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Thermal Analysis of Cornea Heated with Terahertz Radiation

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Featured Application: This work may find potential applications in cornea reshaping in the field of ophthalmology, as well as THz radiation safety and regulation for biomedical imaging or therapy.

Abstract: We numerically investigate the thermal effects in a cornea illuminated by terahertz radiation. By modifying the bioheat and Arrhenius equations, we studied the heat-transfer and temperature distributions in the corneal tissue, and evaluated the potential thermal damage. The influence of the beam radius and power density are discussed. We also estimated the effective cornea-collagen shrinkage region, and evaluated the degree of thermal damage in the cornea. We expect this work to open up a novel effective and safe thermal-treatment approach based on THz radiation for cornea reshaping in the field of ophthalmology.

Keywords: terahertz heating; bioheat transfer; cornea; ophthalmology

1. Introduction

The cornea is a key component of the eye's optical system since it has a curved shape and ensures the refractive function [1]. An effective way to correct refractive disorders of the eye, such as myopia, keratoconus, and hyperopia, is to steepen the precise curved shape of the cornea [2]. Reshaping the cornea can be done through heating, which is known as thermokeratoplasty (TKP), since the cornea stroma permanently shrinks when temperature is raised to over 55 °C [3]. TKP techniques include heating with microwaves [2], preheated probes applied to the surface or inserted in the cornea [4], radio-frequency (RF) currents [5], or laser [6]. Although microwave heating combined with surface cooling can produce a significantly deep region of shrinkage, the shrinkage effect is extremely sensitive to the applicator–cornea gap, making it difficult to implement in the clinic [2]. Preheated probes and RF currents are invasive approaches, so accompanying hazards include infection or even destruction of the cornea [4,5]. For laser-based TKP, the shrinkage effect is not deep enough because of the rather limited heating depth of the laser into the cornea [7]. In other words, there exist many problems for conventional heating techniques, demanding the exploration of novel approaches for the effective and safe thermal treatment of cornea reshaping.

Recently, terahertz (THz) technology has emerged as a novel and promising noninvasive candidate in biomedical applications [8]. A typical application is cornea diagnostics in the field of ophthalmology [9]. Since THz waves are extremely sensitive to water content in tissue and are believed to be harmless for biological entities, THz spectroscopy and imaging techniques have been applied in ex vivo or in vivo corneal hydration sensing [9–14]. These studies suggest that THz sensing is an ophthalmological diagnostic tool that deserves further clinical tests. Another emerging application is related to THz-induced bioeffects, which were mediated primarily through photothermal mechanisms, i.e., thermal effects. Kristensen et al. [15] derived the analytical solution for the Kirchoff's heat equation based on a static (steady-state) model, and showed that heating efficiency is about 40% if THz radiation heats the top layer of the water disc. Wilmink et al. [16] investigated the biological effects associated with human dermal fibroblasts exposed to 2.52 THz radiation. Ganesan et al. [17] calculated the terahertz heating effects in realistic tissue (brain and breast tissue). Zilberti et al. [18] analyzed the transient skin heating induced by terahertz radiation. Bottauscio et al. [19] evaluated the thermal response of human tissue exposed to a focused-beam terahertz electromagnetic radiation by solving the coupled electromagnetic–thermal problem. Encouraged by these studies, quite recently, Smolyanskaya et al. [20] investigated heat transfer of the eye cornea in the THz field. However, their model was relatively simple and thus insufficient to understand the transient behavior of heating effects. Questions remain, such as whether there exists thermal damage, and how THz radiation parameters influence the transient heating effect in the cornea.

In this work, we theoretically investigate the thermal effects in the cornea when heated with terahertz radiation. We develop a model to describe transient temperature distributions and to evaluate the potential thermal-damage effects in the cornea heated with THz ratiation. We also discuss the influence of key parameters, including the radius and power density of the THz beam.

2. Materials and Methods

In order to investigate the time-dependent heat transfer and temperature distributions in the cornea illuminated by terahertz radiation, we developed a two-dimensional (2D) axisymmetric model, as illustrated in Figure 1. This model includes the surrounding fluids, like tears and aqueous humor, similar to the models for thermal effects in the cornea under microwaves [2] or RF heating [5]. A continuous-wave terahertz beam of 3 mm radius and 1 THz frequency impinges onto the center of the cornea. Based on the structure of the human eye, the cornea is treated as a homogeneous and curving layer with 0.4∼0.7 mm thickness [21] and 7.5 mm radius [2,5]; the tear film with a thickness of 5∼15 µm, and the aqueous humor with a thickness of 2 mm [2,5] were modeled as the major water content.

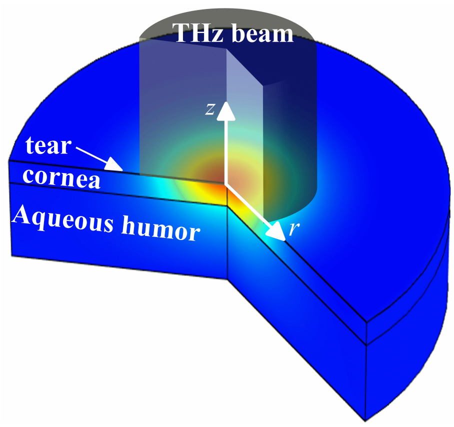

Figure 1. Schematic diagram of THz thermal treatment of the cornea (out of scale).

We made use of the bioheat equation to govern the terahertz bioheat effects in the cornea, which can be written as [22]:

$$\rho C \frac{\partial T}{\partial t} = \nabla(k \nabla T) + q\,. \tag{1}$$

Here, ρ is the density of the corneal tissue (kg/m^3), C is the specific heat of the corneal tissue(J/(kg·K)), T is the corneal tissue's local temporal temperature (K), and k is the thermal conductivity of the corneal tissue (W/(m·K)). Heat source q is related to absorbed THz radiation (W/m^3), which can be given by the Beer–Lambert law [23]:

$$q(z,r) = \alpha(1 - R_f)I_0 \exp\left(-\alpha|z|\right). \tag{2}$$

Here, R_f is the reflectivity of THz radiation by the corneal tissue, which is taken to be $R_f = 0.02$ @1 THz [11], I_0 is the induced localized THz power intensity ($I_0(z,r) = \frac{2P}{\pi w_0^2}\exp(\frac{-2r^2}{w_0^2})$, P is THz laser power in Watts, w_0 is the radius of the THz beam with Gaussian distribution), α is the absorption coefficient of the biotissue, and $\{z, r\}$ denotes the coordinates. For convenience in the following discussion (i.e., influence of the THz beam radius and power density), P_d represents the power density of the THz beam in Watts per square centimeter ($P_\mathrm{d} = \frac{P}{\pi w_0^2}$). Heated by THz radiation, the cornea experiences a rise in temperature, and could suffer irreversible thermal damage if temperature rises above a threshold. According to the Arrhenius formulation, the damage degree can be quantified by a parameter, $\Omega(t)$, which is expressed as [24]

$$\Omega(t) = \ln\left(\frac{c(t_0)}{c(t)}\right) = \frac{k_\mathrm{B}}{\hbar}\exp \Delta S/R \int T(t)\exp\left(-\frac{\Delta E}{R \cdot T(t)}\right)\mathrm{d}t. \tag{3}$$

where $c(t0)$ is the initial concentration of undamaged corneal-tissue molecules, $c(t)$ is the concentration of remaining corneal tissue at time t, k_B is Boltzmann's constant, $\hbar$ is Planck's constant, $R = 8.313$ J/(mol·K) is the universal gas constant, $\Delta S = 106$ kJ/mol and $\Delta E = 39$ J/(mol·K) are the entropy and the enthalpy of collagen denaturation [22,24], respectively. With Equation (3), the spatial distribution of thermal damage can be obtained.

The bioheat equation, i.e., Equation (1), is solved using the finite-element method (COMSOL). The initial temperature and the temperature at the bottom surface of the aqueous humor were set to be 35 °C. We recorded the temperature as the damage degree at each time step. Physical and thermal parameters of the water (tear and aqueous humor) and the cornea [5,22,24] that were used in the model are summarized in Table 1.

Table 1. Physical and thermal parameters of tear and aqueous humor (modelled as water), and the cornea [5,22,24] used in the model.

Property	Material	Value	Material	Value
Density ρ (kg/m^3)	Water	1000	Cornea	1060
Thermal conductivity k (W/m/K)	Water	0.578	Cornea	0.556
Specific heat C (J/kg/K)	Water	4180	Cornea	3830
Absorption coefficient [1] α (1/m)	Water	24,067	Cornea	14,400
Convection coefficient h (W/m^2/K)	Water-air	20	Water-cornea	500
Film thickness t (μm)	Tear film	10	Cornea	600

[1] Absorption coefficient is at a frequency of 1 THz.

Additionally, we used an axisymmetry boundary condition at $r = 0$ in our model. The effects of heat convection in all interfaces (tear–air, cornea–tear, cornea–aqueous humor) of the model were taken into account using thermal-transfer coefficients. According to published reports [5,22,24], convection boundary conditions at tear–air, cornea–tear, cornea–aqueous humor interfaces were assigned as $h_{tear-air} = h_{Water-air} = 20$ W/(m^2·K), $h_{cornea-tear} = h_{Water-cornea} = 500$ W/(m^2·K), $h_{cornea-humor} = h_{Water-cornea} = 500$ W/(m^2·K), respectively. Initially, the tissue was assumed to be at a uniform temperature of 35 °C, and the ambient temperature of air (above the cornea) was kept at a constant value of 25 °C. Temperature at the bottom surface of the aqueous humor was also kept constant at 35 °C.

3. Results and Discussion

3.1. Dynamic Temperature Distributions

We took the terahertz beam radius to be $w_0 = 3\,\mathrm{mm}$, and power density to be $P_\mathrm{d} = 0.6\,\mathrm{W/cm^2}$. Figure 2 shows the time-dependent evolution of temperature distribution in the tear, cornea, and aqueous humor. This shows that the maximum temperature is at the top center of the tear film; temperature gradually decays in both the radial (r) and vertical (z) directions. Since the tear film is very thin, only 10 µm, the temperature difference between the tear film and the top layer of the cornea is negligible. The temperature in all layers increased very quickly when terahertz heating time was shorter than 60 s, and then gradually saturated. With terahertz heating of 180 s, the maximum temperatures in the tear, cornea, and aqueous humor could reach 70.86, 68.38 , and 48.6 °C, respectively.

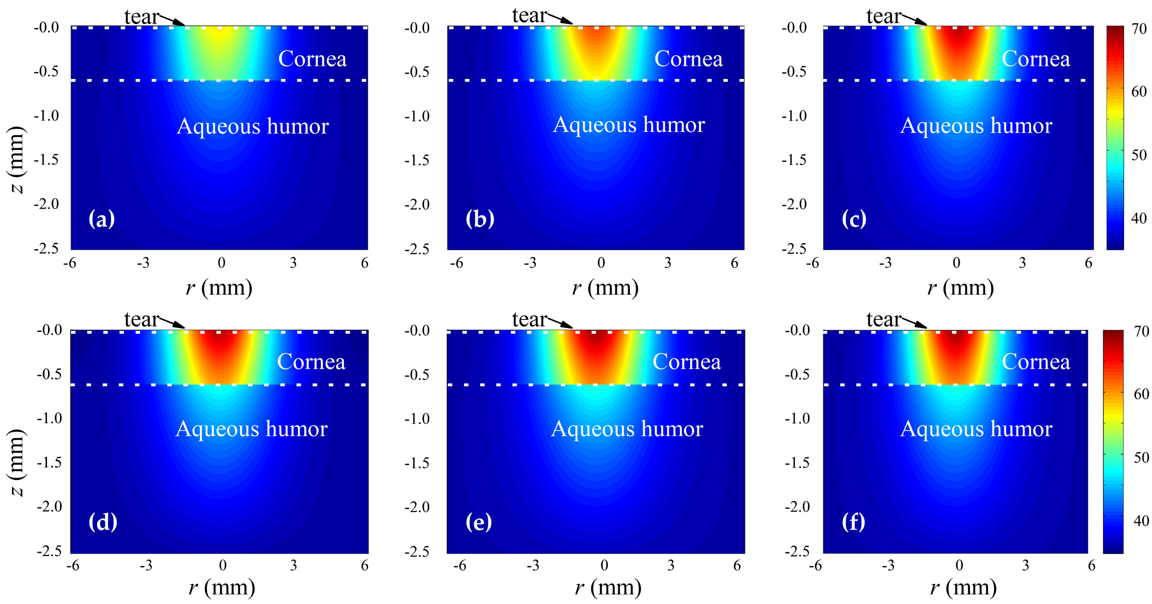

Figure 2. Time-dependent evolution of temperature distributions under terahertz heating with beam radius $w_0 = 3\,\mathrm{mm}$, power density $P_\mathrm{d} = 0.6\,\mathrm{W/cm^2}$, and exposure time of (**a**) 10 s; (**b**) 30 s; (**c**) 60 s; (**d**) 180 s; (**e**) 300 s; and (**f**) 1200 s.

Furthermore, based on Figure 2f, we could also obtain the temperature distribution across the surface beneath the terahertz beam (Figure 3). As expected, it is clearly seen that maximum heating occurs just in the center of where the THz beam is incident. This is because the intensity distribution of the THz beam is hypothetically a Gaussian distribution.

3.2. Influence of THz Beam Radius and Power Density

We now discuss the influence of the terahertz beam radius and power density on the heating effects in the cornea. Figure 4 plots the transient-temperature behaviors at the top center of the cornea layer under different beam sizes and power densities. This shows that, for different beam sizes and power densities, temperature rises very quickly for less than 60 s and then saturates; the higher the power density, or the larger the beam size, the higher the saturated temperature. The difference between saturated temperatures for neighboring power densities is a constant, and the constant linearly increases with beam size. These linear behaviors occur because the heat absorbed by the cornea increases linearly with both power density and beam radius.

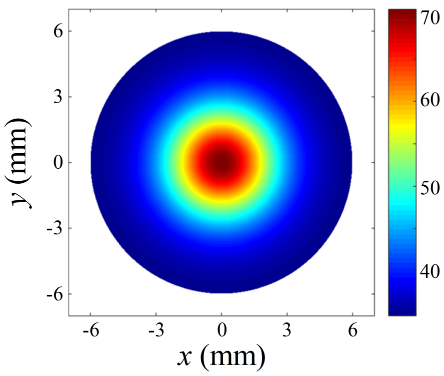

Figure 3. Temperature distribution across the surface beneath the THz beam (beam radius $w_0 = 3$ mm, power density $P_d = 0.6$ W/cm^2, and exposure time 1200 s).

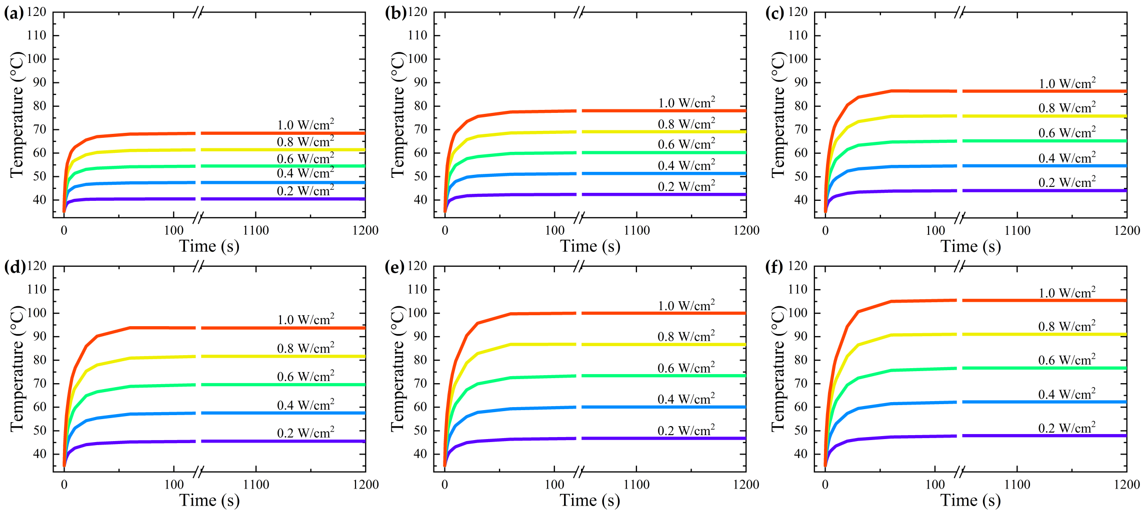

Figure 4. Time-dependent temperature evolution of at the top center of the cornea layer under different power densities (0.2∼1 W/cm^2 as marked in the figure) and terahertz beam radius of (**a**) $w_0 = 1.5$ mm; (**b**) $w_0 = 2.0$ mm; (**c**) $w_0 = 2.5$ mm; (**d**) $w_0 = 3.0$ mm; (**e**) $w_0 = 3.5$ mm; and (**f**) $w_0 = 4.0$ mm.

In order to ensure collagen shrinkage, Fyodorov et al. [3] reported that the minimal cornea temperature should be 55 °C, Haw and Manche [25] suggested the maximal allowed temperature is 75 °C, and Asbell et al. [26] reported that the best temperature for optimal shrinkage of the cornea collagen is ∼65 °C. Moreover, Aksan and McGrath [27] showed that to avoid high temperatures and excessive denaturation is crucial so as to prohibit stiffness decrease of the tissue. Therefore, we can take 55∼75 °C as the safe shrinkage temperature range, and 65∼70 °C as the optimal shrinkage-temperature range. With these ranges, we can identify the suitable power density and beam size for achieving collagen shrinkage. For example, for a beam size of $w_0 = 3.5$ mm (Figure 4e), the suitable power density should be 0.38∼0.6 W/cm^2, and optimal power density should be 0.5 W/cm^2.

3.3. Cornea-Shrinkage-Region Estimation

Since the temperature in the cornea can rise to a certain range for collagen shrinkage, terahertz radiation can be used as a novel corneal thermal therapy. Here, we estimate the effective region of cornea shrinkage based on the above spatial and temporal temperature distributions under THz heating with a beam radius of $w_0 = 3$ mm and power density of $P_d = 0.6$ W/cm^2. As we discussed earlier, 55∼75 °C is the safe shrinkage temperature range. Therefore, we can define the region within this temperature range as the shrinkage region. According to the spatial and temporal temperature distributions, we obtained the time-dependent evolution of the corresponding collagen shrinkage regions, as shown in Figure 5. Results show that the tomography of the collagen-shrinkage region evolves from a funnel-like shape into the cylindrical profile. After temperature saturation, the diameter of the collagen-shrinkage region is about 3 mm, which is comparable to that of the microwave-heating approach (diameter is about 1.3∼2.8 mm [5]).

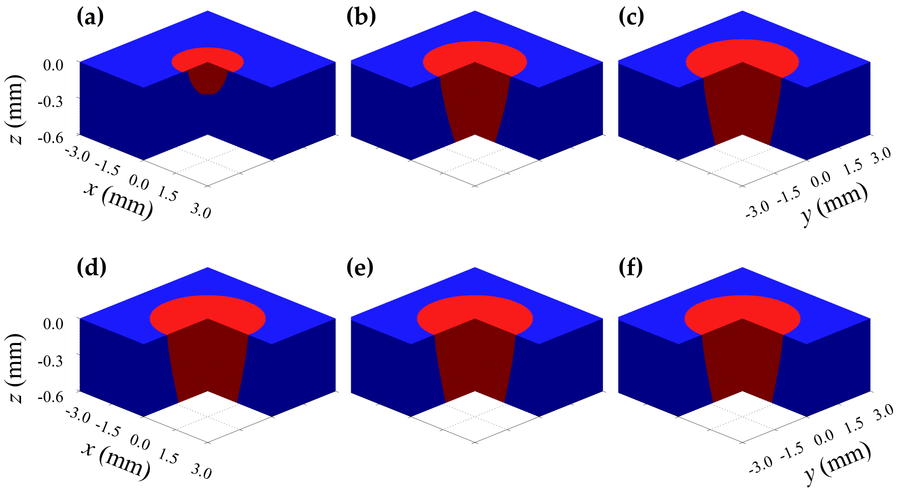

Figure 5. Time-dependent evolution of collagen-shrinkage tomography under terahertz heating with beam radius $w_0 = 3\,\text{mm}$, power density $P_\text{d} = 0.6\,\text{W/cm}^2$, and exposure time of (**a**) 10 s; (**b**) 30 s; (**c**) 60 s; (**d**) 180 s; (**e**) 300 s; and (**f**) 1200 s. Blue regions indicate nonshrinkage regions, and red regions the shrinkage regions. Shrinkage threshold value was taken to be 55 °C.

Given the similarity of heating with THz and infrared (IR) lasers (near-surface heating in both cases), we compared our results with typical IR modeling studies and experiments in the literature [7,23]. The comparison of heating the cornea with THz and typical IR lasers is summarized in Table 2. For IR laser-based heating, the shrinkage effect is not deep enough because of the rather limited heating depth of the laser into the cornea (only ∼50%). Therefore, laser irradiation using THz wavelengths may heat deeper into the cornea than IR wavelengths.

Table 2. Comparison of heating cornea with THz and typical infrared (IR) lasers.

	THz Laser (This Work)	**Near IR Laser [7]**	**Far IR Laser [23]**
Method	Theory	Experiment	Theory
Laser wavelength (μm)	300	2.10	10.6
Depth [1] (μm)	600	300–400	<100
Profile [2]	cylinder	wedge	–
Max. temp.	68.38 °C	–	56.5 °C

[1] Depth of shrinkage effect in experiment, depth of temperature ≥55 °C in theory; [2] Profile of shrinkage effect in experiment, profile of temperature ≥55 °C in theory.

Although reshaping the cornea using IR lasers is well-established, there still exist some problems for IR-heating techniques. According to the comparison summarized in Table 2, IR heating techniques cannot produce enough heating depth (only ∼50%) and a good profile of the shrinkage effect (wedge), which are very important for cornea reshaping based on thermal techniques. However, the THz heating technique can produce a significantly deeper region and a better shrinkage profile. Therefore, we expect this result can clarify the potential benefits of using THz radiation compared with using IR lasers in cornea reshaping in ophthalmology.

3.4. Degree of Thermal Damage

Figure 6 shows the spatial and temporal dependence of the damage degree in the cornea under terahertz heating with a beam radius of $w_0 = 3\,\text{mm}$ and power density $P_\text{d} = 0.6\,\text{W/cm}^2$. We found that the spatial distribution of the damage degree was similar to the temperature distribution in Figure 2e. The maximal degree of thermal damage ($\Omega = 0.17$) occurred at the top center of the cornea, consistent with the literature [28]. Because $\Omega = 0.1$ corresponds to the onset of collagen denaturation, and $\Omega > 1$ denotes irreversible thermal damage (quantified in terms of collagenous-tissue denaturation) [24,28], we found that collagen denaturation had already happened since $\Omega = 0.17$ in Figure 6. Therefore, one should take appropriate precautions. Fortunately, the degree of thermal damage is a function of both time and temperature [24]. Thus, we can prevent collagen denaturation by limiting the duration of terahertz heating, i.e., $t < 720$ s so that $\Omega < 0.1$ throughout the cornea.

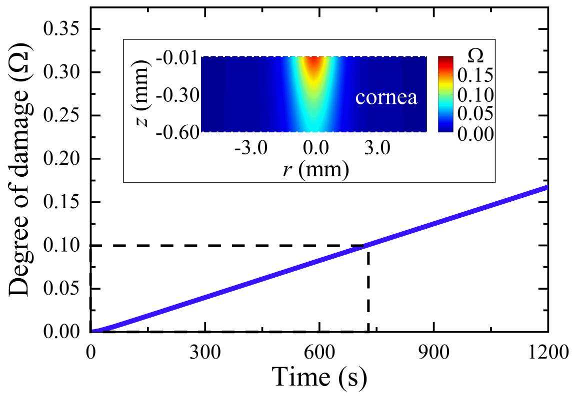

Figure 6. Time-dependent degree of damage at the top center of the cornea. The inset shows spatial distribution in the cornea at $t = 1200$ s. The results were calculated under THz radiation with a beam radius of $w_0 = 3\,\text{mm}$ and power density of $P_\text{d} = 0.6\,\text{W/cm}^2$.

4. Concluding Remarks

In summary, we investigated terahertz thermal effects in the cornea. By developing a 2D axisymmetric model based on terahertz bioheat effects, we calculated the time-dependent evolution of temperature distribution in the cornea. We also showed that both the power density and the beam radius of the terahertz beam are important for achieving an appropriate temperature range, within which the cornea can experience collagen shrinkage. Based on the evolution of temperature distribution in the cornea, we evaluated the effective region of collagen shrinkage and the degree of thermal damage. Our results suggest that THz radiation could be used as a potential and promising noncontact heat source that is suitable for the thermal treatment of the cornea in the ophthalmology field. Before this expectation can be realized, further research should also include (i) studying the influence of other parameters, such as THz frequency; (ii) experimentally quantifying the relationship between collagen shrinkage of the cornea and temperature; and (iii) conducting in vitro THz exposure to the cornea to verify the obtained results from the developed model in this work.

Author Contributions: conceptualization, W.L. and Y.L.; methodology, W.L., Y.L., and G.L.; software, R.S., G.W., G.J., and G.L.; investigation and data analysis, all authors; writing—original-draft preparation, W.L. and G.L.; writing—review and editing, all authors; supervision, Y.L., J.L., and G.L.

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Conflicts of Interest: The authors declare no conflict of interest.

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