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# Measurement of the anisotropic thermal conductivity of the porcine cornea

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ABSTRACT

Accurate thermal models for the cornea of the eye support the development of thermal techniques for reshaping the cornea and other scientific purposes. Heat transfer in the cornea must be quantified accurately so that a thermal treatment does not destroy the endothelial layer, which cannot regenerate, and yet is responsible for maintaining corneal transparency. We developed a custom apparatus to measure the thermal conductivity of *ex vivo* porcine corneas perpendicular to the surface and applied a commercial apparatus to measure thermal conductivity parallel to the surface. We found that corneal thermal conductivity is 14% anisotropic at the normal state of corneal hydration. Small numbers of *ex vivo* feline and human corneas had a thermal conductivity perpendicular to the surface that was indistinguishable from the porcine corneas. Aqueous humor from *ex vivo* porcine, feline, and human eyes had a thermal conductivity nearly equal to that of water. Including the anisotropy of corneal thermal conductivity will improve the predictive power of thermal models of the eye.

## 1. Introduction

Researchers have developed analytical and numerical models of heat transfer in the eye to analyze thermally-based methods for vision correction and other scientific purposes (Ooi et al., 2009; Ooi and Ng, 2009; Karampatzakis and Samaras, 2010; Wang and Qin, 2010). Karampatzakis and Samaras, 2010 included hypothetical values of anisotropic thermal conductivity in the cornea in their model. In this article, we report measured values of the anisotropic thermal conductivity of the cornea as a function of corneal water fraction. Quantification of anisotropy will permit more accurate analysis of heat transfer in the cornea.

Thermally-based methods of vision correction exploit the fact that collagen in the cornea shrinks when elevated above 60° C (Stringer and Parr, 1964; Spörl et al., 1996). The proper choice of heating pattern on the corneal will change central corneal topography to correct certain vision disorders. An early method of thermal keratoplasty applied a hot probe to the cornea to produce collagen shrinkage (Aquavella, 1974; Goldblatt et al., 1989). Later, radio-frequency thermokeratoplasty (RFTK) employed electrical currents to heat the cornea for the same purpose (Doss and Albillar, 1980; Asbell et al., 2001). Clinical trials of RFTK for correction of hyperopia and keratoconus have been described by many authors (Alio et al., 2005; Claramonte et al., 2006; Du et al., 2007; Lyra et al., 2007; Hashemi and Habibollahi, 2008; Ehrlich and Manche, 2009; Kato et al., 2010). Supporting the clinical application of RFTK are the theoretical analyses performed with thermal or thermal-electrical models (Berjano et al., 1997, 1998, 2002, 2003; Pearce, 2002; Pearce and Panescu, 2004; Berjano et al., 2005; Pearce and Ikei, 2007; Jo and Aksan, 2010); two models of Berjano and colleagues include hypothetical values of anisotropic thermal conductivity in the cornea (Berjano et al., 1998, 2002). Such models would be most useful when they incorporate actual measured values of anisotropic thermal conductivity.

Laser thermokeratoplasty (LTK) was first described by Seiler et al. (1990), and clinical trials followed (Park et al., 2004; Rehany and Landa, 2004; Holzer et al., 2009). A semi-analytical model (Manns et al., 2003) and a numerical model based on the classical (parabolic) heat equation (Ooi et al., 2008) have been developed for transient heat transfer in the cornea in response to a laser pulses. Others solved the hyperbolic heat equation with laser or RFTK pulses of extremely short duration driving the heating process

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*Abbreviations:* LSP, Line Source Probe; GHP, Guarded Hot Plate; TK, Thermal Keratoplasty; RFTK, Radio-Frequency Thermal Keratoplasty; LTK, Laser Thermokeratoplasty; MTK, Microwave Thermal Keratoplasty.

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**Nomenclature**

| | |
|---|---|
| $A_\perp$ | cross-sectional area of corneal sample ($m^2$) |
| $h_{fg}$ | latent heat of vaporization of water = 2430 kJ $kg^{-1}$ at 330 K |
| $k_\perp$ | thermal conductivity perpendicular to corneal surface (W $m^{-1}$ $K^{-1}$) |
| $k_{II}$ | thermal conductivity parallel to corneal surface (W $m^{-1}$ $K^{-1}$) |
| $k_w$ | thermal conductivity of water (Incropera and DeWitt, 1996) = 0.611 (W $m^{-1}$ $K^{-1}$) |
| $k_c$ | thermal conductivity of collagen (Kampmeier et al., 2000) = 0.188 (W $m^{-1}$ $K^{-1}$) |
| $M_d$ | mass of dehydrated corneal sample (gm) |
| $M_c$ | mass of hydrated corneal sample (gm) |
| $Q$ | heat flux out of upper plate of Guarded Hot Plate apparatus (W) |
| $Q_E$ | systematic error in heat flux (W) |
| $R_2$ | radius of curvature of lower plate = 0.008 m |
| $R_1$ | radius of curvature of upper plate = 0.007 m |
| $S$ | separation of upper and lower plates at centerline with corneal sample present (m) |
| $\Delta T$ | temperature difference across corneal sample (K) |
| $\Delta x$ | thickness of general sample in Cartesian coordinates (m) |
| $t(\theta)$ | thickness of corneal sample as a function of angular location $\theta$ (m) |
| $\Delta$ | deviation of corneal thickness at centerline from the ideal value equal to $R_2 - R_1$ |
| $\rho$ | mass density of corneal sample (kg $m^{-3}$) |
| $\rho_w$ | mass density of water (Incropera and DeWitt, 1996) = 1000 (kg $m^{-3}$) |
| $\rho_c$ | mass density of collagen (Kampmeier et al., 2000) = 1536 (kg $m^{-3}$) |
| $\theta$ | angular location in spherical coordinate system (rad) |
| $\omega_w$ | mass fraction of water in cornea |

(Trujillo et al., 2009; Tung et al., 2009); the hyperbolic heat equation assumes a limited speed of propagation of thermal effects in a medium.

The first microwave thermokeratoplasty (MTK) system employed a surface cooling system to spare the epithelium of the cornea, while attaining shrinkage temperature in the corneal stroma (Trembly and Keates, 1991). A later MTK system flattened the central zone of *ex vivo* porcine corneas to correct myopia, while preserving the epithelium with a cooling system (Trembly et al., 2001). A commercial MTK system produced central flattening in *ex vivo* porcine corneas (Ryan et al., 2009), human eye bank corneas (Barsam et al., 2010), and human patients (Celik et al., 2013). An electrical-thermal model with isotropic thermal conductivity was developed to predict the transient temperature distribution of this commercial MTK system (Pertaub and Ryan, 2009). With an accurate thermal model, an MTK system may be designed to preserve the epithelium and endothelium, while attaining a shrinkage temperature in the stromal collagen. The anisotropy of the thermal conductivity of the cornea must be known, in order to quantify the balance of heat transfer toward the epithelial and endothelial layers and parallel to them.

Investigators of thermal refractive techniques usually assume that the thermal conductivity of the cornea is isotropic. Levin (Levin, 1987) measured an isotropic thermal conductivity in *ex vivo* porcine corneas of 0.556 W $m^{-1}$ $K^{-1}$ using a transient, thermistor probe developed by Balasubramaniam and Bowman (1974), Bowman et al. (1975), Bowman and Balasubramaniam (1976), Valvano et al. (1984). This paper advances Levin's work by quantifying the anisotropy of corneal thermal conductivity and its relation to the corneal state of hydration.

## 2. Methods

### 2.1. Theoretical

Poppendiek et al. (1966) described a theoretical model for the thermal conductivity of a material comprising orderly layers of different materials. For heat flow in the direction *parallel* to repeated layers of *N* different materials, the thermal conductivity is given by

$$k_{II} = \rho \sum_{j=0}^{N} \frac{k_j \omega_j}{\rho_j} \tag{1}$$

We modeled the cornea as collagen layers alternating with water layers to reduce the preceding equation to

$$k_{II} = \rho \cdot \left( \frac{k_w \cdot \omega_w}{\rho_w} + \frac{k_c \cdot (1 - \omega_w)}{\rho_c} \right) \tag{2}$$

where $k_w = 0.611$ W $m^{-1}$ $K^{-1}$ (Incropera and DeWitt, 1996) and $k_c = 0.188$ W $m^{-1}$ $K^{-1}$ (Kampmeier et al., 2000).

For heat flow in the direction *perpendicular* to repeated layers of N different materials Poppendiek et al. (1966) gives the thermal conductivity as:

$$k_\perp = \left( \rho \sum_{j=0}^{N} \frac{\omega_j}{k_j \rho_j} \right)^{-1} \tag{3}$$

For alternating layers of water and collagen, we adapted this to yield

$$k_\perp = \left[ \rho \cdot \left( \frac{\omega_w}{k_w \cdot \rho_w} + \frac{(1 - \omega_w)}{k_c \cdot \rho_c} \right) \right]^{-1} \tag{4}$$

We computed thermal conductivity with these theoretical expressions for a range of values of water fraction. In the Results section, we compare such theoretical values of thermal conductivity to our own measured values of thermal conduction, in the directions parallel and perpendicular to the collagen fibers. The next section describes our experimental methods.

### 2.2. Experimental

#### 2.2.1. Line Source Probe

We applied: a) a transient technique, the Line Source Probe, to measure the thermal conductivity parallel to the corneal surface, and b) a steady-state technique, the Guarded Hot Plate, to measure the thermal conductivity perpendicular to the corneal surface. The Line Source Probe (LSP) is a source of axially-uniform heat flux