Mathematical modeling of ultrashort pulsed laser irradiation in the cornea

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Abstract---A simple mathematical model for the temperature evolution in the cornea exposed to short-pulsed Ho: YAG laser under Laser Thermo Keratoplasty (LTK) treatment is developed by incorporating the heat flux phase-lag in the Fourier's heat transfer model and laser source term is described by Lambert Beer's law. An analytical solution to the mathematical model is obtained using the Laplace transformation technique. The computational results for the temperature profile and the temperature variation with time are presented through the graphs. The effect of some typical parameters: the heat flux phase-lag, convection coefficient and thermal conductivity on the temperature distribution and temperature variations are illustrated and discussed.

Keywords---Temperature, Laser, Cornea, LTK, Laplace Transformation technique, Hyperbolic Model.

Introduction

Laser thermo keratoplasty (LTK), a corneal refractive surgery technique, is directed towards altering the corneal curvature using laser energy to heat the peripheral corneal collagen. The laser heating results in the shrinkage of the peripheral and paracentral stromal collagen, which causes flattening of the peripheral cornea, and steepening of the central cornea leading to an increase in the corneal curvature and an improvement in corneal refractive power without any cutting or removal of the tissue.

LTK eye surgery has been plagued, however, by the regression of the refractive effect. Thus, the results of LTK surgery are not permanent. Also, it is not the

preferred choice for clinical treatment of hyperopia due to its low predictability and repeatability in producing reliable results. There is a need to introduce some modifications in the procedure to improve LTK which may minimize or counteract the regression of the refractive effect. A thermal refractive surgical procedure that aims to reshape the cornea without the collagen fibres necrosis and with the minimal thermal damage to adjacent tissue may result in a better refractive correction technique with long-term stability.

An understanding of the response of stromal collagen to laser heat enriched through the experimental investigations and theoretical studies of the thermomechanical behaviour of the cornea subjected to LTK surgery to improve its predictability and repeatability may contribute to the design and development of a more effective LTK treatment procedure. In addition to numerous experimental studies of the temperature rise in the corneal tissue during LTK surgery, several mathematical models for the temperature profiles in the eye subjected to laser irradiation have been developed and simulated.

Mainster [1] and Peppers et al., [2] modeled the cornea as a semi-space region where heat transfer during laser irradiation was assumed to be one dimensional. They used Beer's law to model the laser energy absorbed inside the cornea. Zhou et al., [3] and Mainster et al., [4] calculated the temperature distribution using the finite difference method and considered the cornea as a finite cylinder during treatment of LTK. Brinkmann et al., [5] also developed a cylindrical model and solve it using the finite difference method. This model has been used by Brinkmann and his co- workers to understand the thermal responses of the human cornea during LTK treatment under various conditions [6-9]. The cornea was modeled as a rectangular strip of finite thickness by [10]. Analytical expressions were obtained for the corneal temperature during LTK for various conditions, and computational results were obtained and presented through the graphs. Recently, Podol'stev and Zheltov [11] developed a model of the human eye as a multi-layered cylinder to understand the heat transfer process during LTK.

Most of the above researches had been concerned with the thermal analysis of corneal temperature during laser irradiation, and many of them applied the classical Fourier's heat conduction model to evaluate the thermal behaviour of the corneal tissue. Although Fourier's heat conduction model does not give bad results in most of the engineering problems, some experimental results showed that Penne's bioheat transfer (Parabolic model) provides non-physical results such as those involving extremely short times or high heat flux [12-13]. In this case, thermal waves do not propagate at an infinite speed. Jaunich et al., [14] solved the problem of the bioheat transfer of short pulses of laser irradiation on body tissues numerically. Gheitaghy et al., [15] developed the hyperbolic model for the heat transfer in a non-perfused homogeneous transparent cornea under ultrashort pulsed laser irradiation in the LTK treatment. The model was solved by exploiting the mathematical analogy between thermal and electrical systems. They concluded that the hyperbolic wave model predicts a higher temperature than that predicted by Fourier's model.

The present work is concerned with the development of a mathematical model for the temperature evolution in the corneal tissue subjected to the ultrashort pulsed

laser irradiation under the LTK surgery by incorporating the relaxation time of heat flux in the Fourier's law of heat conduction and using Beer's law for the laser heat source. An analytical solution to the mathematical model was obtained in infinite series form using the Laplace transform technique. The computational results for the corneal temperature variation with time and temperature distribution were presented through graphs and the effects of some model parameters on the temperature variation and distribution have been illustrated and discussed.

Physical model and mathematical formulation

The cornea is modelled as homogeneous non-perfused tissue a finite domain that is exposed to a short-laser heat pulse at its anterior surface the front surface (Left boundary of Fig.1) as in the LTK surgery. The energy of the laser beam which is incident at the centre of the cornea is assumed to be absorbed in the stroma. One-dimensional heat transfer is assumed.
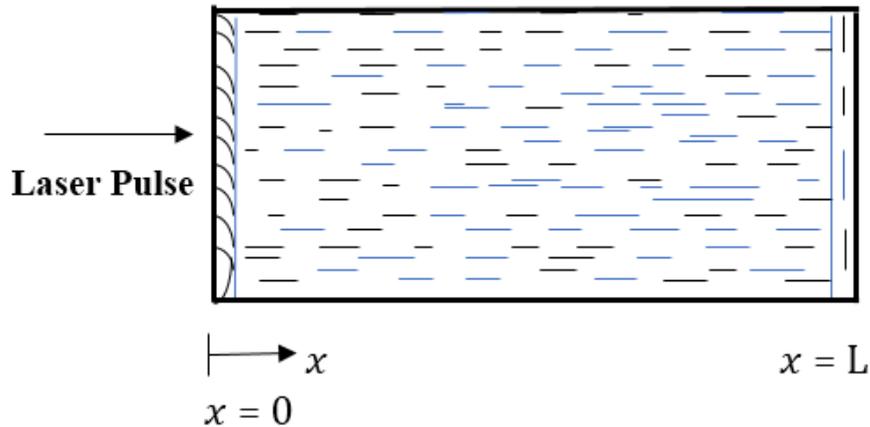

Fig. 1. Schematic diagram of the cornea modeled as finite domain exposed to Ho: YAG short Pulse laser

The heat transfer in living biological tissues is governed by Penne's Eq. [16],

$$\rho c \frac{\partial T(x,t)}{\partial t} = -\nabla.q + \rho_b c_b \omega_b (T_b - T) + q_{mb} + Q(x,t) \tag{1}$$

where, $q(Wm^{-2})$ is the heat flux, $\rho_b(Kg\,m^{-3})$ the blood density, $c_b(JKg^{-1}{}°C^{-1})$ the blood specific heat, $\omega_b(s^{-1})$ the volumetric blood perfusion rate per unit volume, $T_b(°C)$ the blood temperature, T (°C) the tissue temperature, $q_{mb}(Wm^{-3})$ the heat generation due to metabolism, $\rho(Kg\,m^{-3})$ the tissue density, c ($JKg^{-1}{}°C^{-1}$) the tissue-specific heat and $Q(x,t)(Wm^{-3})$ the heat generated to laser energy. Due to a small amount of metabolic heat compared to the heat generated from laser accidents, it could be neglected [17]. Also, the blood perfusion rate at the selected region is almost zero because the corneal tissue is avascular.

Therefore $\qquad q_{mb} = 0, \quad \omega_b = 0,$

Now, Eq. (1) reduces to the following form:

$$\rho c \frac{\partial T(x,t)}{\partial t} = -\nabla . q + Q(x,t) \qquad (2)$$

The Fourier's law of heat conduction, which is a simple linear empirical relation between the heat flux vector and the temperature gradient is given by

$$q(x,t) = -k \frac{\partial T(x,t)}{\partial x} \qquad (3)$$

where, k $(Wm^{-1}{}^{\circ}C^{-1})$ is the corneal tissue thermal conductivity.
Adding relaxation time of heat flux, τ_q in variable t in term $q(x,t)$ of Fourier's law (3), we obtain:

$$q\left(x, t + \tau_q\right) = -k \frac{\partial T(x,t)}{\partial x} \qquad (4)$$

Using the first-order approximation of Taylor's series expansion of $q\left(x, t + \tau_q\right)$, the following Eq. is obtained:

$$q(x,t) + \tau_q \frac{\partial q(x,t)}{\partial t} = -k \frac{\partial T(x,t)}{\partial x} \qquad (5)$$

On solving Equations (2) and (5), we get a hyperbolic model of heat transfer in the corneal tissue.

$$\tau_q \frac{\partial^2 T(x,t)}{\partial t^2} + \frac{\partial T(x,t)}{\partial t} = \alpha \frac{\partial^2 T(x,t)}{\partial x^2} + \frac{1}{\rho c}\left[Q + \tau_q \frac{\partial Q(x,t)}{\partial t}\right] \qquad (6)$$

where, $\alpha = \frac{k}{\rho c}$ is the thermal diffusivity of the corneal tissue.
The laser heat source is modelled by Beer-Lambert law
$$Q(x,t) = I(t)(1-R)\,\mu\,e^{-\mu x}$$

where, R is Fresnel surface reflectance, $\mu(m^{-1})$ the absorption coefficient of the corneal tissue, $I(t)\,(Wm^{-2})$ the laser intensity. The laser heat source $Q(x,t)$ is assumed to be Gaussian and has been separated into variables in time and space. The appropriate physically realistic and mathematically consistent conditions for the problem under consideration are as follows:

Initial conditions

$$T(x,t)|_{t\,=\,0} = T_0, \qquad\qquad \frac{\partial T(x,t)}{\partial t}\bigg|_{t\,=\,0} = 0,$$

$7(a,b)$
Boundary conditions

$$-k \frac{\partial T(x,t)}{\partial x}\bigg|_{x\,=\,0} = h(T - T_0) + \sigma\epsilon\left(T^4 - T_0{}^4\right) + E, \qquad (8)$$

$$\frac{\partial T(x,t)}{\partial x}\bigg|_{x\,=\,L} = 0, \qquad (9)$$

where, $E (Wm^{-2})$ is the evaporative heat loss, $\sigma (Wm^{-2}K^{-4})$ the Stefan Boltzmann constant h $(m^{-2}K^{-1})$ the convection coefficient and ε the emissivity of the cornea.

The boundary condition (8) represents that the heat loss at the anterior surface of the cornea occurs due to convection, emission and evaporation. The boundary condition (9) represents that the posterior surface of the cornea is thermally insulated.

Non-dimensionalization

To non-dimensionalize the governing equation (6) the following scheme is introduced:

$$X = \frac{\omega x}{2\alpha}, \quad \tau = \frac{t}{2\tau_q}, \quad \psi = \frac{Q\tau_q}{\rho c T_0}, \quad \theta = \frac{T}{T_0},$$

The normalized form of Eqn. (6) is given by

$$\frac{\partial^2 \theta}{\partial \tau^2} + 2\frac{\partial \theta}{\partial \tau} = \frac{\partial^2 \theta}{\partial X^2} + 4\psi_0\,\eta(\tau)\,e^{-\beta X} + 2\frac{\partial \psi_0 \eta(\tau) e^{-\beta X}}{\partial \tau} \tag{10}$$

where $\Psi(X,\tau) = \psi_0\,\eta(\tau)\,e^{-\beta X}$, $\psi_0 = \frac{\beta\,I_r(1-R)}{2\omega\rho c T_0}$, $\beta = 2\,\omega\tau_q\,\mu$

and $\eta(\tau)$ is the dimensionless rate of energy absorbed in the tissue, the laser heat source term
is expressed in terms of arbitrary reference laser intensity I_r as $I(\tau) = I_r\,\eta(\tau)$

The normalized forms of the initial and boundary conditions are

$$\theta(X,\tau)|_{\tau=0} = 1, \quad \frac{\partial \theta(X,\tau)}{\partial \tau}\bigg|_{\tau=0} = 0, \tag{11(a,b)}$$

$$-B\frac{\partial \theta}{\partial X}\bigg|_{X=0} = F\,(\theta-1) + H(\tilde{\theta}^2+1)(\tilde{\theta}+1)\,(\theta-1) + G,$$

$$\frac{\partial \theta}{\partial X}\bigg|_{X=L'} = 0, \quad \text{where } L' = \frac{\omega L}{2\alpha} \tag{12(a,b)}$$

where $F = \frac{hT_0}{I_r}$, $H = \frac{\sigma\epsilon T_0^4}{I_r}$, $G = \frac{E}{I_r}$, $B = \frac{\omega\rho c T_0}{2I_r}$

Taking the Laplace transform of Eq. (10) and using initial conditions 11(a, b), we get the equation:

$$\frac{d^2\overline{\theta(X,u)}}{dX^2} - u(u+2)\,\overline{\theta(X,u)} = -(u+2) - 2\,\psi_0 e^{-\beta X}\,\overline{\eta(u)}(u+2) \tag{13}$$

where
$$\overline{\theta(X,u)} = L[\theta(X,\tau)]$$
$$\overline{\eta(u)} = L[\eta(\tau)]$$

The Laplace transformation of boundary conditions 12(a, b) results in the following equation:

$$-B\frac{\partial \overline{\theta}}{\partial X}\bigg|_{X=0} = F\left(\bar{\theta}-\frac{1}{u}\right) + H(\tilde{\theta}^2+1)(\tilde{\theta}+1)\left(\bar{\theta}-\frac{1}{u}\right) + \frac{G}{u},$$

$$\frac{\partial \overline{\theta}}{\partial X}\bigg|_{X=L'} = 0, \quad \text{where } L' = \frac{\omega L}{2\alpha} \tag{14 (a,b)}$$

The solution of ordinary differential Eq. (13) subject to the boundary conditions 14 (a, b) is given below:

$$\overline{\theta(X, u)} = A_1(u)\, e^{\lambda X} + A_2(u)\, e^{-\lambda X} + A(u)\, e^{-\beta X} + \frac{1}{u} \tag{15}$$

where, $\lambda^2 = u(u + 2)$, $U = B\lambda + (F + \mathbf{R})$, $V = B\lambda - (F + \mathbf{R})$, $\mathbf{R} = H(\tilde{\theta}^2 + 1)(\tilde{\theta} + 1)$

$$A(u) = -2\psi_0 \overline{\eta(u)}\, \frac{(u + 2)}{((\beta^2 - \lambda^2))},$$

$$A_1(u) = \frac{G\, e^{\lambda L'}}{u(V\, e^{\lambda L'} - U\, e^{-\lambda L'})} - \frac{A\, e^{\lambda L'}(B\beta - F - \mathbf{R})}{(V\, e^{\lambda L'} - U\, e^{-\lambda L'})} - \frac{AU\beta\, e^{-\beta L'}}{\lambda(V\, e^{\lambda L'} - U\, e^{-\lambda L'})},$$

$$A_2(u) = \frac{A\beta\, e^{-\beta L'}}{\lambda\, e^{\lambda L'}} - \frac{AU\beta\, e^{-\beta L'}\, e^{-\lambda L'}}{\lambda\, e^{\lambda L'}(V\, e^{\lambda L'} - U\, e^{-\lambda L'})} + \frac{G\, e^{-\lambda L'}}{u(V\, e^{\lambda L'} - U\, e^{-\lambda L'})} + \frac{A\, e^{-\lambda L'}(B\beta - F - \mathbf{R})}{(V\, e^{\lambda L'} - U\, e^{-\lambda L'})},$$

For taking the inverse Laplace transform of Eq. (15) and to find the solution in the time domain, we expand the terms $A_1(u)\, e^{\lambda X}$ and $A_2(u)\, e^{-\lambda X}$ in Binomial series

$$A_1(u)\, e^{\lambda X} = A\, U\beta\, e^{-\beta L'}\, e^{\frac{-\lambda(L' - X)}{\lambda}} + A\, U\beta\, e^{-\beta L'} \sum_{n=0}^{\infty} \frac{e^{-\lambda((1 - 2n)L' - X)}}{\lambda} - \frac{G}{Bu} \sum_{n=0}^{\infty} \frac{e^{\lambda(2nL' + X)}}{\lambda}$$
$$+ \frac{A(B\beta - F - \mathbf{R})}{B} \sum_{n=0}^{\infty} \frac{e^{\lambda(2nL' + X)}}{\lambda}$$
$$A_2(u)\, e^{-\lambda X} = -\frac{G}{Bu} \sum_{n=0}^{\infty} \frac{e^{\lambda(2nL' + 2L' - X)}}{\lambda} + \frac{A(B\beta - F - \mathbf{R})}{B} \sum_{n=0}^{\infty} \frac{e^{\lambda(2nL' + 2L' - X)}}{\lambda}$$
$$+ A\,\beta\, e^{-\beta L'} \sum_{n=0}^{\infty} \frac{e^{\lambda(2nL' + L' - X)}}{\lambda}$$

The inverse Laplace transform of Eq. (15) is obtained by using the Binomial series of the terms $A_1(u)\, e^{\lambda X}$ and $A_2(u)\, e^{-\lambda X}$, we get the solution:

$$\theta(X, \tau) = e^{-\beta X} \quad \psi_0 f_H \quad + \psi_0\, \beta\, e^{-\beta L'} h_i(L' - X,\ \tau) + \psi_0\, \beta\, e^{-\beta L'} \sum_{n=0}^{\infty} h_i((1 - 2n)L' - X, \tau) -$$
$$\frac{G}{B} \sum_{n=0}^{\infty} h(-(2nL' + X),\ \tau) + \psi_0\, \frac{(B\beta - F - \mathbf{R})}{B} \sum_{n=0}^{\infty} h_i(-(2nL' + X),\ \tau) +$$
$$\psi_0\, \frac{(B\beta - F - \mathbf{R})}{B} \sum_{n=0}^{\infty} h_i(-(2L' + 2nL' - X),\ \tau) + \psi_0\, \beta\, e^{-\beta L'} \sum_{n=0}^{\infty} h_i(-(L' + 2nL' -$$
$$X),\ \tau) - \frac{G}{B} \sum_{n=0}^{\infty} h(-(2L' + 2nL' - X),\ \tau) + 1$$

where

$$h_i(p, \tau) = \begin{cases} 0 & for & p \geq \tau \geq 0 \\ \int_p^\tau e^{-v} I_0[(v^2 - p^2)]^{\frac{1}{2}} f_H(\tau - v)\, dv & for & \tau > p \end{cases}$$

$$h(p, \tau) = \begin{cases} 0 & for & p \geq \tau \geq 0 \\ \int_0^\tau e^{-(\tau - v)} I_0[(\tau - v)^2 - p^2]^{\frac{1}{2}}\, dv & for & \tau > p \end{cases}$$

$$f_H(\tau) = \frac{\gamma_p^2 e^{\gamma_m \tau} - \gamma_m^2\, e^{-\gamma_p \tau} - 4\gamma}{\gamma \gamma_m \gamma_p}$$

$$\gamma = [1 + \beta^2]^{\frac{1}{2}}$$
$$\gamma_p = \gamma + 1$$
$$\gamma_m = \gamma - 1$$

Results & Discussion

The computational results of the hyperbolic model for the temperature profile and temperature variation with time in the corneal tissue irradiated by Ho: YAG laser under LTK treatment is obtained using the values of typical parameters given in the table and presented through the graphs.

Table 1
Parameters used in Computations

Parameter	Symbol	Magnitude	Dimension
Corneal density	ρ	1062	$Kg\,m^{-3}$
Corneal thermal conductivity	k	0.556	$Wm^{-1\circ}C^{-1}$
Fresnel surface reflectance	R	2.4%	-
Absorption coefficient	μ	2000	m^{-1}
Thermal diffusivity	α	0.001452	$cm^2 s^{-1}$
Emissivity of cornea	ε	0.975	_
Stefan Boltzmann constant	σ	5.67×10^{-8}	$Wm^{-2}K^{-4}$
Wavelength	λ	$1.85 - 2.1$	μm
Specific heat	c	3830	$J\,Kg^{-1}K^{-1}$
Initial temperature	T_0	35	°C
Evaporative heat loss	E	40	$W\,m^{-2}$
Phase - lag in heat flux	τ_q	1	sec.
Thickness of cornea	L	0.55	Mm
Reference laser intensity	I_r	2×10^4	Wm^{-2}
Convection coefficient	h	20	$W\,m^{-2}K^{-1}$
Pulse duration	t_i	200	μ s

The temperature rises with time in the corneal tissue subjected to the ultra-short pulsed laser irradiation under LTK surgery during the very short heating phase is almost spontaneous and it is difficult to represent the temperature response of the cornea by graphs. The computational results of this hyperbolic model for the temperature as a function of space and time variables are presented only for the cooling phase.

A comparison of the corneal temperatures variation with time predicted by the parabolic model and the hyperbolic model is illustrated in Fig.2. The temperature response predicted by Fourier's Model (parabolic model) decreases with time rapidly whereas the temperature predicted by the hyperbolic model decreases with time slowly. Most of the time, the temperature predicted by the hyperbolic model is higher than that predicted by the parabolic model.
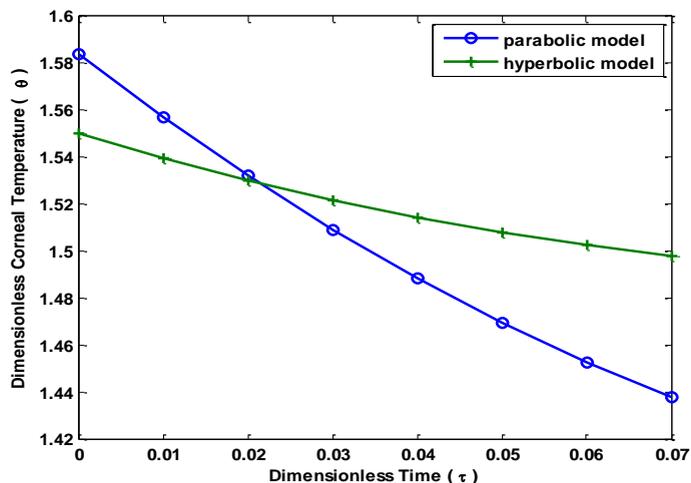
Fig.2. Comparison of the dimensionless temperature variations with time predicted by Fourier's model and hyperbolic model at x = 0.5 mm depth of the corneal tissue during pulsed Ho: YAG laser irradiation

The effect of convection coefficient on the parabolic and hyperbolic temperature variations at different depths is shown in Fig.3 (a) and 3(b), respectively. It is observed that the convection coefficient does not have a significant effect on the temperature variations. The effect of the convection coefficient on the hyperbolic temperature variation is slightly more than that on the temperature parabolic variation. The effect of convection coefficient on the temperature variation gets on decreasing along with the corneal depth, and it is negligible away from the anterior corneal surface.
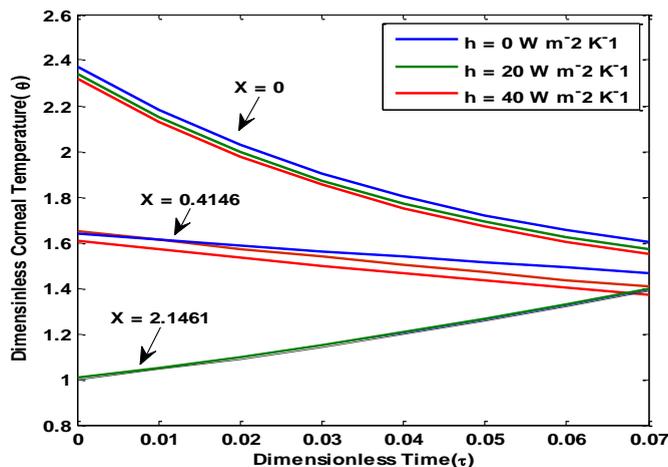
Fig.3 (a). The effect of convection coefficient on the temperature variation with time predicted by the parabolic model at different depths during the cooling phase when laser energy is not applied
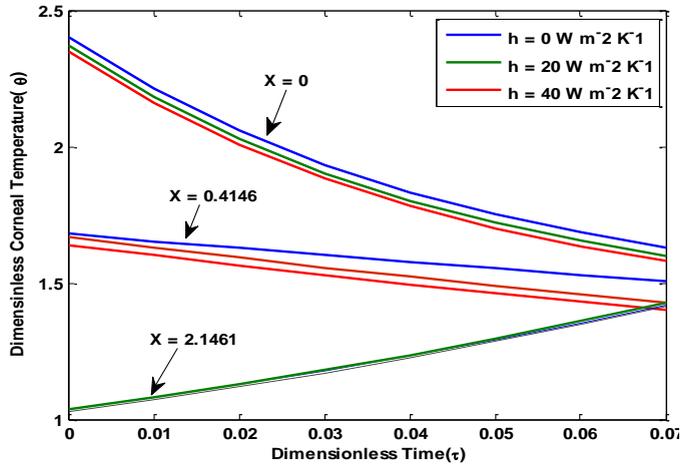
Fig.3(b). The effect of convection coefficient on the temperature variation with time predicted by the hyperbolic model at different depths during the cooling phase when laser energy is not applied

The temperature in the cornea far from its anterior surface increases linearly with time in contrast to the temperature decrease with time at or near the anterior surface during the time under consideration. This occurs due to the diffusion of laser heat energy inwards in the corneal tissue.

The effect of relaxation time on the temperature variation at the anterior corneal surface predicted by the hyperbolic model is illustrated in Fig.4. It is evident from the Fig. that an increase in relaxation time decreases the temperature. However, these temperature distributions become similar in the steady-state. If the heating duration is shorter than the phase lag time, the thermal waves can be generated and predict the maximum temperature.
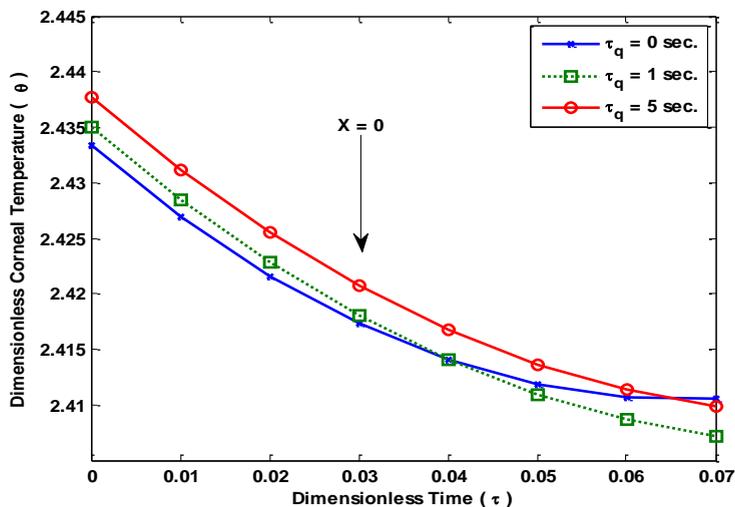

Fig.4. The effect of relaxation time on the temperature variation with time at the anterior surface of the cornea

The influence of temperature-dependent conductivity on the temperature variation with time predicted by the hyperbolic model at different depths of the cornea is presented in Fig.5. The temperature-dependent thermal conductivity of the homogeneous cornea has been assumed as given shown below:
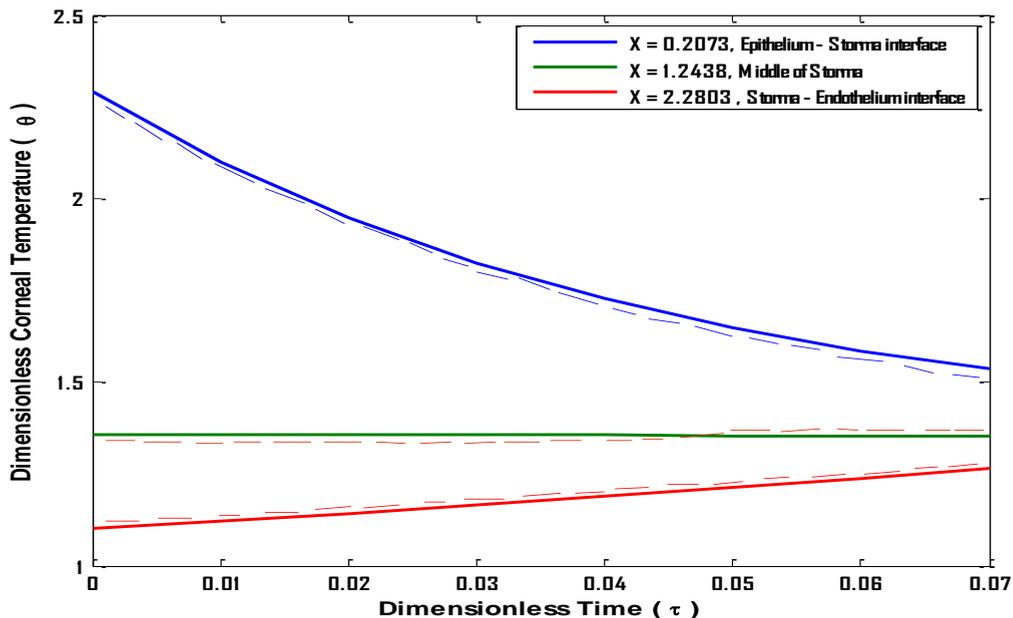
$$k = 0.556 + 0.0031(T - T_0)$$

Fig.5.   Effect of temperature-dependent conductivity on hyperbolic temperature variation with time:

Continuous lines represent $k = 0.556\ Wm^{-1}°C^{-1}$, dashed lines represent
$$k = 0.556 + 0.0031(T - T_0)$$

It is observed from the curves in Fig.(5) That the thermal conductivity has little effect on the temperature variation with time after laser heating. By assuming the linear increase of thermal conductivity with temperature, the conduction of laser energy in the surface layers as a better result, cooling increases. On the other hand, the diffusion of energy in the inner layer increases the temperature.

In Fig. 6 the curves show the distribution of dimensionless temperature along with the dimensionless corneal depth following each laser pulse of the treatment. It is seen that the temperature in the epithelium layer of the cornea estimated by the hyperbolic model lies in the range of 85℃-94℃. Whereas the stromal temperature estimated is seen to lie in the range 68℃-90℃. The temperature in the endothelial layer is predicted to lie between 60℃ and 73℃. The temperature in the layers of the corneal tissue increases with the number of pulses under LTK treatment.
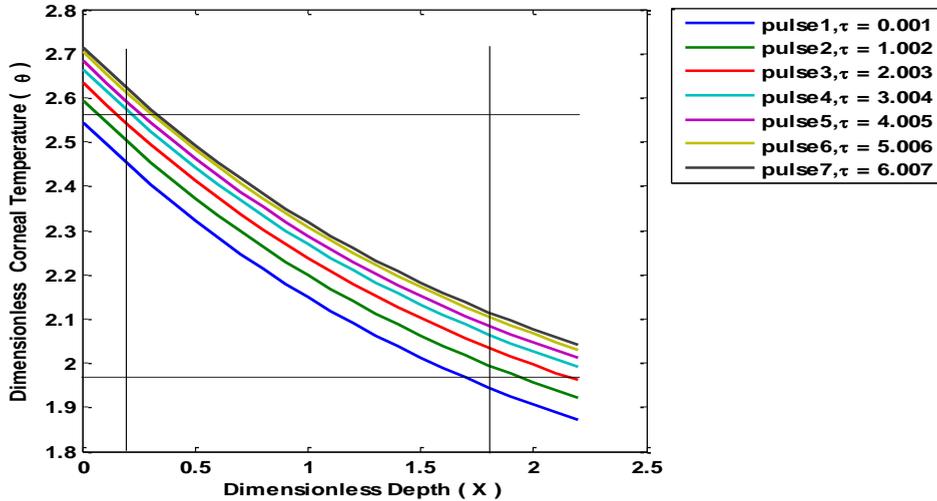
Fig.6. Dimensionless temperature profiles after each laser pulse, predicted by the hyperbolic model

The dimensionless corneal temperature distributions at different times t = 2, 4, 6, 8 and 10 sec. are depicted in Fig.7. The vertical solid lines separate the plotted area into epithelium, stroma and endothelium. The upper (65.79℃) and lower (55.40℃) threshold limits for corneal shrinkage to occur are denoted by the solid horizontal lines. During the course of laser irradiation, the temperature at the majority of the stroma is found to lie between 55.40℃ and 65.79℃. At the epithelium, the temperature ranges from 65.40℃ to 75.10℃. Comparing this to the temperature produced when using a continuous-wave laser, it seems that the continuous wave laser avoids the problem of over-heating. Similar to continuous wave laser heating, no endothelial cell damages are found when the pulsed laser is used.
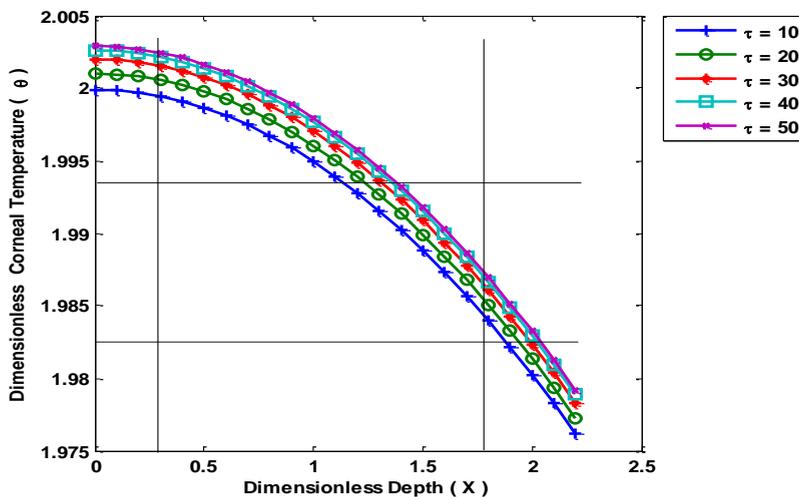

Fig.7. The dimensionless temperature profiles at various time levels

Fig.8 depicts the effect of the relaxation time on the dimensionless corneal temperature profile. It is observed from Fig. 7 that an increase in the relaxation time of heat flux reduces the temperature and that the wavefront is more observable in the case of larger τ_q . Since τ_q is normally interpreted as the non-zero time that accounts for the effect of "thermal inertia", τ_q is responsible for the delay in establishing heat flux and associated conduction through the medium.
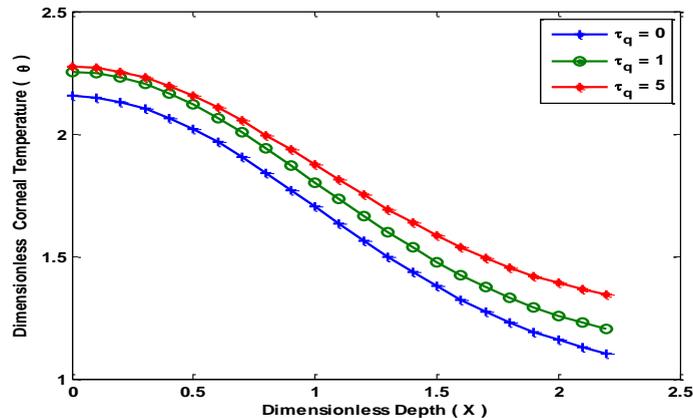

Fig.8. The effect of relaxation time on the corneal temperature profile at the time $\tau = 0.05$

Conclusion

The hyperbolic heat conduction model is used to describe the temperature changes in the human cornea exposed to short-pulsed Ho: YAG laser heating under LTK surgery and to investigate the effects of the phase-lag in the heat-flux on the corneal temperature distribution and temperature variation with time in this study. As observed, from the computational results the temperature in the epithelium layer lies between 85℃ and 94℃, the stromal temperature lies between 68℃ and 90℃ and the temperature in the endothelium lies between 60℃ and 73℃. An increase in the heat flux phase-lag causes a rise in the corneal temperature. There is a need to validate the reliability of the present results by comparing these analytical results with the experimental data. Once the model is validated, it may be used for the design and development of better laser surgery to treat hyperopia.

Acknowledgement

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