Analysis of thermal damage caused by retinal implant in a feline eye

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Abstract. The advancement of the technology in the detection of some pathologies has provided several types of treatments that have been studied and applied to humans. Even hereditary diseases with no cure prognosis can be alleviated with the use of implanted devices. This is the case of Retinitis Pigmentosa, which has no cure. However, the use of retinal implants can help in partial recovery of the patient's vision. Several types of treatments have been studied and applied in humans. The present work was developed with the objective of obtaining insights that can help and guide a safe procedure for retinal implantation in patients with Retinitis Pigmentosa. In this process, certain precautions must be taken to avoid thermal damage of the patient's residual vision. Therefore, this work aims to calculate the thermal damage that may occur due to temperature increases as a result of the electrical power dissipated by the implant. To validate the three-dimensional geometry of the human eye, a previous study was carried using a feline eye model with an epiretinal chip. Numerical simulations were performed to analyze temperature profiles and calculate thermal damage. In addition to temperature values, thermal damage is a function that quantifies the degree of cellular denaturation as a function of the power applied to the implant and its use time. Among some results presented, the main one proved that with the continuous application of an electrical power of 36.6 mW, the feline eye presented irreversible thermal damage after 5h12min. Furthermore, even after the implant is turned off, the thermal damage continues to increase, until the entire eye returns to its former thermal equilibrium. With the same methodology, an additional study is being carried out to calculate the advancement of the thermal damage in a human eye submitted to the ARGUS II implant, which was approved by the FDA (Foods and Drugs Administration – USA) for use in humans. In this work, the SolidWorks® software was used for three-dimensional geometric modeling of the eyeball, its respective tissues and the epiretinal implant. The Ansys-Fluent® was adopted for simulation of temperature profiles. The calculation of the thermal damage as well as the heat source term due to the blood perfusion were programmed and inserted into the Ansys-Fluent® program, using the Finite Volume Method and unstructured meshes.

Keywords: retinitis pigmentosa, numerical simulation, thermal damage, epiretinal implant, macular degeneration.

1 Introduction

The use of the ARGUS II implant in people, nowadays regulated by the FDA, has led to new lines of research being developed. One of these lines addresses to the calculation of temperatures within the human eye and possible damage that a temperature increase may cause. The so-called retinal implant is essential to improve the visual acuity of patients diagnosed with Retinitis Pigmentosa (RP) or with Macular Degeneration (MD).

RP is a genetic condition that leads the patient to experience losses of the visual field. As the name im-plies, in these cases the patient starts to present a cluster of pigments that are not seen in a common retina (Fig. 1). Patients with this condition experience loss of peripherical and night vision. The visual field gradually reduces to form a “tunnel vision”.

The retinal implant represents a strategy to stimulate damaged cells. Through surgery, the prosthesis is

carefully placed on the epiretinal surface of the human eye – between the retina and the vitreous body. A camera fixed close to the user's viewing angle – usually installed in glasses – captures the image of the environment and sends it to a video processing unit. The image is then transformed into data, replacing points of interest by pixels. The data is sent to the internal implant which, through electrical stimulus, informs the optic nerve of the image that previously could not be "computed" by cones and rod cells [1].

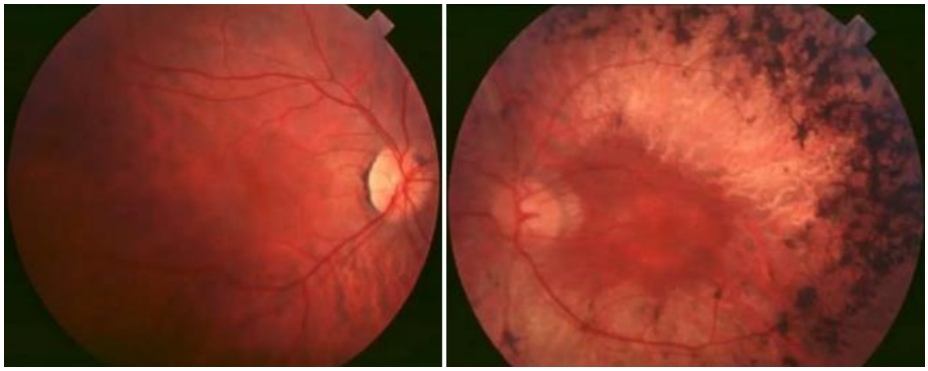


Figure 1. Fundus images of a patient with RP in the initial (left) and advanced (right) stages, [2]

Authors in [3] simulated the temperature changes caused by an implant in a feline's eye, as well as they performed measurements in vivo and in vitro. The authors took as basis the Australian standard AS EN 45502.1-2002 which imposes as a safety margin for surface temperatures in biological implants up to 2°C above body temperature around any surface of the implant. Using this standard, the referred authors found that the implant can reach a value of 36.6mW continuously without damaging neighboring tissues.

The standard previously mentioned is not concerned with the calculation of the thermal damage function, which is traditionally used to quantify the damage to living tissues that may be caused in hyperthermic processes. The calculation of this variable differentiates the present analysis from the work presented by [3] and validate the results of its geometric and mathematical model. The thermal damage function is properly presented and discussed in the following section. The thermal damage function has been studied and is suitable to several biological tissues, always looking for a way to control the rate of protein denaturation in order to measure the probability of damage and allow to control the irreversibility of the process. [4, 5] for example, analyzed the effects of the treatment of choroidal melanoma using Transpupillary Thermal Therapy (TTT) and calculated the thermal damage function to determine the amount of laser radiation energy necessary for treating some eye tumors.

Later, [6] extended the same study, calculating the thermal damage function in a three-dimensional geometry, finding different effects in treatments for patients with advanced age, whose vitreous humor mood starts to liquefy, thus modifying the process of heat transfer inside the eye.

This thermal damage function is universally accepted to calculate any damage that may be caused by hyperthermic procedures in living tissues. The study by Henriques and Moritz (1947) [7] defined the function, which is based on the rate of the protein denaturation in an Arrhenius chemical reaction originated by an increase of the temperature in the tissues motivated by external sources of heat. This function was developed to calculate the denaturation of proteins and to quantify burns in living tissues.

2 Materials and methods

2.1 Mathematical and Geometric Modeling

Temperature elevations of the human body during hyperthermic processes cause the denaturation of a series of proteins, which represents a common process of necrosis in cells as described in [8]. This denaturation depends not only on high temperatures, but also on the time that the foreign body remains warm.

The thermal damage model in living tissues was originally established by Henriques and Moritz [7] for the analysis of skin burns and since then it has been widely accepted and used to describe the quoted damages. Many

other models were developed from this first one, but few differ from the original. One exception is the Birngruber model [9], specifically developed and used for ocular tissues [4].

The authors of [7] and [9] sought a way to simplify the protein denaturation model in a temperature-dependent equation, which when integrated over time would result in thermal damage. The Birngruber model, which is specifically focused on thermal eye damage, was used in the present article and is detailed below.

As shown in [10], the result of the logarithm of the concentration ratio of undamaged cells after a time t is called the thermal damage Ω. This function starts at t=0, at a body temperature of 37°C, and is integrated until a time t=t', when the temperature of the eye returns to body temperature, after the power is turned off, ie , when there is no longer a significant contribution to the denaturation process. In this case, the equation is suitable for a temperature range from 37 °C to 100 °C [10].

$$\Omega = \frac{R}{N_A.h} exp\left(1 + \frac{\Delta S}{R}\right) \int_0^t T(t).exp(\frac{-\Delta E_{act}}{RT(t)})dt \tag{1}$$

where R is the universal gas constant, N_A Avogadro's constant, h Planck's constant, ΔS the change of entropy during the reaction, T the absolute temperature and ΔE_{act} the activation energy for the denaturation process.

From the skin burns, both authors in [7] and those in [9], consider Ω=1 as an indicator of total irreversible damage. According to Birngruber, the activation energy for the retinal tissue is $\Delta Eact = 2.9.10\text{^}5\, J.mol^{-1}$and the entropy change is $\Delta S = 595\, J.mol^{-1}K^{-1}$. More mathematical details can be found in [6,11-15].

The present work calculates the thermal damage due to retinal implants and determines the maximum time of continuous use of an implant, in order to avoid permanent damage to the cells. The maximum time will vary according to the power dissipated by the implant. The feline eye designed by the authors of [3] was taken as a basis for the development of the three-dimensional model shown in the present work (Fig. 2). SolidWorks® was used to build the geometrical model of the eye and the volume of the respective tissues, in order to compare with Table 1 provided by Opie et al.

Table 1 is subdivided into: Tissues, Volumes proposed by Opie et al. (V. Op.), Volume of the authors' design (V. Aut.), Volume difference (Dif.), Thermal conductivity (k), Specific mass (ρ) and Thermal capacity at constant pressure (c_p).

Table 1. Tissue Volume ([3] and Author), percentage difference and tissue properties used in the modeling of the feline eye.

Tissue	V. Op.	V. Aut.	Dif.	k	ρ	c_p
Unit.	mm3	mm3	%	W/m ºC	kg/m3	J/kgºC
Anterior Chamber	572.9	573.0	0.01	0.600	1009	3430
Lens	613.0	614.0	0.16	0.400	1100	3000
Vitreous Body	1534.0	1534.0	0.02	0.600	1009	3430
Retina	346.6	346.5	0.04	0.565	1039	3680
Choroid	45.57	45.96	0.86	0.600	1050	4178
Cornea, Sclera and Iris	1123.0	1141.0	1.56	0.580	1075	4178
Epiretinal	4.783	4.710	1.53	400	8700	385

As the analyzed regions are biological tissues, a model of the heat diffusion equation proposed by [16] and presented in Eq. (2) was used. Terms to consider the volumetric rates of heat generation from blood perfusion, metabolic heat and volumetric rate from external sources were added.

$$\rho c_p \frac{\partial T}{\partial t} = \bigtriangledown(k. \bigtriangledown T) + A - B(T - T_b) + Q \tag{2}$$

where ρ represents the specific mass of the tissue, c_p the specific heat, k the isotropic thermal conductivity, A characterizes the metabolic generated heat, B the blood perfusion coefficient, T_b the temperature of the arterial blood and Q is the volumetric power heat dissipated by implant. All temperatures in this work are in Kelvin. The volumetric rate of metabolic heat generation (A) in the retina is represented by:

$$A = A_R.(1.1)^{(\tau - \tau_b)} \tag{3}$$

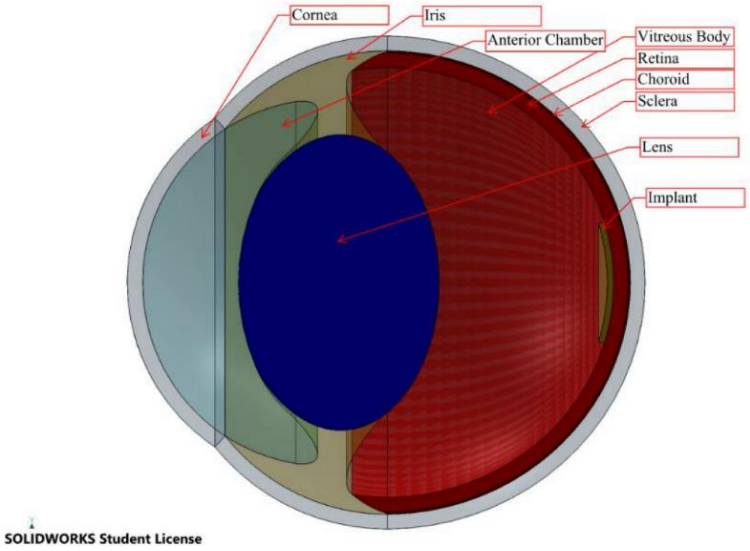


Figure 2. Feline eye model.

and blood perfusion (B) in the choroid and retina are represented by

$$B = \begin{cases} B_R & for T \leq 39^oC \\ B_R[1 + 0.8(T - 39)] & for 39^oC \leq T \leq 39^oC \\ 5B_R & for T \geq 44^oC \end{cases} \tag{4}$$

The values of A_R and B_R are specified in Table 2. As boundary conditions the authors of [3] considered that the sclera, for being located mostly inside of the eyeball, is at a constant surface temperature of 37°C and that the corneal surface is in contact with the air, exchanging heat by convection, according to the data also reported in Table 2.

Table 2. Data for numerical simulation [3]

Boundary conditions		
Description	Unit	Value
A_R – Retinal metabolic rate	W/m^3	10,000
B_R – Retinal blood perfusion rate	$W/(m^3\,^oC)$	35,000
Coefficient of heat exchange by convection on the corneal surface	$W/(m^2\,^oC)$	65
Room temperature	ºC	20
Fixed temperature on the sclera surface	ºC	37

2.2 Methodology

A numerical calculation of the temperature profiles and thermal damage was performed using the commercial software Ansys Fluent® which uses general heat diffusion equations in each distinct region of the eye. A convergence analysis of the unstructured mesh was made using the mean square error. After comparing with the epiretinal temperature profile presented in [3] (Fig. 4-a), an unstructured mesh with polyhedral elements of uniform size of 2·10(-4) meters was chosen (see Fig.3).

The Eq. (1), which calculates the thermal damage, was inserted in Fluent® through the User-Defined Function (UDF), since this function is not calculated by the software. This discretized function was based on the algorithm proposed by [4]. In addition to thermal damage, the equations for the metabolic heat rate and blood perfusion have been adapted and included in the retinal and choroid layers using UDF's.

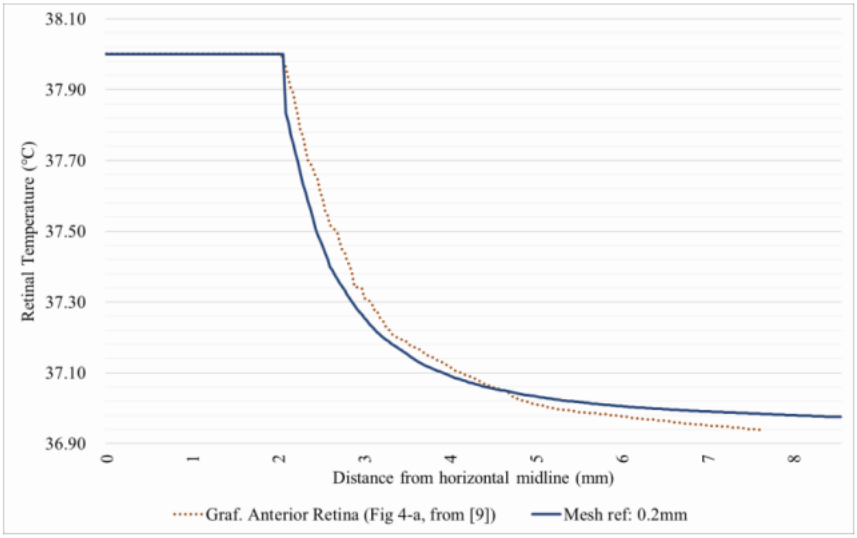


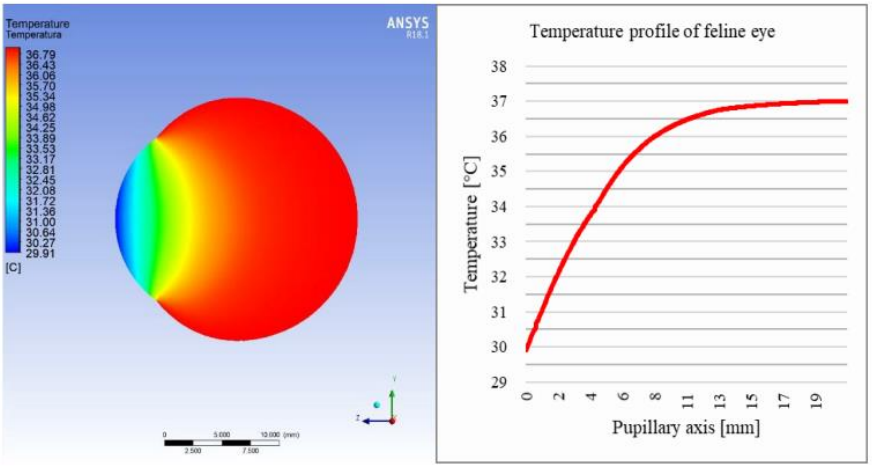
Figure 3. Comparison between temperature profile presented on figure 4a of [3] and the result of the used mesh in the present work.

3 Results and discussion

The duration of the numerical calculation was chosen based on the assumption the use the implant is continuous, for a period of approximately 8 hours. The power generated by the epiretinal implant was the maximum power simulated by [3] whose value corresponds to 36.6mW. As explained earlier, with this electric power the authors of [3] guarantee that the maximum temperature of the globe is below the 2 °C margin.

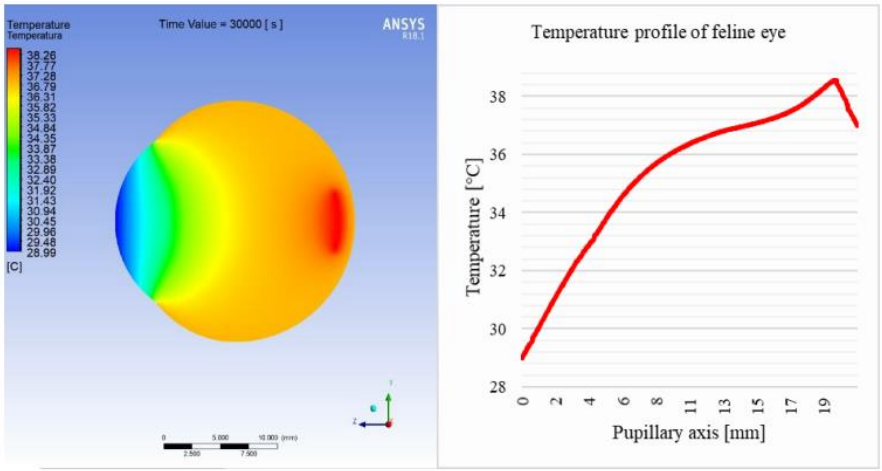
The temperature profile of the eye at steady state was considered as the initial condition for this problem. The steady state was simulated by considering the boundary conditions shown in Table 2, without the implant effect, as shown in Fig. 4. The pupillary axis starts in the center for cornea external surface and ends at the fundus of the eye.

Considering the profile shown in Fig. 4 as the initial condition of the transient simulation, the problem was calculated over a time of 8h20min with a continuous power generated by the implant equal to36.6mW. The calculated thermal damage is shown in Fig. 6.



$T_{máx}$ (°C)	T_{min} (°C)	ΔT
37.00	29.91	7.09

Figure 4. Simulation of the feline eye in steady state; the temperature distribution (left) and the temperature profile on the pupillary axis (right).

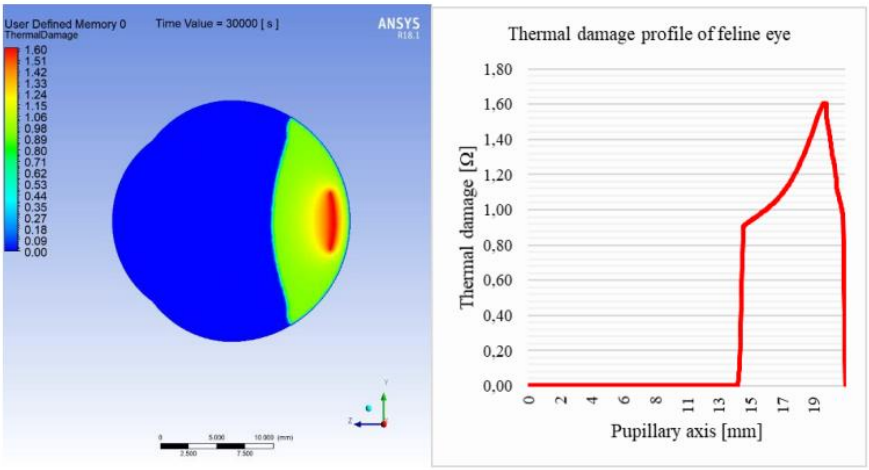


$T_{máx}$ (°C)	T_{min} (°C)	ΔT
38.55	28.99	9.56

Figure 5. Temperature profiles of the feline eye in a transient state after 8h20min of continuous application of 36.6mW of the epiretinal implant: temperature distribution (left) and temperature profile of the pupillary axis (right).

The presence of the implant caused a gradual increase in the temperature of the eye. Considering the blood perfusion, that are present in the retina and in the choroid, and the conventional processes of heat transfer already included in the ANSYS modules, the maximum temperature remained below 39°C. According to the Australian standard AS EN 45502.1-2002, the implant would not cause a risk of thermal damage to the neighboring biological tissue, being within the maximum margin of 2°C of temperature increase. However, the results obtained by the present study show that despite the temperatures being within the range calculated by [3], during the calculated time, irreversible damage can appear in regions of the eye around the implant.

Fig. 6 shows that during the analyzed time, the implant would cause permanent damage to the retinal tissue due to the longtime of warming. In order to be more accurate, the exact moment when the thermal damage exceeds the safety margin was calculated. So, according to the calculated results, the maximum time that the feline eye could sustain without suffering damage, receiving a constant power of 36.6mW, was 18,700 seconds, which is equivalent to 5 hours, 11 minutes and 40 seconds.



$\Omega_{máx}$	Ω_{min}	ΔΩ
1.604	0.000	1.604

Figure 6. Thermal damage in the eye (left) and profile of thermal damage in the pupillary axis (right).

4 Conclusions

The present study presents a way to increase information about safety during continuous use of retinal implants by patients with retinitis pigmentosa or macular degeneration. Using the proposed methodology in a feline eye, the results were compared with the one presented in [3] to validate the whole process. The commercial software Ansys Fluent® was used to calculate the thermal damage, which was introduced by the authors. With this new model it is possible to calculate when irreversible damage at the retina may occur, which opens the possibility for better applications for implant's use or even improve the patient's chances of visual recovery. The model presented for thermal damage quantifies in a simple way the degree of cell degeneration according to the power applied in the implant and its time of use. With the presented method, the use of controllers stored in the video processing unit could be suggested, which makes it possible to adjust the level of the electrical power emitted by the chip, in order to avoid the problem described. With the validation of the mathematical and numerical model. The human eye has been submitted to the Argus II implant, released by the FDA (Food and Drug Administration) in the United States and produced by Second Sight Medical Products®. A similar study is been carried out for a human eye [17].

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