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Additional Information

Radio-frequency heating of the cornea: Theoretical model and *in vitro* experiments

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Abstract

We present a theoretical model for the study of cornea heating with radio-frequency currents. This technique is used to reshape the cornea to correct refractive disorders. Our numerical model has allowed the study of the temperature distributions in the cornea and to estimate the dimensions of the lesion. The model incorporates a fragment of cornea, aqueous humor and the active electrode placed on the cornea surface. The finite element method has been used to calculate the temperature distribution in the cornea by solving a coupled electric-thermal problem. We analyzed by means of computer simulations the effect of: a) temperature influence on the tissue electrical conductivity, b) the dispersion of the biological characteristics, c) the anisotropy of the cornea thermal conductivity, d) the presence of the tear film, and e) the insertion depth of the active electrode in the cornea, and the results suggest that these effects have a significant influence on the temperature distributions and thereby on the lesion dimensions. However, the cooling of the aqueous humor in the endothelium or the realistic value of the cornea curvature did not have a significant effect on the temperature distributions.

An experimental model based on the lesions created in rabbit eyes has been used in order to compare the theoretical and experimental results. There is a tendency towards the agreement between experimental and theoretical results, although we have observed that the theoretical model overestimates the lesion dimension.

Index Terms: Thermokeratoplasty, cornea, numerical model, computer model, radio-frequency (RF) heating, finite element method, theoretical model.

I. INTRODUCTION

Thermal techniques for changing the shape of the cornea are commonly referred to as thermokeratoplasty (TKP) and they are based on the fact that the cornea stroma permanently shrinks when temperature is raised to 55-63 °C [1]. These techniques have been used to reshape the cornea to correct disorders such as keratoconus [2], hyperopia [3], and astigmatism [4]. They are based on applying energy as thermal conduction from pre-heated probes applied to the surface [2] or inserted in the cornea [3], laser [5], ultrasound [6], or microwave energy [7]. Also radiofrequency (RF) currents have been used in TKP [8,9]. In 1980, Doss and Albillar [8] proposed a TKP technique by using RF currents (RF-TKP). They used a large diameter electrode combined with surface cooling in order to correct the keratoconus. In a clinical study using this technique, Rowsey observed unpredictability and regression of the shrinkage effect [10]. However, Mendez-G and Mendez-Noble [9] have recently proposed a RF-TKP technique using a smaller diameter electrode without surface cooling. The first clinical results using this technique achieve hyperopia correction that was stable and had little regression through time. On the other hand, we presented a preliminary study showing thermal lesions created by RF currents using a small diameter electrode [11]. We showed the geometric and histologic characteristics of these lesions on an *in vivo* model based on rabbit eyes.

To our knowledge, there are no theoretical or experimental studies about the influence of different factors on the lesions characteristics in the cornea heating with RF currents. Only Trembly and Keates [7] have presented a numerical model for the theoretical analysis of the temperature distribution in the cornea during microwave heating combined with surface cooling and studied the effect of changing the applied microwave power level and the applicator characteristics on the temperature profiles.

In this paper, we present a realistic non-linear numerical model for the simulation of tissue temperature distribution during RF-TKP using a surface electrode. The first objective of this study has been to construct the theoretical model and to carry out computer simulations in order to compare the computer results with the lesions created on an in vitro model. The second objective has been to use our model in order to study the temperature profiles in the cornea during RF-TKP. The effect of different parameters such as the corneal curvature, the thermal transfer in the interfaces of the model, the electrical and thermal characteristics of the tissues, and the presence of a tear film has been considered.

II. MATERIALS AND METHODS

A. Description of the theoretical model

In RF-TKP, electrical currents ranging from 500 kHz to 1 MHz flow between an active electrode placed on the cornea surface and a dispersive electrode of big dimensions placed on the back of the patient's head. Fig. 1 (top) shows the geometry and dimensions of the active electrode considered in this study. It is made of stainless steel and has a 200 μm diameter in the point placed on the cornea. The length of the sharp-edge zone of the active electrode is 5 mm, the diameter of the active electrode body is 1.5 mm, and the total length is 100 mm. Fig. 1 (bottom) shows the physical situation during RF-TKP considered in this study. The active electrode is situated on the center of the cornea. Therefore the model presents axisymmetric characteristics, and a two-dimensional approach is possible. The rectangle in Fig.1 (bottom) indicates the region where our theoretical model applies. Fig. 2 shows the theoretical model proposed. The model represents the active electrode, the cornea and the aqueous humor (fluid included in the anterior chamber), and it is similar to the model proposed by

Trembly and Keates [7] for microwave heating. Corneal thickness of 600 μm was considered [7]. The value of the model parameters L, R and Z have been calculated by sensitivity analysis in order to avoid boundary effects, which will be presented in the results and discussion section.

Although the literature contains scarce data about the electrical and thermal characteristics of the cornea and aqueous humor, Table 1 shows a brief review of this topic and indicates (in bold) the value of the physical characteristics used in the model [7,12-17]. We have not modeled the several layers of the cornea, due to the fact that only average measured values for the whole cornea are available. The interface between the cornea and air will be referred to the epithelium, and the interface between the cornea and the aqueous humor as the endothelium. In our model, a change of the electrical conductivity of the cornea and the aqueous humor with temperature of $+2\%/^{\circ}\text{C}$ has been considered [18]. The temperature profiles for RF-TKP have been calculated using the finite element method (FEM). The ANSYS 5.3 commercial finite element package running on an IBM-PC with a 233-MHz processor has been used for computer simulations. The temperature distribution in the tissue was obtained by solving the bio-heat equation [19]

$$\rho \cdot c \cdot \frac{\partial T}{\partial t} = \nabla \cdot k \nabla T + q - Q_p + Q_m \quad (1)$$

where ρ is the mass density (kg/m^3), c is the specific heat capacity ($\text{J}/\text{Kg}\cdot\text{K}$), k is the thermal conductivity ($\text{W}/\text{m}\cdot\text{K}$), T is the temperature ($^{\circ}\text{C}$), q is the heat source (W/m^3), Q_p is the perfusion heat loss (W/m^3), and Q_m is the metabolic heat generation (W/m^3). The situation has been simplified by ignoring Q_p and Q_m as they are negligible for RF heating [19].

At the frequencies (500 kHz) and over the distance of interest (the electrical power is deposited in a small radius around the active electrode) the medium can be considered resistive, because the displacement currents can be neglected. Therefore, it is possible to use a quasi-static approach to the electrical problem [20-21]. The distributed heat source (Joule loss) is given by

$$q = \mathbf{J} \cdot \mathbf{E} \quad (2)$$

where \mathbf{J} is the current density (A/m^2), and \mathbf{E} is the electric field intensity (V/m). These were evaluated using Laplace's equation

$$\nabla \cdot \sigma \nabla V = 0 \quad (3)$$

where V is the root mean squared (r.m.s.) voltage (V) and σ is the electrical conductivity (S/m).

The model presented, as are other models of RF heating, is based on a time domain analysis of an electric-thermal coupled problem [17,22-23]. The temperature for the surfaces away from the active electrode (right and bottom limit of the model in the Fig.2) was assumed to be 20 °C (using Dirichlet boundary conditions). An initial temperature of 20 °C was used in all the model. The electrical potential was fixed on the active electrode to a value equal to the total applied voltage (root-mean-square value in a experimental set-up), while the potential in the dispersive electrode was fixed to zero volts. The effect of heat convection in both the interfaces (epithelium and endothelium) of the model have been taken into account using thermal transfer coefficients (h_1 for the epithelium and h_2 for the endothelium). At such interfaces the temperature obeys

$$\nabla T \cdot d\mathbf{S} = h k^{-1} (T_b - T) \quad (4)$$

where T is the tissue temperature, \mathbf{S} is the directed surface, k is the thermal conductivity of the tissue, h is the thermal transfer coefficient, and T_b is the temperature far from the

interfaces (air temperature for epithelium interface, and tissue quiescent temperature for the endothelium interface).

The value of the maximal temperature achieved in the tissue (T_{\max}) has been used as a control parameter in the sensitivity analysis. In order to assess the effect of different factors studied in this work, we will consider an effect to be significant when the inclusion of this factor induces a change of ± 4 °C in T_{\max} . This temperature range is similar to the dispersion of the shrinkage temperature (55–63 °C) found by Stringer and Parr experimentally [1]. The geometry of the temperature profiles has been assessed by means of the depth and width of the 40 °C isothermal line.

B. Description of the experimental model

An *in vitro* model based on an isolated rabbit eye was developed in order to validate the theoretical model. Fig. 3 shows the components of our experimental model which is similar to that used by Doss and Albillar [8]. A 200 μm diameter stainless steel active electrode was placed on the center of the cornea, and a RF generator (model RFG-3D, Radionics Inc, Massachusetts, USA) was used to deliver 500 kHz RF currents to the tissue. The output voltage (root mean square value without load impedance) was programmed from the front panel for each case. All the experiments were carried out on enucleated rabbit eyes. The eyes were obtained four to eight hours post mortem and stored in a cold saline solution (5-10 °C) to minimize swelling or autolysis [24]. We made one lesion on each eye by programming the output voltage and the time duration. After heating, the cornea was excised from the eye, preserved in formalin, sliced at 4 μm thickness through the centre of the lesion, stained with hematoxylin and eosin, and mounted in a slide for photographing. The lesions were assessed using the coagulation contour observed in the histologic samples. Brickmann et al. [25] have shown that this

coagulation contour occurs in a temperature range around 100 °C using short heating times. The depth and width of each lesion were measured on the histologic samples under a optical microscope (X100) with a calibrated reticle (1 μm divisions). All the dimensions are indicated as % of corneal thickness. Finally, to compare the experimental and numerical results the experimental dimensions of the lesion are compared to the 100 °C isothermal lines from the computer simulations.

III. RESULTS AND DISCUSSION

A. Construction of the theoretical model

The parameters R, Z and L of the model (Fig. 2) can not be inferred from the physical dimensions shown in Fig. 1, because only a portion of the physical stage is included in the theoretical model. In order to avoid numerical artifacts in the FEM model, we tested the model by increasing the value of these parameters. Computer simulations were carried out setting the applied voltage to 8 V, time duration to 1 s (standard conditions of applied voltage and duration), h_1 to 20 $\text{W}/\text{m}^2\text{ }^\circ\text{C}$, h_2 to 500 $\text{W}/\text{m}^2\text{ }^\circ\text{C}$ and the time step to 50 ms. The effect of heat convection at the active electrode-air interface has been taken into account using a thermal transfer coefficient of 20 $\text{W}/\text{m}^2\text{ }^\circ\text{C}$ for all the computer simulations. Computer simulations were made by increasing equally the values of R and Z from 1 mm to 5 mm in steps of 1 mm. When the difference between the maximal temperature achieved in the tissue (T_{max}) after 1 s and the temperature in the previous simulation was less than $\pm 0.5^\circ\text{C}$, we considered the former values of R and Z to be adequate. A value of 3 mm was obtained for R and L. These dimensions are similar to the dimensions of the model used by Trembly and Keates [7]. A similar method to calculate the dimensions of the model has been used by Labonté [22] in a model for cardiac ablation and by Trembly and Keates [7] in a model

of TKP using microwave heating. The same method was used to estimate the optimum value of L . Values from 0.5 to 2 mm in steps of 0.5 mm were used, and a value of 1 mm was found to be sufficient. The time step used for all the transient analysis was set to 50 ms. The difference between T_{\max} obtained with this step time and a lower step time (25 ms) was less than ± 0.5 °C. We have used a Cauchy convergence test to determine whether the model mesh is of appropriate size. This method has been described by Tungjtkusolmun *et al.* [26] in a RF cardiac ablation model. We have considered the maximum temperature in all the tissue as the parameter for the convergence test. A grid size of 10 μm in the finest zone (cornea–active electrode interface) was found to be adequate. Unlike, the spatial resolution was of 0.6 mm near the dispersive electrode. The finite element model had near 2000 nodes and used over 3600 triangular elements.

B. Effect of the thermal transfer coefficients

The effect of transfer coefficients in the interfaces (h_1 and h_2) were tested using computer simulations using values suggested in the literature [27-28] because no experimental study presents measured values. Computer simulations using standard conditions (8 V, 1 s) were made with h_1 set to 2, 12 and 25 W/m^2 °C. These are typical values for thermal free convection between solid (cornea) and air [27-28]. While, h_2 was set to 20, 500 and 1000 W/m^2 °C, these are typical values for thermal free convection between solid (cornea) and liquids (aqueous humor) [28]. Fig. 4 shows temperature profiles obtained on the axis of symmetry in the cornea zone. The temperature profiles were not significantly effected by the variation of h_1 , and the maximal difference of the T_{\max} was of 0.5 °C (not shown in the Fig. 4). However, temperature profiles were slightly effected when h_2 changed. Temperature profiles varied near 4 °C in the endothelium. Moreover, this effect was more significant when the time duration was

increased (near 2 °C after 500 ms and 4 °C after 1 s in the endothelium). To our knowledge there are no experimental data of the thermal transfer capability of the aqueous humor on the endothelium (h_2), but because this fluid is almost static, we have considered that the thermal transfer is due to a free convection process. The use of convective boundary conditions (h_1 and h_2) is an approximation often used in the thermal modelling of RF heating [22,27]. The results suggest that only the thermal transfer in the cornea-aqueous humor interface (h_2) could be significant in a theoretical model for RF-TKP, especially if RF currents are applied for a long time (several seconds). If short time durations are used, this effect could be negligible.

C. Linear versus non-linear model

In order to study the effect of the change of the electrical conductivity of biological tissues (cornea and aqueous humor) with the temperature, computer simulations were carried out under standard conditions (8 V, 1 s) in two different cases: a) linear model (without variation of σ) and b) considering a change of +2 %/°C [18] for the electrical conductivity (non-linear model). The parameters h_1 and h_2 were fixed to 20 W/m² °C and 500 W/m² °C respectively. A highest value of T_{\max} (increase of 15 °C) was obtained when the effect of the temperature was considered. This critical result is in agreement with Labonté [22] and Shahidi and Savard [23] using their models for RF cardiac ablation. This result indicates that it is necessary to include the effect of temperature for all the simulations in order to obtain more realistic temperature profiles in the model. The value of +2 %/°C indicated in this section will be used for the cornea and the aqueous humor in all the simulations presented in the following sections, except in the section H when a linear model will be again considered.

D. Influence of the corneal curvature

The model in Fig. 2 is similar to the model of Trembly and Keates [7]. In order to study the effect of considering a more realistic shape of the cornea, the model was modified. Fig. 5 (a) shows the modified model with a geometry based on biometry data. A cornea curvature radius of 8 mm was used [29]. Control simulation (with realistic curvature) and simulation using a model with a flat surface were made under standard conditions (8 V, 1 s). We observed a difference of near 4 °C for T_{\max} between the two simulations. The result indicates that this factor could be significant under non standard conditions, such as longer time or higher programmed voltage. New computer simulations could be used to test this hypothesis.

E. Effect of tear film

In order to consider a realistic approach of the RF-TKP, we have studied the effect of the presence of a thin tear film on the cornea and around the active electrode. Fig. 5(b) shows the location of the tear film in the model. In this study, the electrical characteristics of this film were considered to be similar to aqueous humor (table I) because we have not found any study reports the thermal or electrical characteristics of the tear film. Two different thickness of this film (50 and 100 μm) were considered. Also two values (500 and 1000 $\text{W}/\text{m}^2\text{°C}$) of the thermal transfer coefficient between the cornea and tear film and between the electrode and tear film (h_{TEAR}) were considered in simulations under standard conditions (8 V, 1 s). These values of coefficients are in the range of typical values of the free convection heat transfer coefficient between solids (cornea) and liquids (tear film) [28]. The convection coefficient between the tear film and air was of 20 $\text{W}/\text{m}^2\text{°C}$. Table III shows the T_{\max} , the depth and $\frac{1}{2}$ width of the 40 °C isothermal line after 1 s. The results indicate that as the thickness of the tear was

decreased from 100 μm to 50 μm , T_{max} increased 3.7 and 3.5 $^{\circ}\text{C}$ for h_{TEAR} 500 and 1000 $\text{W}/\text{m}^2\text{C}$ respectively, the width of the 40 $^{\circ}\text{C}$ isothermal line increased 5% for h_{TEAR} 500 and 1000 $\text{W}/\text{m}^2\text{C}$, and the depth increased 5 and 15 % for h_{TEAR} 500 and 1000 $\text{W}/\text{m}^2\text{C}$ respectively. Furthermore these three parameters (T_{max} , width and depth of the 40 $^{\circ}\text{C}$ isothermal line) increased when h_{TEAR} decreased from 1000 to 500 $\text{W}/\text{m}^2\text{C}$. T_{max} increased 4.2 and 4.0 $^{\circ}\text{C}$, width increased 21 and 20%, and depth increased 2 and 12 %, for a tear film thickness of 50 and 100 μm respectively. Moreover, the largest difference was found between the control case and when a tear film was considered: minimal difference of T_{max} of 14.7 $^{\circ}\text{C}$, and minimal increase of the 40 $^{\circ}\text{C}$ isothermal line dimensions of 16.0 % and 8.3 % for the width and depth respectively. These results suggest that the presence of the tear film performs like a thermal and electrical leak path removing the heat away from the tissue and scattering the electrical current across the tear.

F. Insertion depth of the active electrode

When a small diameter active electrode is placed on the surface of the cornea a slight strain occurs in the tissue. This makes a small portion of the active electrode (tip zone) to remain inserted in the cornea. The influence of this effect on the temperature profiles has been studied using the modified model of the Fig. 5(c). Table IV shows the 40 $^{\circ}\text{C}$ isothermal line dimensions and T_{max} for several studied depth of insertion (ID) of the active electrode in the cornea under standard conditions (8 V, 1s) after 1 s. As we increased ID (from 0 to 100 μm), we found that the 40 $^{\circ}\text{C}$ isothermal line dimensions increased from 350 to 460 μm in depth and from 375 to 460 μm in $\frac{1}{2}$ width. Plots of temperature profiles were obtained for each ID. We observed that the location of the point with maximal temperature was always found around the perimeter of the active

electrode. Since an increase of ID placed the points of maximal temperature in deeper locations, the lesion can be deeper, and this fact could justify these results. On the contrary, T_{\max} decreased from of 85.6 to 72.4 °C when ID increased from 0 to 100 μm . When ID decreased, the value of maximal density current in the tissue (not shown) increased due to the well known “edge effect” studied by other authors [17,33]. This increase of the current density involved an increase of the temperature achieved. In summary, the results indicate that the depth of insertion of the active electrode has a significant effect on the temperature profiles.

The current RF heating theoretical models have often considered a good quality contact between the electrode and the tissue [22-23]. However, it is known that this parameter has an important effect on lesion characteristics [34-35] and sometimes, for example in RF-TKP, it is difficult to predict its behaviour in a clinical situation. Only Jain and Wolf [36] have studied the effect of ID using a theoretical model for RF cardiac ablation, and they obtained results similar to ours. They found that when ID increased, depth and width of the temperature profiles increased because the location of the hot spot shifted deeper into the tissue. However, their results are not directly comparable to ours since they used a constant temperature protocol, and our study set a constant applied voltage.

G. Anisotropy of the corneal thermal conductivity

In the study of Trembly and Keates [7] for microwave heating of the cornea, the agreement between the theoretical and experimental studies was only approximate. The width of the lesion was roughly twice as high in experiment as in theory. They indicated that this disagreement might be due to the anisotropy of cornea thermal conductivity. Their work also suggests that conductivity is larger in the longitudinal direction

(parallel to the corneal surface) than transverse direction. In order to study the influence of this thermal anisotropy, we have carried out computer simulations under standard conditions (8 V, 1 s) including this effect. To our knowledge, there are no experimental values of this kind of anisotropy. With k_x , the longitudinal thermal conductivity of the cornea, and k_y , the transverse thermal conductivity, (see Fig. 6), we fixed k_y to 0.556 W/m·k [7], k_x was set to three values: $k_x=k_y$ (control, non-anisotropy), $k_x=2\cdot k_y$, and $k_x=3\cdot k_y$. Fig. 6 shows the obtained temperature profiles and indicates the situation of the 40 °C isothermal line for each studied case. The results (shown in Table II) suggest that an increase of the longitudinal thermal conductivity ($k_x=2\cdot k_y$) involves lower values of T_{\max} (a difference near 17 °C), and the reduction of 21 % of depth and 4 % of width in 40 °C isothermal lines. Also the temperature profiles shown in Fig. 6 suggest that an increase of this anisotropy in thermal conductivity involves temperature profile geometry with a more ellipsoidal shape (width/depth ratio of 1.3). A similar effect was observed when k_x was set to $3\cdot k_y$ but with major differences (see Table II). The value of T_{\max} decreased near 25 °C, depth and width in 40 °C isothermal line reduced in 42 % and 15% respectively, and the width/depth ratio was 1.6. Our results suggest that wider lesions could be created if a condition of thermal anisotropy is considered. Thereby this effect could explain the discrepancy between experimental and theoretical results observed by Trembly and Keates [7]. On the other hand, our results suggest also that there is a direct relation between T_{\max} and the temperature profile dimensions and they agree with the observations of Labonté [22] in a theoretical model for RF cardiac ablation.

H. Electrical conductivity dispersion

We have studied the effect of changes in electrical conductivity (σ) of cornea and aqueous humor due to biological dispersion. Computer simulations under standard conditions (8 V, 1 s) were carried out considering values of dispersion of $\pm 50\%$ of σ at the beginning of the simulation. We have also considered two models: a) linear model, and b) non-linear model including the effect of the temperature on the electrical conductivity ($+2\%/^{\circ}\text{C}$). Fig. 7 shows the temperature profiles after 0.5 s and 1 s for the linear model (a) and the non-linear model (b). Since we increased σ ($+50\%$), significant differences between the two models were found. T_{\max} was maximal for the non-linear model and long time durations (differences of $25\text{ }^{\circ}\text{C}$ after 0.5 s and near of $45\text{ }^{\circ}\text{C}$ after 1 s). This discrepancy between the two models and durations is due to the so called thermal feedback in electrosurgical heating [30]. When the tissue is heated and an electrical protocol based on a constant applied voltage is used, the tissue electrical resistance declines. Then, more current is delivered from the generator, the temperature in the tissue increases, creating a positive feedback loop. Fig. 7 also shows that when we decreased σ by -50% at the beginning of the simulation, a minor difference of T_{\max} between models and time durations was found ($4\text{ }^{\circ}\text{C}$ after 0.5 s and $7\text{ }^{\circ}\text{C}$ after 1 s). Moreover, Fig. 7 shows that the effect of the time duration is less significant when σ decreased. Panescu and Webster [30] have studied the influence of the dispersion of σ ($\pm 50\%$) on the temperature distributions in RF heating using a linear model, achieving similar results to our linear model (Fig. 7(a)). However, our results suggest that the studies about biological characteristic dispersion should include the dependence with temperature (non-linear model) especially when positive changes of σ and long time durations are considered. Recently, Tungjitkusolmun et al. [26] have studied the effects of changes in electrical conductivity (σ) of the cardiac tissue ($\pm 50\%$) on the temperature profiles in a RF cardiac ablation model. They have considered a change in

σ of 2 %/°C (non-linear model), but they have not studied the differences between using a linear model and non-linear model when the dispersion in σ is considered.

I. Comparison between computer simulations and in vitro experiments

A realistic theoretical model has been considered for the comparison between computer simulations and the in vitro experimental results. This theoretical model includes the cornea curvature, an insertion depth of the active electrode of 50 μm , a value for the anisotropy of the corneal thermal conductivity ($k_x=2\cdot k_y$), and a 100 μm thickness tear film. The thermal transfer condition of the tear film (h_{TEAR}) in the computer simulations was considered using three values: 20, 100 and 500 $\text{W}/\text{m}^2\text{ }^\circ\text{C}$, because of the lack of experimental data. Moreover, the value of the electrical conductivity of the cornea in the theoretical model was varied from 2.56 S/m (proposed initial model, see table I) to 1 S/m in order to achieve a good agreement with the experimental electrical impedance of 1 $\text{k}\Omega$ measured between the active and dispersive electrode. Computer simulations and *in vitro* experiments were made setting the applied electrical voltage to 16 and 21 V, and the time duration to 1 s. These values of voltage are higher than the standard condition (8 V) in order to obtain temperatures in the cornea, high enough to create a observable thermal lesion. Three lesions were created for each voltage in rabbit eyes. Only one lesion was made in the centre of each eye. Table V shows the lesion dimensions in depth and width obtained using in vitro model and the dimensions of the 100 °C isothermal line in the computer results. Fig. 8 and 9 also show the computer simulations and the experimental lesions respectively in the two studied cases. Table V indicates that an increase of the applied voltage from 16 to 21 V produced in the experimental model an increase of the lesion depth from 21 ± 1 to 30 ± 3 % of corneal thickness. Using the theoretical model, the depth of the 100 °C isothermal

line changed from 39 to 70 % of corneal thickness for h_{TEAR} of $100 \text{ W/m}^2 \text{ }^\circ\text{C}$. This increase of the applied voltage involved an increase of the lesion width from 106 ± 5 to 108 ± 9 % of corneal thickness in the experimental model, and from 95 to 190 % of corneal thickness for h_{TEAR} of $100 \text{ W/m}^2 \text{ }^\circ\text{C}$ in the theoretical model. The results indicate that the value of the applied voltage has a significant effect on the temperature distributions theoretically, but experimentally the applied voltage has a significant effect only on the lesion depth. The best agreement between the $100 \text{ }^\circ\text{C}$ isothermal line depth in the theoretical model and the lesion depth in the experimental model was found when the value of h_{TEAR} was set to $100 \text{ W/m}^2 \text{ }^\circ\text{C}$. A value of $100 \text{ W/m}^2 \text{ }^\circ\text{C}$ for h_{TEAR} has been stated for the temperature profiles showed in Fig. 8 and 9. The significant effect of the applied voltage on the temperature profiles observed in our computer results has also been indicated by Labonté for a theoretical model for RF cardiac ablation [22]. Our results (see table V, Fig. 8 and 9) show that the theoretical model predicts greater lesions than the experimental model. In general, there is a tendency towards agreement between experimental and theoretical results, although the numerical model overestimates the lesion dimension, especially the width. We think that these differences could be due to several causes. First, the variation of tissue characteristics in the vicinity of the active electrode during heating, because the experimental heating was associated in all the cases with a strong desiccation, detachment of tissue and adhesion to the active electrode around its perimeter. For this reason, this zone of the tissue tends to have a low value of electrical conductivity, and that could be the cause of less increase of the lesion width in the experimental model. Second, the thermal and mechanic characteristics of the cornea change strongly during the heating [1], and this aspect has not been considered in the numerical model. Other possible causes of this disagreement could be: a) the difference between the corneal thickness in the numerical

model (600 μm) and the actual thickness in the experimental model; and b) the lack of more precise experimental data about the thermal and electrical characteristics of the biological tissues used in this study (including the different membranes of the cornea). In spite of the limitations, the proposed numerical model qualitatively predicts the process of the heating of the cornea using RF currents, and it could be used in order to study the effect of different electrode shape or applied voltage values and time duration conditions on the temperature distributions.

On the other hand, in order to compare the results of the theoretical model with the in vitro experiments, only the isothermal line (100 °C) and the coagulation contour observed in the histology samples were used. It would be necessary to carry out further studies in order to describe a thermal damage function more specific to the heating of the cornea. To our knowledge, only the study of Brickmann et al. [25] offers these experimental data on thermal damage of the cornea heated with lasers. Moreover, different techniques proposed for the experimental validation of numerical models in RF heating like the use of a tissue phantom [22] or the recording of point temperatures with sensors inserted in the tissue [8] have not been considered in this study. Future studies should include experiments in order to describe a thermal damage function more specific for the heating of the cornea, and to measure the thermal and electrical characteristics of the cornea under several heating conditions. Also, future studies should investigate more realistic models including the behaviour of the interface tissue-electrode under high temperature conditions and strong tissue desiccation.

In order to interpret the results of computer simulations presented in this study, it is important to take into account that our model only represents a limited zone of the physical situation in RF-TKP (Fig.1 and 2). However, to our knowledge, the majority of the numerical models of RF heating using an active electrode include only a limited

fragment of biological tissue and active electrode [17,19,22,26,36-39]. Computer simulations have been carried out in all these cases in order to determine the appropriate model dimensions. The objective of these numerical models was to study the effect of different factors on the temperature distributions in the lesion zone. Due to the lesion is created in the vicinity of the active electrode, it was not necessary to model all the physical situation, but only a limited zone of the tissue and active electrode. Under this approach, the conclusions obtained were useful.

IV. CONCLUSION

This paper presents a theoretical model for the study of RF-TKP using a small active electrode for surface application. We have studied the influence of different factors. Each factor was considered significant when its inclusion induces a change of maximum temperature in the tissue in ± 4 °C. Based on this criterion, the dependence of electrical conductivity with the temperature, the dispersion of this parameter, the thermal anisotropy of the cornea, the presence of the tear film, and the depth insertion of the active electrode in the cornea have a significant effect on the maximal temperature achieved in the tissue. However, the cooling of aqueous humor on the cornea, as well as the cornea curvature, do not have a significant effect.

Finally, an in vitro model based on a rabbit eye has been used in order to compare the theoretical and experimental results. There is a tendency towards the agreement between experimental and theoretical results, although the theoretical model overestimates the lesion dimension (especially width). We have proposed and discussed several causes of this fact. Nevertheless, the proposed theoretical model allows one to study qualitatively the heating of the cornea with RF currents.

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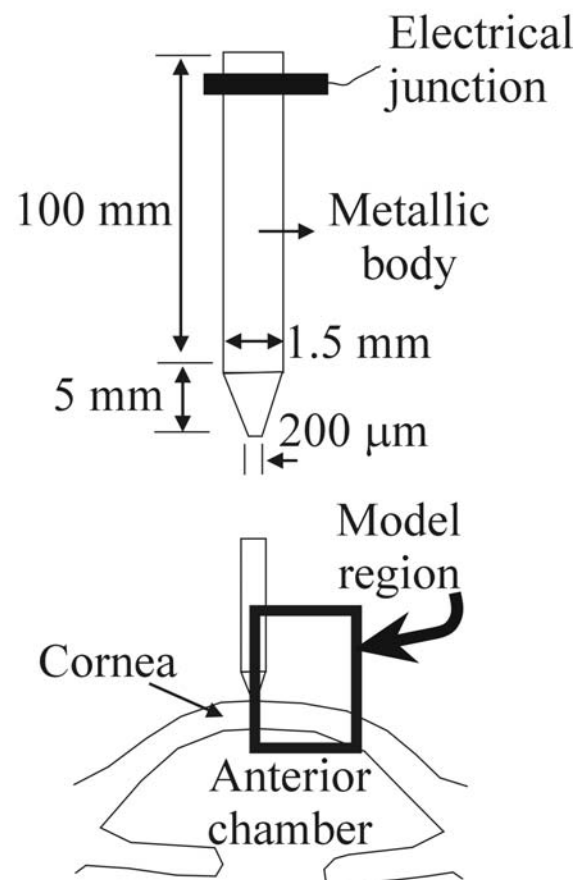


Figure 1. Top: Active electrode used in this study (not to scale) and its dimensions. Bottom: Physical situation considered in the study of the thermokeratoplasty with radio-frequency currents.

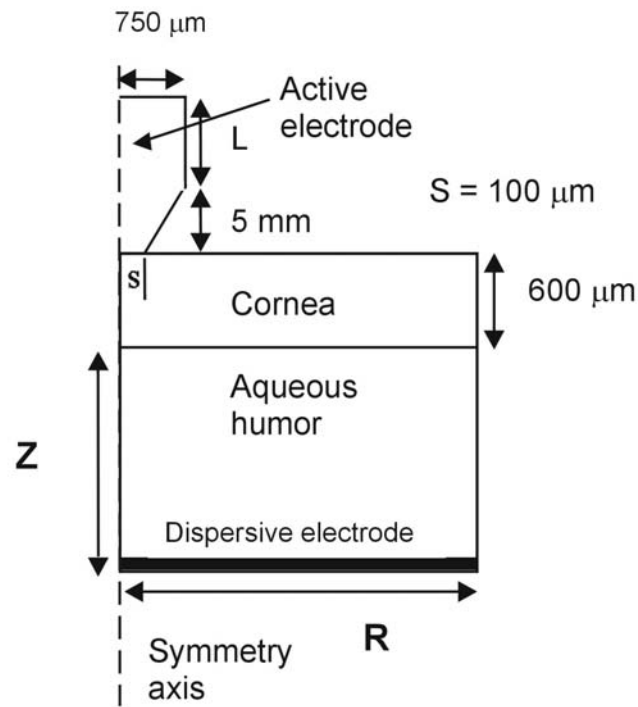


Figure 2. Theoretical model proposed (out of scale). Z and R : outer dimensions of the model; s : active electrode radius in contact zone ($100\ \mu\text{m}$); and L : length of the active electrode included in the model. Corneal thickness of $600\ \mu\text{m}$.

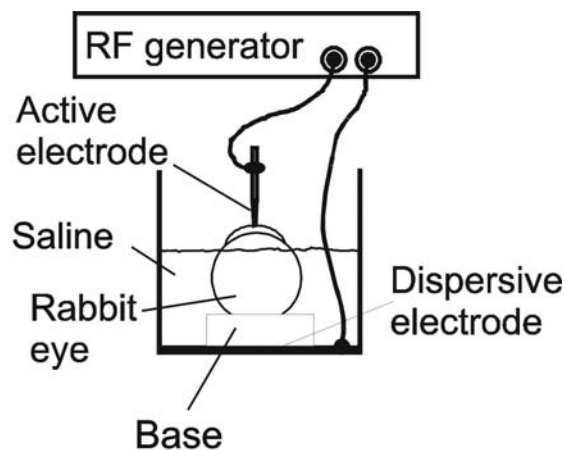


Figure 3. *In vitro* model used in the experiments.

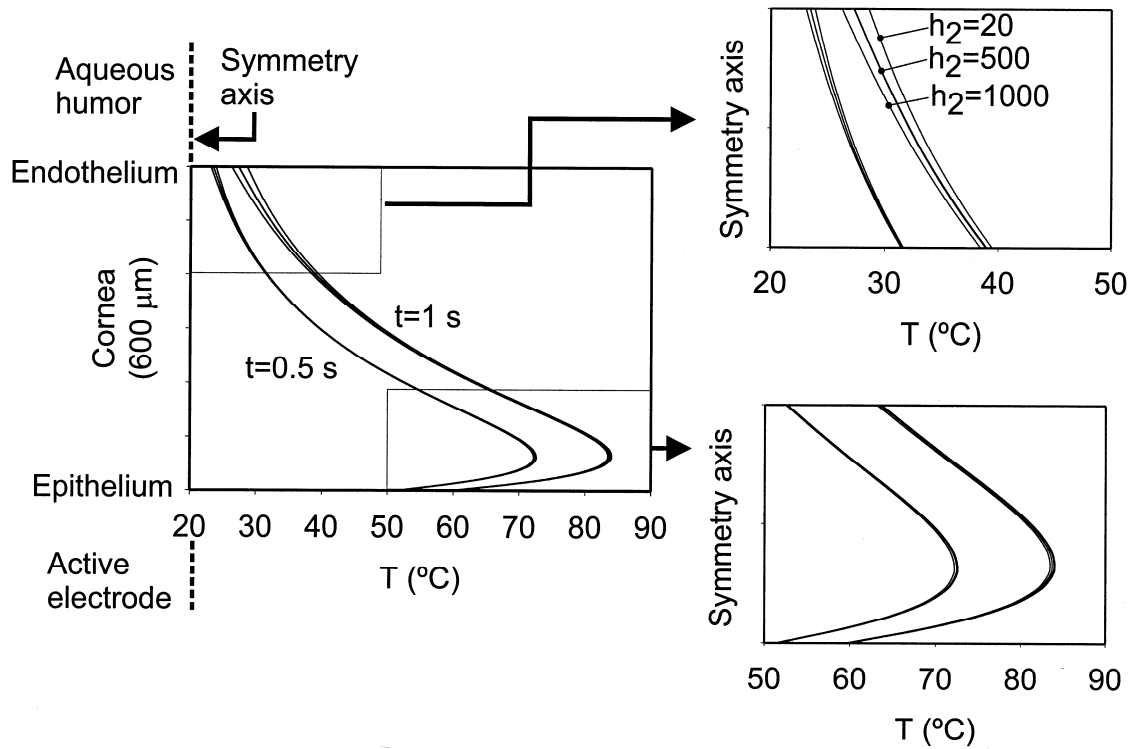


Figure 4. Left: Temperature profiles on the cornea symmetry axis for different conditions of thermal transfer in the endothelium - aqueous humor interface (h_2). Values for h_2 set to 20, 500 and 1000 $\text{W}/\text{m}^2 \text{ } ^\circ\text{C}$. Right: Zoom of the endothelium and epithelium zone. Applied voltage set to 8 V during 1 s.

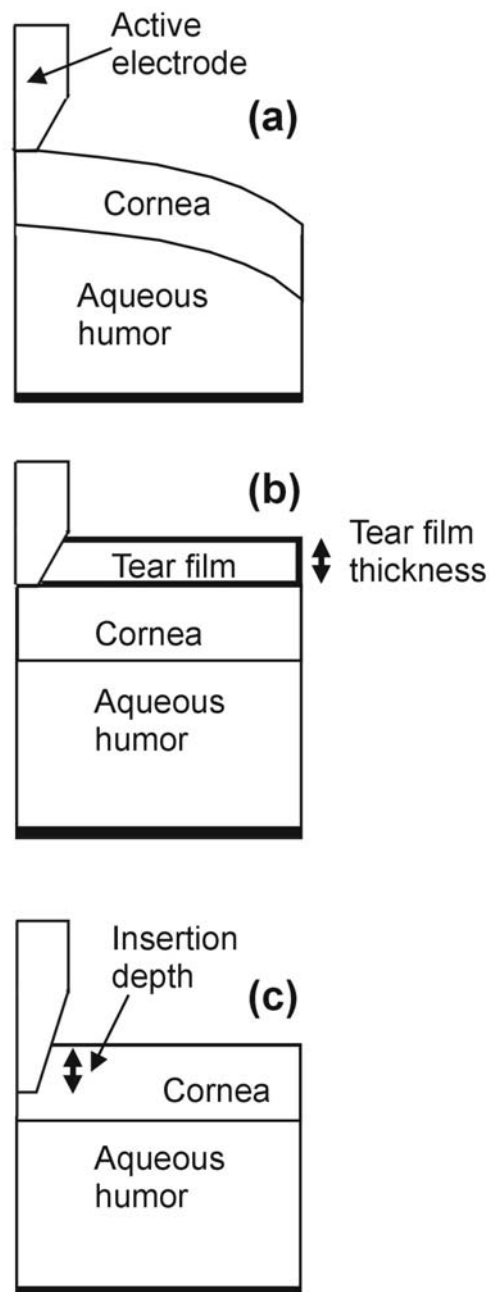


Figure 5. Modifications in the proposed theoretical model (out of scale) in order to study the effect of the realistic shape of the cornea (a), the presence of a tear film on the cornea surface (b), and the insertion depth of the active electrode in the cornea (c).

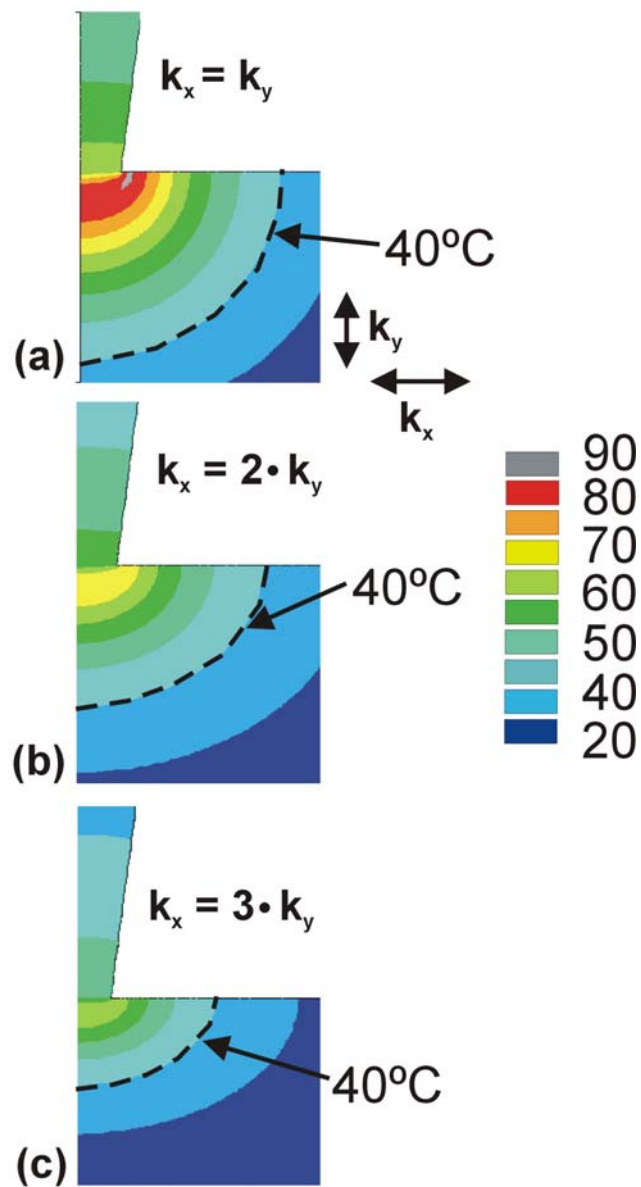


Figure 6. Temperature profiles (°C) in the cornea for different anisotropy conditions in the cornea thermal conductivity: (a) $k_x = k_y$ (control, non-anisotropy), (b) $k_x = 2 \cdot k_y$, and (c) $k_x = 3 \cdot k_y$. k_x is the longitudinal thermal conductivity, and k_y the transverse thermal conductivity. The 40°C isothermal line is indicated in order to compare the geometry of the temperature profiles for each case studied.

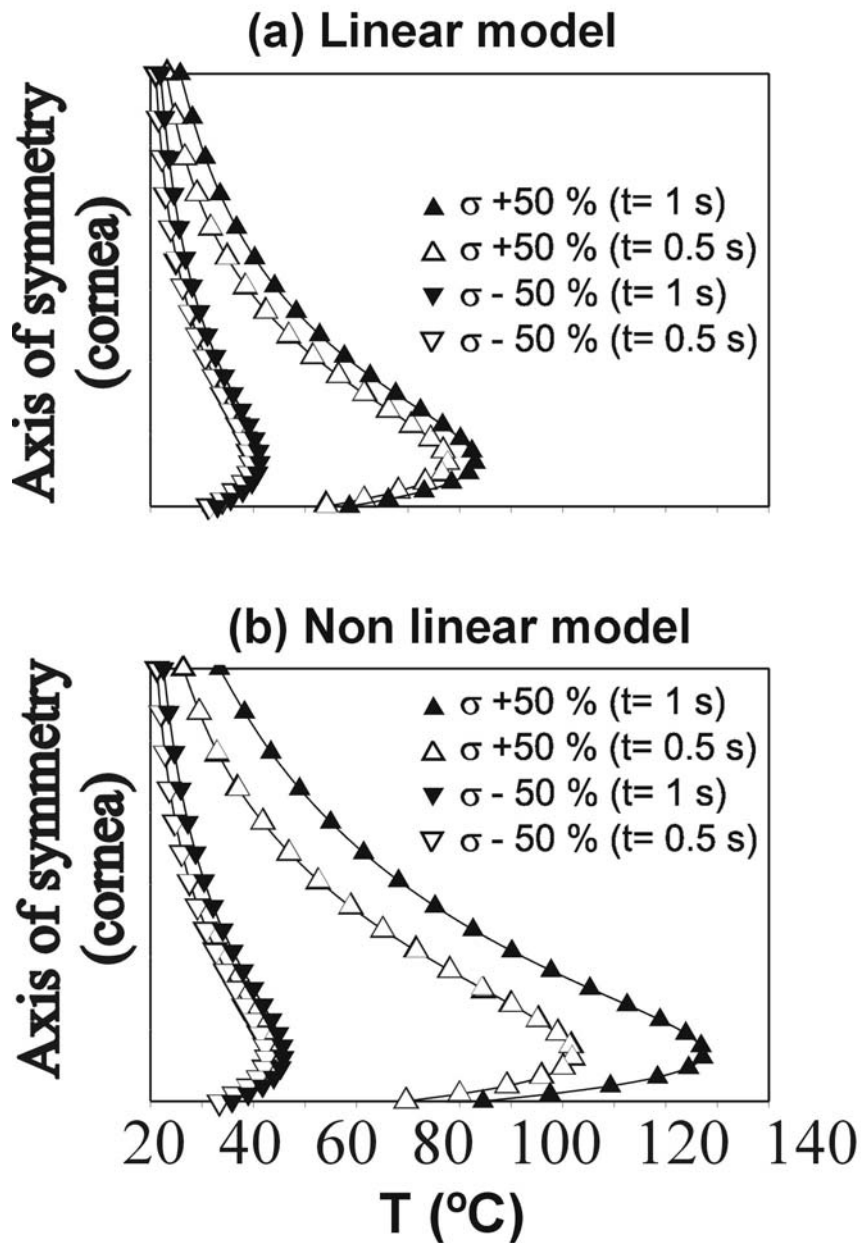


Figure 7. Temperature profiles on the cornea symmetry axis for a change of the electrical conductivity (σ) of the cornea and aqueous humor ($\pm 50\%$) after 0.5 and 1 s, applied voltage set to 8 V. Two different models are shown: (a) linear and (b) non-linear (including a change of σ with temperature of $+2\%/^{\circ}\text{C}$).

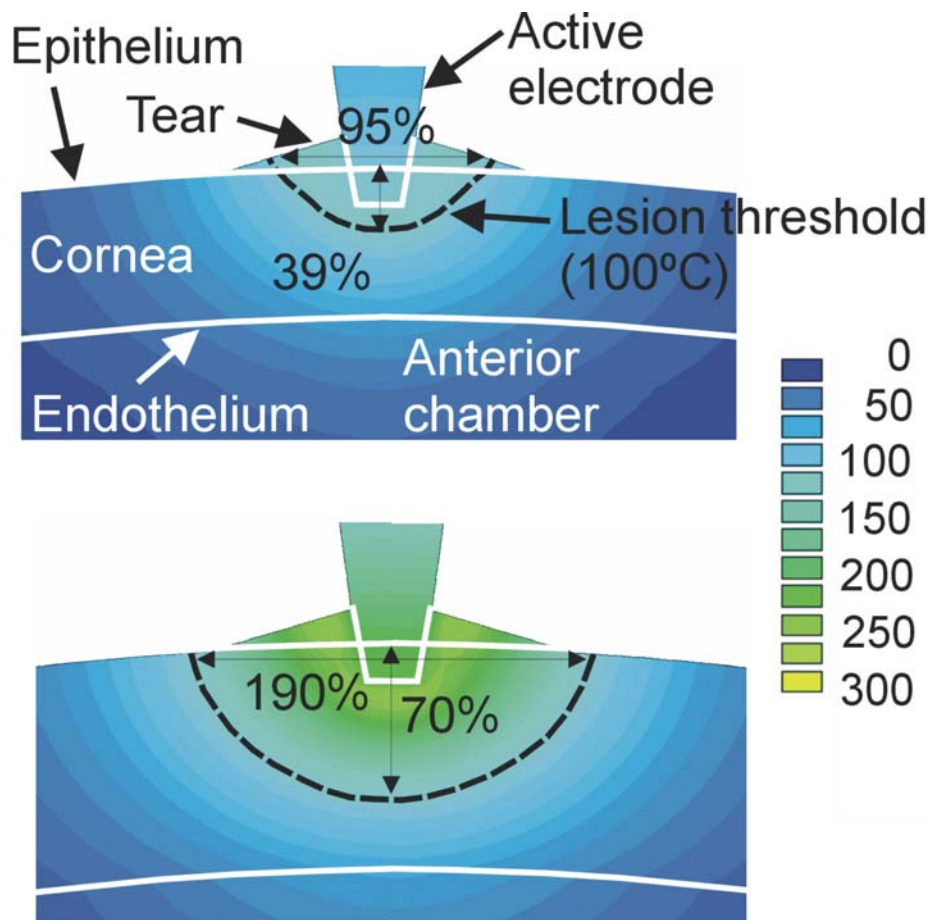


Figure 8. Temperature profiles in the cornea for two conditions of applied voltage (computer simulations based on the proposed theoretical model). Top: 16 V after 1 s. Bottom: 21 V after 1 s. The assessment of the lesion dimensions (central depth and surface width) are stated as % of corneal thickness using the 100°C isothermal line. Temperature scale is in °C.

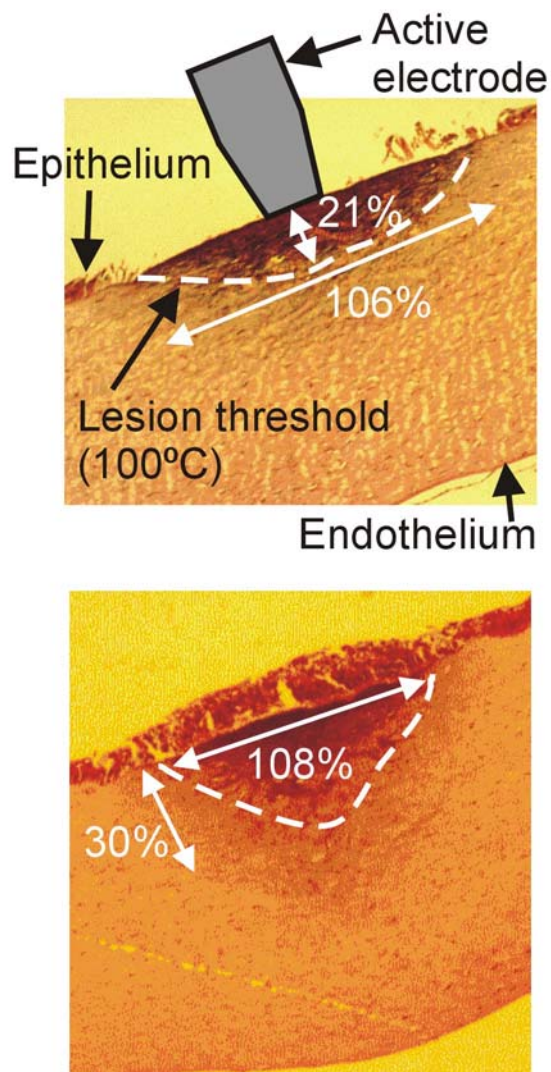


Figure 9. Cross-section of corneas heated with an electrode of 200 μm diameter (hematoxylin and eosin, X 40). Top: 16 V after 1 s. Bottom: 21 V after 1 s. The lesion dimensions (central depth and surface width) are given as % of cornea thickness.

TABLE I

CHARACTERISTICS OF THE MATERIALS. IN BOLD TYPE THE DATA USED IN OUR THEORETICAL MODEL. σ : ELECTRICAL CONDUCTIVITY; ρ : MAS DENSITY; c : SPECIFIC HEAT CAPACITY; AND k : THERMAL CONDUCTIVITY.

MATERIAL	σ (S/m)	ρ (Kg/m ³)	c (J/Kg·K)	k (W/m·K)	Reference
CORNEA * Steer * Rabbit * Pig * Rabbit	0.54 ¹ 2.08- 2.56 ² 1.2 ³	1000	3830	0.556	[Trembly, 1991] [7] [Watanabe, 1993] [12] [Jürgens, 1996] [13] [Gabriel, 1983] [14]
AQUEOUS HUMOR * Sheep * Sheep * Pig	1.6 ²	1000	4180	0.578 0.578	[Bowman, 1975] [15] [Poppendiek, 1966][16] [Jürgens, 1996] [13]
ELECTRODE *Stainless steel	7.4E+6	8E+3	480	15	[Panescu, 1995] [17]

Frequencies of measurement:

⁽¹⁾ 10 kHz-100 MHz; ⁽²⁾ 10 kHz -10 MHz; and ⁽³⁾ 500 kHz (extrapolated)

TABLE II

EFFECT OF THE ANISOTROPY IN CORNEAL THERMAL CONDUCTIVITY ON MAXIMUM TEMPERATURE REACHED IN THE TISSUE (T_{\max}) AND ON THE DEPTH AND 1/2 WIDTH OF THE 40 °C ISOTHERMAL LINE. SIMULATIONS UNDER STANDARD CONDITIONS (8 V, 1 s).

K_x IS THE LONGITUDINAL THERMAL CONDUCTIVITY, AND K_y THE TRANSVERSE THERMAL CONDUCTIVITY.

Thermal anisotropy	T_{\max} (°C)	½ Width (µm)	Depth (µm)	Width/depth
Non-anisotropy, $k_x=k_y$	85.65	375	350	1.07
$k_x=2 \cdot k_y$	68.53	360	275	1.31
$k_x=3 \cdot k_y$	61.61	320	200	1.6

TABLE III

EFFECT OF THE TEAR FILM CHARACTERISTICS ON MAXIMUM TEMPERATURE REACHED IN THE TISSUE (T_{\max}) AND ON THE DEPTH AND 1/2 WIDTH OF THE 40 °C ISOTHERMAL LINE. SIMULATIONS UNDER STANDARD CONDITIONS (8 V, 1 s).

Tear characteristics		T_{\max} (°C)	½ Width (μm)	Depth (μm)
THICKNESS	THERMAL TRANSFER COEFFICIENT (h_{TEAR})			
No tear (control case)		85.6	375	350
100 μm	500 $\text{W}/\text{m}^2\text{°C}$	67.2	307	307
	1000 $\text{W}/\text{m}^2\text{°C}$	63.2	253	273
50 μm	500 $\text{W}/\text{m}^2\text{°C}$	70.9	323	323
	1000 $\text{W}/\text{m}^2\text{°C}$	66.7	266	316

TABLE IV

EFFECT OF THE INSERTION DEPTH (ID) OF THE ACTIVE ELECTRODE IN THE CORNEA ON
 MAXIMUM TEMPERATURE REACHED IN THE TISSUE (T_{\max}) AND ON THE DEPTH AND 1/2

WIDTH OF THE 40 °C ISOTHERMAL LINE.

SIMULATIONS UNDER STANDARD CONDITIONS (8 V, 1 s).

ID (μm)	T_{\max} ($^{\circ}\text{C}$)	$\frac{1}{2}$ Width (μm)	Depth (μm)
0 (Control)	85.6	375	350
25 μm	80.0	425	400
50 μm	76.9	430	430
75 μm	74.5	450	440
100 μm	72.4	460	460

TABLE V

COMPARISON BETWEEN COMPUTER SIMULATIONS AND IN VITRO EXPERIMENTS FOR DIFFERENT CONDITIONS OF APPLIED VOLTAGE AND THERMAL TRANSFER COEFFICIENT OF THE TEAR FILM (h_{TEAR}). LESION WIDTH AND DEPTH ASSESSED USING THE COAGULATION CONTOURS IN THE CORNEA CROSS-SECTION FOR THE EXPERIMENTAL MODEL, AND THE 100 °C ISOTHERMAL LINE IN THE COMPUTER SIMULATIONS. ALL THE DIMENSIONS STATED AS % OF CORNEAL THICKNESS

	EXPERIMENTAL RESULTS		Computer simulations					
	Mean (Standard deviation). n=3		Depth (%)			Width (%)		
	Depth (%)	Width (%)	Depth (%)			Width (%)		
h_{TEAR} (W/m ² °C)	-	-	20	100	500	20	100	500
16 V, 1s	21 (1)	106 (6.5)	40	39	32	106	95	50
21 V, 1s	30 (3.6)	108.3 (8.9)	74	70	68	194	190	149