th>N</th>
<th>Mean</th>
<th>Std Dev</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Lower 95% CL for Mean</th>
<th>Upper 95% CL for Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>13mm</td>
<td>30</td>
<td>0.35</td>
<td>0.84</td>
<td>-1.30</td>
<td>1.83</td>
<td>0.04</td>
<td>0.66</td>
</tr>
<tr>
<td>14mm</td>
<td>30</td>
<td>0.94</td>
<td>1.61</td>
<td>-1.67</td>
<td>6.35</td>
<td>0.34</td>
<td>1.54</td>
</tr>
<tr>
<td>15mm</td>
<td>30</td>
<td>0.59</td>
<td>1.07</td>
<td>-1.50</td>
<td>2.82</td>
<td>0.19</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Table 41. Difference values between mean relative static condition data and mean relative dynamic condition data for the 13.0, 14.0, and 15.0 mm diameter contact lenses, with standard deviations, minimum and maximum values, and 95% confidence limits for the mean.

<table>
<thead>
<tr>
<th>Location</th>
<th>N</th>
<th>Mean</th>
<th>Std Dev</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Lower 95% CL for Mean</th>
<th>Upper 95% CL for Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>45</td>
<td>0.90</td>
<td>1.24</td>
<td>-1.18</td>
<td>6.35</td>
<td>0.52</td>
<td>1.27</td>
</tr>
<tr>
<td>Peripheral</td>
<td>45</td>
<td>0.35</td>
<td>1.17</td>
<td>-1.67</td>
<td>2.82</td>
<td>0.00</td>
<td>0.71</td>
</tr>
</tbody>
</table>

Table 42. Difference values between mean relative static condition data and mean relative dynamic condition data for the central and peripheral cornea, with the standard deviations, minimum and maximum values, and 95% confidence limits for the mean.

<table>
<thead>
<tr>
<th>Location</th>
<th>Lens</th>
<th>N</th>
<th>Mean</th>
<th>Std Dev</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Lower 95% CL for Mean</th>
<th>Upper 95% CL for Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>13mm</td>
<td>15</td>
<td>0.36</td>
<td>0.79</td>
<td>-1.18</td>
<td>1.64</td>
<td>-0.08</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>14mm</td>
<td>15</td>
<td>1.39</td>
<td>1.76</td>
<td>-0.98</td>
<td>6.35</td>
<td>0.42</td>
<td>2.36</td>
</tr>
<tr>
<td></td>
<td>15mm</td>
<td>15</td>
<td>0.94</td>
<td>0.73</td>
<td>-0.11</td>
<td>2.42</td>
<td>0.54</td>
<td>1.34</td>
</tr>
<tr>
<td>Peripheral</td>
<td>13mm</td>
<td>15</td>
<td>0.34</td>
<td>0.91</td>
<td>-1.30</td>
<td>1.83</td>
<td>-0.16</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>14mm</td>
<td>15</td>
<td>0.49</td>
<td>1.36</td>
<td>-1.67</td>
<td>2.75</td>
<td>-0.27</td>
<td>1.24</td>
</tr>
<tr>
<td></td>
<td>15mm</td>
<td>15</td>
<td>0.24</td>
<td>1.26</td>
<td>-1.50</td>
<td>2.82</td>
<td>-0.46</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Table 43. Repeated measures analysis to assess the impact of lens diameter and location on the difference values between mean relative static condition data and mean relative dynamic condition data. There was no difference with respect to lens diameter (p=0.12) or location (p=0.059).
Figure 1. Dynamic central relativized oxygen uptake by diameter
Figure 2. Static central relativized oxygen uptake by diameter
Figure 3. Dynamic peripheral relativized oxygen uptake by diameter

Figure 4. Static peripheral relativized oxygen uptake by diameter