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In-vitro method for determining corneal tissue friction and damage due to contact lens sliding

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ABSTRACT

It is postulated that frictional energy due to contact lens rubbing against corneal tissue correlates positively with cell damage; where the damage is due to a fatigue mechanism (repeated stressing). Efforts were made to develop a relatively rapid in-vitro method capable of exploring this postulate. Measurements of the dynamic coefficient of friction (DCoF) between corneal epithelium and contact lenses, associated frictional forces, frictional energy, and corresponding cell damage were made using SkinEthic (Lyon, France) human corneal epithelial (HCE) constructs and commercially available contact lenses. Five silicone hydrogels (SiHs) and two polyhydroxyethlymethacrylate (p-HEMA) lens types were employed. Frictional forces were measured while the lens was rubbed against a construct that was moistened using a tear-like fluid. The exposed constructs were stained, imaged, and processed using a custom Matlab code. The range of DCoF values observed here extended from about 0.04 to 0.07. The frictional energy varied from about 0.03 mJ to 0.08 mJ. The results indicated a moderate correlation (Pearson's R = 0.79, P = 3.4%) between the frictional energy and cell damage. The authors believe that these results support the notion that cell damage can be caused by fatigue. Future efforts should explore how cell damage relates to a potentially more relevant metric, power density.

1. Introduction

It has been shown that contact lens comfort is strongly correlated with contact lens dynamic coefficient of friction (DCoF) data [1] and it has been suggested that the frictional energy input to the corneal tissue, also referred to as sliding work, may be related to comfort [2]. Additionally, mechanical interactions between a contact lens and ocular tissue can result in damage to corneal epithelial tissue [3–7]. As such, a detailed understanding of the contact lens–eye tribological system is needed; in particular, how lens–eye tribology relates to cell damage that can affect both comfort and ocular health.

Several studies have examined ocular tribology systems in general [8–10]. Rennie, Dickrell, and Sawyer measured the DCoF and frictional forces between a contact lens (Etafilcon-A) and borosilicate glass [8]. They found the DCoF to vary between 0.025 and 0.075 and a range of frictional forces between about 0.5 and 2.0 mN, depending on normal load and sliding speed [8]. Zhou et al. examined the DCoF between senofilicon-A and a stainless steel surface as a function of sliding speed (V) and normal load. They found that the DCoF was proportional to $V^{0.23}$ and a value of about 0.1 was observed at sliding speeds of 1 mm/s [9]. Dunn et al. measured the DCoF of delefilcon-A samples against a borosilicate glass probe [10]. At lower normal loads the DCoF was found to be low ($\mu = 0.02$) but at higher loads (about 2 mN) a transition to higher DCoF values ($\mu = 0.5$) occurred; likely due to the collapse of the thin, high water content, copolymer hydrogel layer [10]. Since the DCoF and frictional forces will depend on the contact pair, including the influence of the materials on the prevailing lubrication conditions, these data may not be relevant to either the upper eyelid–contact lens or lens–ocular surface tribological systems. With this in mind, and given the lack of a standard method for measuring the lens–ocular surface DCoF, the need to mimic the in-vivo system as closely as possible is essential.

Roba et al. employed mucin-coated glass slides and contact lenses, which they believed mimicked the interaction between the lens front surface and upper eyelid [11]. They reported DCoF values ranging from 0.011 to 0.562 depending on contact lens type [11]. While they used a more relevant contact pair, the mucin-coated glass slide will not deform, as would tissue, and their method was not able to assess cell damage. Tosatti et al. augmented the Roba method by exposing the contact lenses to a tear mimicking fluid and found DCoF values extending from 0.008 to 0.231 depending on lens type [12]. Wilson et al. employed mucin-coated glass slides against human corneal cadavers; suggesting a more relevant counter surface for lens–cornea DCoF measurements [13].

Dunn et al. demonstrated that DCoF and cell damage estimates can be made by rubbing silicone hydrogel contact lenses against a

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monolayer of living corneal epithelial cells deposited (cultured) on a rigid cell growth substrate [14]. The DCoF range they observed extended from about 0.03 to 0.05 and was seen to increase nearly monotonically, as a function of cycle number [14]. This increase was attributed to accumulated cell damage, including removal of the cell monolayer [14]. While they employed a pertinent contact pair, the use of a monolayer may have resulted in an overestimation of the cell damage due to poor adhesion between the monolayer and cell substrate. Recently, Samson et al. used excised human cadaver cornea and eyelid tissue to measure the DCoF (and static CoF) of three commercially available silicone hydrogels against these tissues and to test the efficacy of proteoglycan 4 as a lubricant [15]. They found DCoF values, without lubricant, ranging from about 0.05 to 0.13 depending on lens type and sliding speed; lower values were reported with the lubricant [15]. While employing a meaningful counter surface they did not measure cell damage [15].

Three dimensional human corneal epithelial (HCE) cell constructs are a good counter surface candidate. Similarities between these constructs and normal human corneal epithelial tissue in terms of morphology and thickness have been demonstrated [16,17]. Scanning electron microscopy revealed the presence of microvilli on the apical cell layer (outer membrane) similar to that found in human corneal epithelial tissue and other (primary cell) HCE constructs [17,18]. The membrane-bound mucin (MUC4) was also shown to be present [17]. Histological characterizations revealed a cellular structure similar to that of human corneal epithelial tissue down to the basal layer, which was attached to the polycarbonate(PC) substrate with mature hemidesmosomes [16]. Biochemical characterization of the tissues indicated the presence of appropriate markers specific for corneal epithelium, such as cornea-specific keratin-3 [16]. These constructs have been characterized extensively for use in toxicological studies, especially related to exposure to benzalkonium chloride (BAC) [16,19–21].

It is reasonable to expect that the in-vivo corneal cell damage in contact lens wear is due to a combination of DCoF, pressure, and lens movement. The DCoF and lens induced pressure are expressed as the frictional force and in combination with the lens movement deliver energy or work to the corneal surface. It is proposed, here, that the frictional energy, or sliding work, input to the corneal epithelial tissue and normalized to the area and time over which the energy is delivered, represents an appropriate metric. Furthermore, this is likely a better metric than DCoF since it includes lens movement and takes into account the factors that influence the frictional forces, such as ocular shape and lens design. In particular, we are postulating a type of fatigue mechanism (repeated stressing) that causes cell damage. Specifically, it is conjectured that frictional energy correlates positively with cell damage.

The efforts described in this document were undertaken to develop a relatively rapid in-vitro method capable of exploring this hypothesis while employing a contact pair relevant to the lens–corneal surface tribological system.

2. Experimental/analysis method

The HCE constructs were received from the supplier in three separate batches. For each batch, two constructs were used as controls: one as a negative control (no tribological exposure) and one as a positive control (exposure to 0.1% BAC for 1 h). Within each batch, different lens types were tested in a random order. Seven lens types were tested (see Table 1). The experiments were not masked.

2.1. Incubation and preparation of HCE constructs

In the current study, HCE constructs were supplied by EpiSkin (Lyon, France) and were comprised of immortalized human corneal epithelial cells that were cultured at the liquid–air interface on PC support substrates. The constructs were typically between about 50–70 μm thick and had an area of about 0.5 cm^2 [16].

Upon receipt, the constructs were removed from the packaging and immediately placed into a well of a six well plate that had been filled with 1 ml of maintenance medium (a proprietary solution supplied by SkinEthic). Care was taken to ensure that no air bubbles were trapped between the tissue construct and the medium. This took place under sterile environment in a laminar flow hood. The HCE constructs were then allowed to incubate overnight in an incubator with the temperature controlled to 37 °C (±0.2 °C) and with an atmosphere containing 5% CO_2 (±0.2%). Typically the constructs were exposed to the tribological testing after incubating for about 24 h; however, in two instances, the testing took place about 48 h after receipt. When this occurred, the maintenance medium was replaced after about 24 h.

Prior to performing the tribological test, about 50 μl of a human tear facsimile (tear like fluid or TLF) was pipetted onto the HCE tissue surface and the HCE constructs were allowed to incubate for about an additional hour at 37 °C in a 5% CO_2 environment. The TLF consisted of an array of lipids (cholesteryl linoleate, linalyl acetate, triolein, oleic acid, undecylenic acid, and cholesterol) and proteins (mucins, acid alpha 1 glycoprotein, bovine serum, gamma globulins, lipocalin, lysozyme, and lactoferrin). The specific concentrations are based on those detailed previously [22,23].

The HCE constructs were then mounted into a custom construct holder system. First, the custom construct holder was placed into a dish, which was specifically designed to work with the tribometer, and about 2.5 mL of maintenance medium was placed inside the dish. This system provided rigidity to the construct during the tribological testing and is believed to help reduce variation due to flexing of the PC backing. About 2.5 mL of maintenance medium was placed inside the dish so that the maintenance medium level was below the construct; slots in the construct holder allowed for transport of the medium to the HCE construct by capillary action. The Petri dish and construct holder were allowed to incubate for an additional 5 min at 37 °C and

Table 1
Contact lenses used in tribology study.

Lens material lens brand	Manufacturer	Number of lenses tested	Base curve radius (mm)	Diameter (mm)
Balafilcon A PureVision® (PV)	Bausch + Lomb	5	8.3	14.0
Etafilcon A w/PVP 1-DAY ACUVUE® MOIST (1DM)	Johnson and Johnson Vision Care, Inc. (JJVCI)	3	8.5	14.2
Lotrafilcon A AIR OPTIX® AQUA (AOA)	Alcon	2	8.6	14.2
Comfilcon A Biofinity® (BF)	CooperVision	3	8.6	14.0
Etafilcon A ACUVUE® 2 (Acv2)	JJVCI	9	8.3	14.0
Narafilcon A 1-DAY ACUVUE® TruEye® (1DTE)	JJVCI	3	8.5	14.2
Senofilcon A ACUVUE OASYS® (AO)	JJVCI	10	8.4	14.0