Thermal Interaction between laser & tissue during retinal photocoagulation

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ABSTRACT

The conventional retinal photocoagulation uses continuous wave (CW) lasers which results in pathophysiologic thermal environment to surrounding normal tissues such as neural retina, choroid, and photoreceptors. Selective photodamage of retinal pigment epithelium (RPE), thus sparing photoreceptors can be achieved by using short pulsed lasers. The problem associated with the usage of short pulsed laser is that it is difficult to determine correct dosimetry parameters. The aim of this study is to quantify the influence of different laser parameters over the therapeutic range and to find their optimum values in order to achieve the selective retinal treatment. The present study investigates the laser-tissue interaction by analyzing the transient temperature rise in ocular tissues during repetitive laser photocoagulation. The absorption coefficients based on combined scattering and absorption characteristics for ocular tissues such as vitreous humour, neural retina, RPE, choroid, and sclera are accounted in order to get accurate temperature rise. The laser parameters: wavelength, pulse width, and the laser profile are critical in determining the selective damage. The temperature rise in the neural retina and RPE are quantified by varying the laser parameters. Results reveal that microsecond (μs) pulsed lasers with green wavelength and Gaussian heat source profile is the most effective in selective treatment.

Keywords: laser photocoagulation, retinal pigment epithelium, selective microphotocoagulation, selective retinal pigment epithelium treatment

1. INTRODUCTION

Laser retinal photocoagulation is used to treat number of macular diseases such as age-related macular degeneration, diabetic maculopathy, central serous retinopathy, choroidal neovascularization, etc. Most of the macular diseases are related to the decline in RPE cell function. Hence therapeutic range of the laser treatment is associated only with the damage of RPE. It has been postulated that cell proliferation after the RPE damage enhances pumping mechanism and produces the clinical effects of reducing subretinal fluid and improving macular pathology.

During radiation treatment, the photons are absorbed in the tissues and it results in the excitation or increase in energy of the molecules. The increase in energy causes the temperature rise, which breaks the weak bonds in protein and enzymes and thereby causing denaturation of proteins. Many proteins are affected in the temperature range of 50 ^{o}C to 80 ^{o}C. The degree of damage to a particular type of tissue is based on two critical parameters namely temperature rise, and time-duration of heating. Tissue damage can be produced either by long exposure to a low temperature rise or by short exposure to a high temperature rise. This reciprocity between exposure duration and temperature rise is the critical factor, which helped in the development of selective retinal treatments. The radiation parameters such as wavelength, pulse width, repetition frequency, number of pulses and the transverse profile affects the temperature rise and the heating duration.

Conventional laser photocoagulation uses continuous wave laser with exposure time in the range of 100-200 ms and with power in the range of 50 – 200 mW. The laser is primarily absorbed by the melanin granules in the RPE tissue. Since the exposure duration is long, the absorbed thermal energy that spreads by diffusion into neural retina and choroid destroys the photoreceptors. The laser scar expands postoperatively which results in decrease in central visual

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sensitivity, epiretinal fibrosis, and reoccurrence of choroidal neovascularization. The main criterion for determining optimum exposure duration for selective damage is thermal relaxation time. It is defined as the time when maximum temperature occurs at a distance r from the source. It is $r^2/6\alpha$ for a point source where α is the thermal diffusivity. By using pulsed lasers with pulse duration of microseconds, which shorter than the relaxation time of melanin granules, the localized damage of RPE is possible[1,2,3]. Further, by using more number of pulses having long exposure with sub-threshold energy with lower temperature rise it is possible to produce selective damage with insignificant damage to photoreceptors[1].

First selective photocoagulation treatment using 5 μs laser pulses with pulse energy in the range of 3-6 μJ at 500 Hz was carried out in rabbits by Roider[2] with 110 mm retinal spot size and with 100 pulse exposures. They analyzed effect of both CW and pulsed lasers with various power sources and exposure durations. They showed that sparing of neural retina is possible only by the repetitive laser while CW laser always produce damage to the surrounding tissue even for very short exposure duration of few milliseconds.

Clinical study in humans performed by Roider[3,4] with 1.7 μs green laser photocoagulation at 500 Hz for retinal spot diameter of 160 μm produced RPE disruption without producing white or grey lesion. The white or gray lesions formed during CW photocoagulation are due to the destruction of photoreceptors, which alters the scattering characteristics of the neural retina. Further, they showed improved therapeutic effect for CSR, drusen maculopathy, diabetic maculopathy. Hence, it is evident that, for these macular diseases, the therapeutic efficacy is only related with destruction of RPE and not with the destruction of photoreceptors. Autofluorescence imaging by Framme[5] showed leakage through the lesions formed by 1.7μs laser, which proved the possibility of damaging RPE barrier by short pulsed lasers.

Mainster[6,7] studied the effect of wavelength based on absorption characteristics of melanin. They conferred the undesirable effects of blue wavelength and the advantage of using green or red laser. Further, they recommended selection of wavelength based on type and severity of disease; Near infrared rays are preferred over the visible lasers for severe subretinal hemorrhage while visible rays are preferred for thin hemorrhage. Amera[8] predicted temperature rise in ocular tissues using finite volume approach for various power sources, spot diameters and wavelengths.

Although there have been several experimental studies, the influence of each laser parameter are not well quantified owing to the difficulty in measuring the actual temperature rise during the photocoagulation. Further variation in RPE thickness, shape and melanin concentration affects the temperature rise to a great extent. Similar laser power could cause suprathreshold values for heavy pigmentation which produces excessive damage or could lead to very subthreshold values for low pigmentation which does not break brunch membrane. The current study aimed at finding the therapeutic range of laser parameters and RPE thickness by studying temporal and spatial variation of temperature rise profiles. The scattering effects of laser in the ocular tissues are included along with the absorption characteristics in order to get accurate temperature rise.

2. METHODS AND MATERIALS

2.1 Geometry

The geometrical description of the eye from Charles[9] is used to create an axi-symmetric model of a complete eye as shown in figure 1. The model consists of nine different parts: cornea, lens, iris, aqueous humour, vitreous humour, neural retina, RPE, choroid, and sclera. The average thicknesses of 10 μm, 190 μm, 250 μm, and 700 μm are used for RPE, neural retina, choroid, and sclera, respectively.

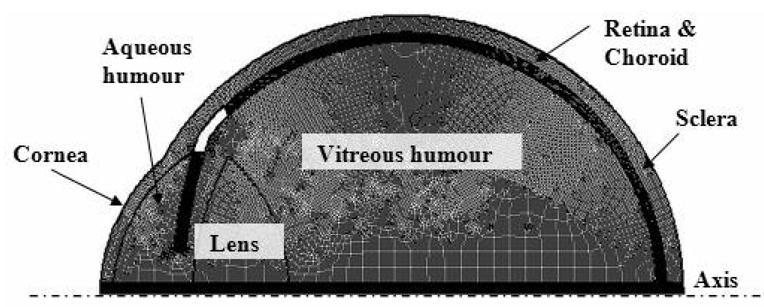

Figure 1. Two dimensional axi-symmetric model

2.2 Governing equation

The simulation of laser-tissue interaction is carried out by solving transient energy equation using finite volume discretization technique.

$$\rho C \frac{\partial}{\partial t}(T) + S(z,r,t) = \nabla.(k\nabla T) \qquad [1]$$

where k – thermal conductivity, ρ – density , C – specific heat capacity, and S – volumetric laser source term which varies spatially and temporally. In numerical analysis by Amera[8] mixed boundary conditions are used. They have analyzed the effect of boundary conditions by applying wide range of heat transfer coefficient and showed that boundary condition has insignificant effect over the solution. Since total time exposure is in the range of few hundred microseconds, the problem is presumed to be semi infinite. This is because of the significant difference in length scale associated with the eye geometry and the size of the laser spot. In order to validate the assumption, two extreme boundary conditions, constant temperature (sink type Dirchlet B.C.) and insulated (no heat transfer) are analyzed. Figure 2 shows temperature profiles obtained for 100 ms CW exposure for both cases. The maximum temperature obtained differs only by 0.02%. Hence constant temperatures at the boundaries are applied for all simulations presented in this study.

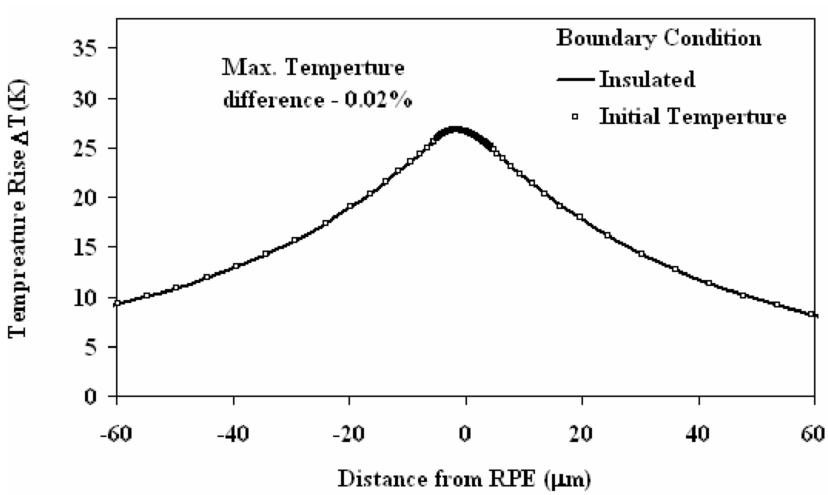

Figure 2: Validation of boundary condition

2.3 Properties

The thermal properties of each ocular tissue are critical for the evaluation of actual temperature rise. The thermal properties of ocular tissues are similar to that of water as all tissues are composed of mainly water. The thermal properties of each ocular tissue are taken from Amera[8]. Thermal conductivity of choroid is very difficult to measure owing to the blood flow through it. Hence thermal properties of choroid are chosen to be similar to that of retina.

2.4 Finite Volume Method

The finite volume mesh is generated in Gambit 2.1.0 using Cooper scheme with ~60,000 cells of quadrilateral elements. Equation 1 is solved using finite volume method. Double precision coupled solver with second-order time implicit scheme is employed to discretize the governing equations. A second order upwind scheme is adapted for energy. Convergence criterion for energy is kept at 10^{-6} an order of magnitude lower than recommended values. Mesh independency is checked by increasing the number of elements in the RPE region by 20% over the current mesh and both the results are compared. The mesh with increased number of elements showed less than 1% difference in temperature rise.

3. RESULTS

The success of selective retinal photocoagulation depends primarily on the proper selection of laser parameters. The results from this study quantitatively express the effect of laser parameters such as 1) Wavelength 2) Laser profile

3) Pulse duration. The effects of wavelength and laser profile are analyzed for CW lasers with 10 mW power and 100ms exposure duration. The effect of pulse width is analyzed using pulsed lasers with 10 mW average power for 100 ms exposure duration. The ratio of maximum temperature rise at RPE to that of neural retina at 5 μm from RPE and neural retina interface, $\frac{\Delta T_{RPE}}{\Delta T_{neural}}$, is used as a measure to study the selectivity. A higher temperature ratio means better selectivity while lower value signifies the spreading of thermal energy to the neural retina.

4.1 Effect of wavelength

Melanin granules in RPE have strong absorption characteristics for wavelengths in the visible range and his absorption decreases with increase in wavelength. In order to evaluate the effect of wavelength the absorption and scattering effect of each ocular tissue should be considered. *In-vitro* measurements using double-integrating and inverse Monte Carlo technique by Hammer[10] included the effect of scattering inside the fundus layer. The value of absorption coefficients for RPE, neural retina, choroid, sclera, and vitreous humour are calculated based on transmission characteristics from the experimental result[10]. The absorption coefficient values used in this study are higher than that of used in previous studies that ignored the scattering effect.

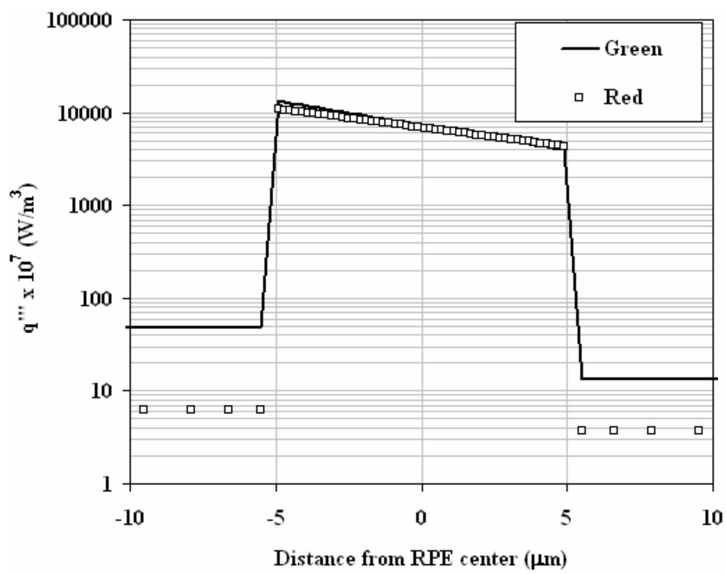

Figure 3: Heat source profile for green and red laser

Two different wavelengths green and red laser are analyzed. The exponentially varying heat source is shown in figure 3. The heat generation is high in RPE and very low in neural retina and choroid for all wavelengths. The advantage of red rays over green wavelength is that heat source at RPE and neural retina interface is lower and the absorption of laser in the neural retina is about 5 times less. The disadvantage of red is the percentage absorption in RPE is less than that of green. Figure 4 shows the temperature rise obtained for CW laser. The green laser produce maximum temperature rise for the same power. However the temperature rise ratio $\frac{\Delta T_{RPE}}{\Delta T_{neural}}$ is higher for red wavelengths due to low heat source near the RPE neural retina interface. Hence based on the temperature rise ratio red wavelengths are found to be more effective in localization of temperature rise.

Another important factor to be considered is the amount of unabsorbed laser energy leaving the sclera, which can produce damage to the optic nerves. The percentage transmission for infrared ray is very high. For green laser almost 88% of incident energy is absorbed whereas it is 80% for red. Hence based on the transmission criteria green laser is preferred over red. Considering both parameters percentage transmission and localization, the red laser is found to be effective for CW.

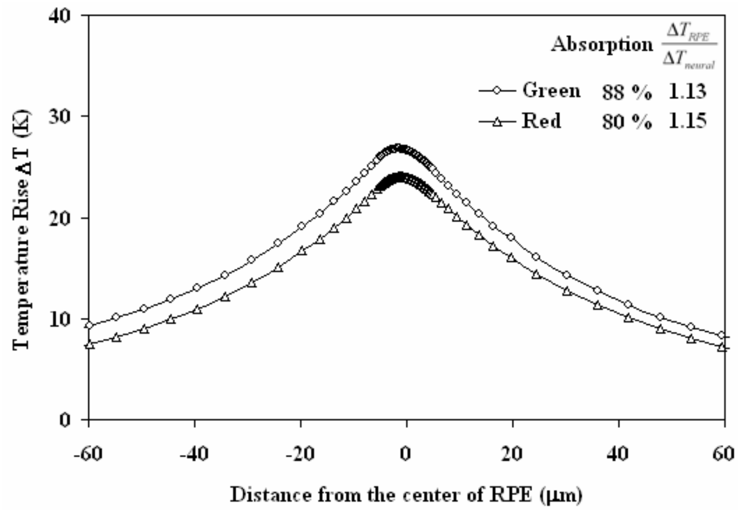

Figure 4: Temperature rise for different wavelengths for CW laser

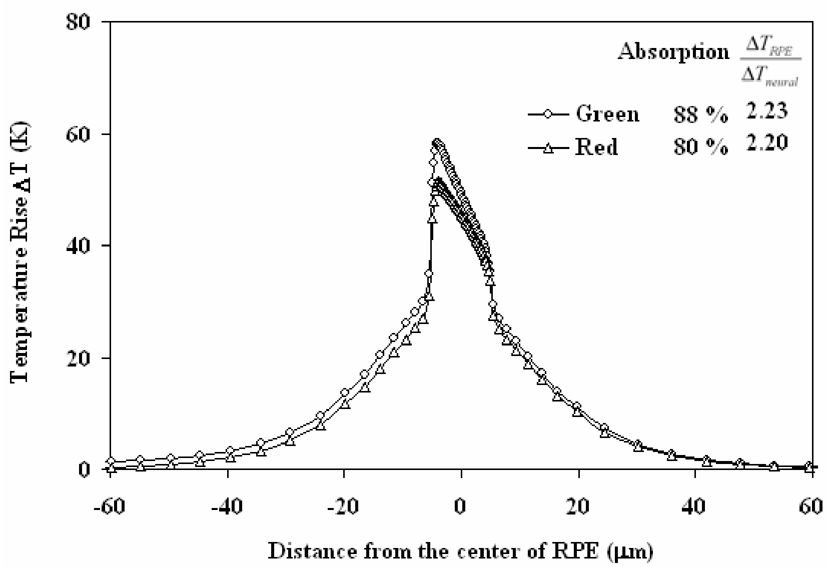

Figure 5: Temperature rise for different wavelength for 2μs pulsed laser at 5000 Hz

The effect of wavelength for pulsed laser is studied by simulating 2 μs pulsed laser at 5000 Hz. For micropulsed lasers, the percentage absorption in the RPE is found to be the main criteria. Figure 5 shows the temperature rise for different wavelengths for pulsed laser which shows high selectivity for green wavelength. Hence, the green laser is more effective for pulsed lasers.

4.2 Effect of laser profile

The traverse laser profile depends on the transverse electromagnetic (TEM) operating mode of the laser. The fundamental mode i.e. TEM00 produces Gaussian profile laser while the multimode produces a near uniform intensity profile (top hat). In this study the effect of the laser profile on the therapeutic effect is analyzed by simulating the laser profiles Gaussian and top hat for CW with 10 mW power for retinal spot diameter of 100 μm. Figure 6 shows comparison of temperature rise along radial direction for 5 ms and 100 ms exposure. The Gaussian profile produces higher temperature at the center of the beam than that of top-hat. The ratio of maximum temperature rise obtained by

Gaussian to that of top hat is 1.24 for 100ms. It is highly dependent on the exposure duration and it increases with decrease in the pulse duration. For 5 ms exposure the power required for Gaussian beam is ~ 28% less than that of top hat to produce same temperature rise. For extremely short pulsed lasers the power required for Gaussian beam will be 50% less than that of the top hat as the laser power at the center of Gaussian is twice as that of top hat profile. Hence Gaussian profile is suitable to achieve better selectivity and to minimize the damage to the neural retina along the radial direction.

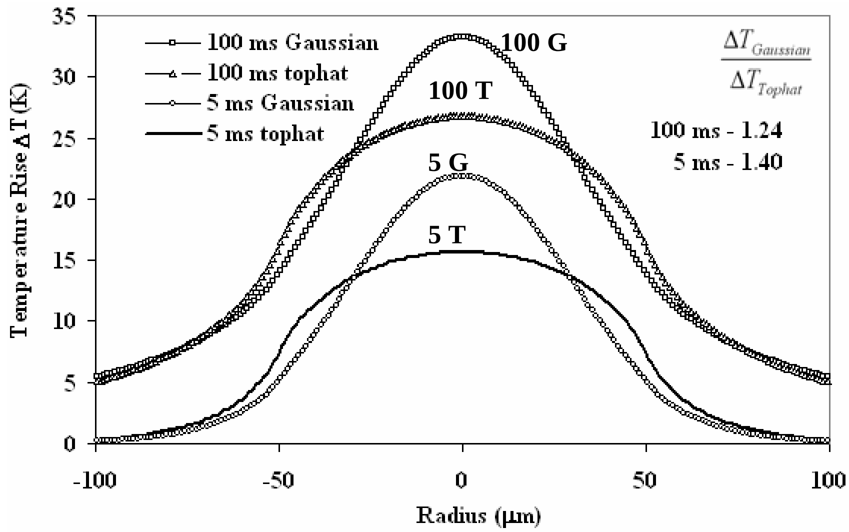

Figure 6: Comparison of temperature profile for Gaussian and top hat profile

4.3 Effect of pulse duration

The effect of pulse duration is studied by analyzing the temperature rise for 2, 200μs pulses at repetition frequency of 1000 Hz for green wavelength. The energy per pulse is maintained at 10 μJ and the average power is maintained at 10 mW. The total number of pulses applied is 100. Figure 7 shows the comparison of temperature rise for different pulse duration at the end of 100^{th} pulse. The maximum temperature rise at the RPE is obtained for 2 μs pulse while 200 μs produces low temperature rise. For 2 μs laser pulse there is no significant conduction and thus, the thermal energy is confined to RPE. This, in turn, results in minimum temperature rise at the neural retina. For 200 μs pulse duration significant spreading of energy is observed. The value of selectivity is 3.11 for 2 μs and it is 1.61 for 200 μs pulse.

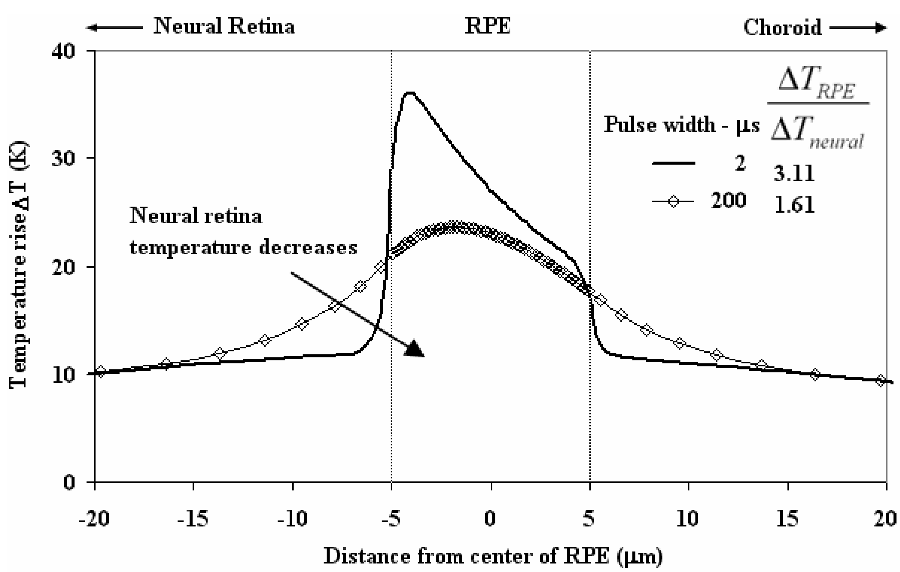

Figure 7: Temperature rise for 2 and 200 μs pulses at 1000 Hz after 100 number of exposures

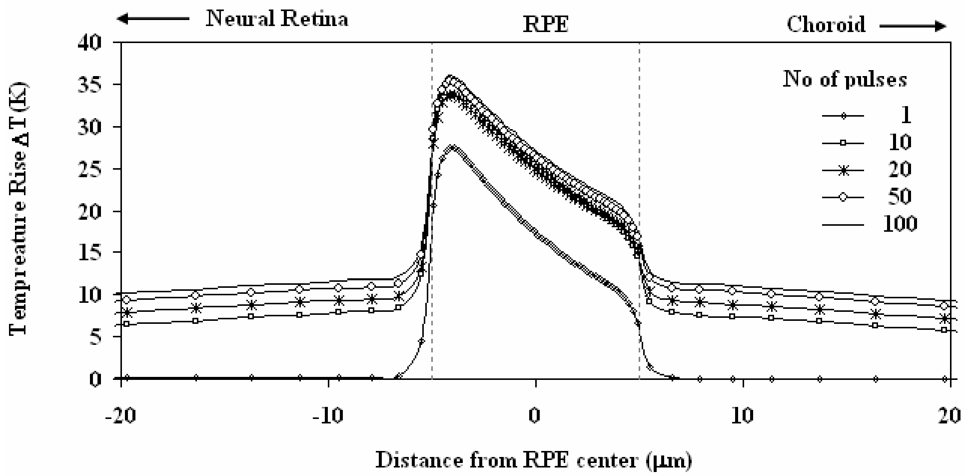

Figure 8a: Temperature rise for 2 μs pulses

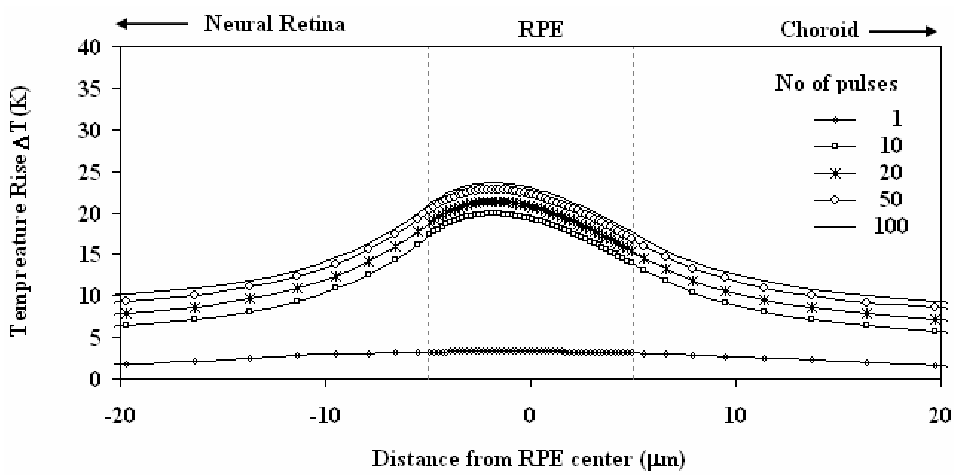

Figure 8b: Temperature rise for 200 μs pulses

Figures 8a and 8b show the temperature traces after different number of pulse exposures for 2 and 200 μs respectively. For all pulse width the maximum temperature augmentation occurs within 10 pulses and only moderate temperature rise occurs between 10^{th} and 100^{th} pulses. The value of temperature rise $\frac{\Delta T_{RPE}}{\Delta T_{neural}}$ after single 200 μs pulse is 1.12 which shows that the spreading of thermal energy to the neural retina takes place significantly within 200 μs. For semi infinite solid with characteristic length of 5 μm and thermal diffusivity of 1.49 x 10^{-7} m^2/s the diffusion time is ~ 160 μs. For 200 μs laser, since the duration is in the order of diffusion time significant conduction occurs. Hence, for better selectivity the pulse duration should be as short as possible.

4. CONCLUSION

The laser tissue thermal interaction during photocoagulation is analyzed by calculating temperature rise for various laser parameters. *Wavelength:* The green wavelength laser is found to be most selective for short pulsed laser as it has high absorption in RPE while red laser produces selective temperature rise for long exposure continuous wave. *Profile:* In comparison to top-hat profile the Gaussian laser profile is most effective in localizing the damage along the radial direction and it reduces the damage to neural retina as it requires ~ 50% less energy for ultra fast lasers than that of top hat profile. *Pulse Width*: The pulse duration is the critical factor and it should be in the order of μs to produce selective retinal photocoagulation.

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