Comsol Multiphysics as a Tool for Reducing Animals in Biomedical Research: an Application in Dermatology

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Abstract: In biomedical research the use of animal models gives rise to several ethical problems. Comsol Multiphysics may be used as a non-animal technique, very useful in overcoming all these concerns. In this presentation a particular application in dermatology is shown. Bioheat equation mode and diffusion approximation were used to design a theoretical model of blue LED light interaction with an abraded rat skin. The geometrical model was used to test the hypothesis underlying the design of a photocoagulator device, to be used as a support tool in laser rejuvenation treatment of facial skin. The use of Comsol enabled us to replace animal tests with the results of a predictive model.

Keywords: bioheat equation, diffusion approximation, LED, dermatology, animal models.

1. Introduction

Research in biomedical fields is necessarily related to the use of animals for testing new technologies prior their applications in human subjects. There are several ethical problems arising from the tests on animals: for these reasons since the end of the fifties of the last century, two British scientists, William Russell and Rex Burch, urged all animal researchers to follow good practices in animal experimentation [1]. In particular they indicated three important concepts, that are now named the "three R's" rules: Replacement, Reduction, Refinement. Comsol Multiphysics may be used as a non-animal technique, included in the first R, the Replacement. In this manuscript we present an application of this concept: the use of Comsol Multiphysics as a simple tool in the design of a light source inducing selective photocoagulation of skin superficial abrasions.

The problem is to develop a compact, low cost device to induce a selective photothermal effect in the blood content of an abraded skin. The system has to be used as a support tool of laser rejuvenation technique of facial skin, where a CO_2 or an erbium laser are used for the photoablation of the superficial layers of the skin [2]. In doing this, the main problem is the bleeding of the dermal capillaries: when bleeding occurs, the blood content may shield the infrared laser radiation, and thus the surgeon needs to stop the treatment for several minutes, till coagulation by local pressure of capillaries is reached. The result is loss of time and, mainly, a not satisfactory aesthetic effect due to scar formation in the bleeding area. A solution to this practical problem is to induce a photothermal effect localized in the blood content, so as to induce a temperature enhancement only in the bleeding capillaries, enabling rapid coagulation of the treated area without collateral thermal effects to the surroundings. This goal is reached by the use of a blue high power LED, emitting at around 400 nm, where the main absorption peak of haemoglobin is located. The light absorption is converted into heat and the coagulation effect is induced only in the directly irradiated bloody area.

Three sources are commercially available in this wavelength range (mod. LED405-66-60, LED435-66-60, LED470-4x4PC66, Roithner LaserTechnik GmbH, Vienna, Austria): they emit at 405 nm, 435 nm, 470 nm, with a typical total radiative power output of 300 mW, 720 mW, 600 mW, respectively. We thus tested the hypothesis of selective photothermal effect in a PDE model of the problem and optimized the light source parameters by the use of Comsol Multiphysics, instead of the use of animal models.

In figure 1(a) we represented the geometrical model of our problem, with capillaries of different diameters; in figure 1(b) another geometrical problem is shown: it was used to study the LED-induced thermal effects in the real conditions (a uniform blood layer on a dermis subdomain).

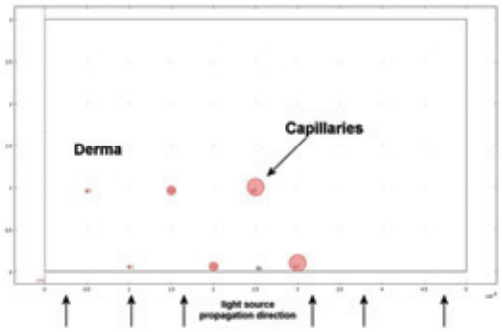

Figure 1(a). A schematic of the problem for testing selectivity absorption in the blood content

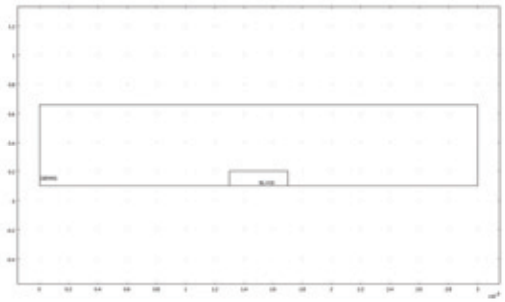

Figure 1(b). A schematic of the problem for testing thermal effects in the blood content of an abraded skin

2. Use of COMSOL Multiphysics

We used the Diffusion and Bioheat Equation Modes to describe light propagation into a biotissue and the induced thermal effects, respectively [3, 4]. The model was drawn in a bi-dimensional geometry with axial symmetry. The analysis was time dependent. The light propagation in the tissue was studied in the diffusion approximation:

$$\frac{\partial\Phi(x,y,t)}{\partial t}-\nabla\left(\alpha^n\nabla\Phi(x,y,t)\right)=-c_n\mu_a^n\Phi(x,y,t)$$

$$\alpha^n=\frac{c_n}{3\left(\mu_a^n+(1-g)\mu_s^n\right)}$$

where $\mu_a{}^n$ and $\mu_s{}^n$ (1/m) are the n-th subdomain (blood, dermis) absorption and scattering coefficient respectively, g is the optical anisotropy factor, c_n (m/s) is the light velocity in the n-th medium; $\Phi(x,y,t)$ is the photon number per area and time. The light source was imposed as a boundary condition, at z=0, while photon flux outwards the boundaries at z= 0.003 and r = 0.005 was imposed. The temperature enhancement was described by the bio-heat equation:

$$\rho_n C_n\frac{\partial T(x,y,t)}{\partial t}-\nabla\left(k^n\nabla T\right)=\rho_b C_b\omega_b\left(T_b-T\right)+Q_{met}+Q_{ext}$$

where the external heat source was set as:

$$Q_{ext}=\mu_a^n\Phi(x,y,t)h_p\nu$$

h_p is the Planck constant and ν (1/s) is the light source frequency (i.e. the light velocity in the subdomain/the light wavelength).

Heat flux was set as a boundary condition at z= 0.003 and r = 0.005, while thermal insulation was imposed at z = 0, because we supposed that the light source was in close contact with the tissue. In both the equations the optical parameters depend on the tissue characteristics and on the wavelength of the light source and were taken from literature [5, 6, 7]. Also the thermal parameters were taken from literature [8, 9, 10].

3. Expected Results

With the geometry described in Figure 1 (a) we tested the hypothesis of selective absorption of the LED light @ 405 nm, 435 nm and 470 nm. We observed that the 405 nm is effectively mainly absorbed by the blood content, localized in the capillaries: the result is a temperature enhancement mainly in the blood vessels (figure 2, figure 3 and figure 4).

We then used the model of figure 1(b) to optimize the LED source parameters and to exploit different geometrical configurations of the device. The expected temperature dynamics in a superficial blood layer are shown in figure 5.

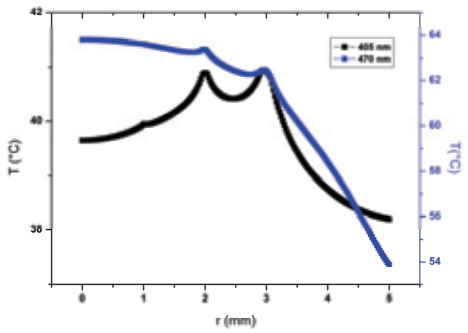

Figure 2. Selectivity of the treatment: the temperature rise is well confined in the capillaries @405 nm, while quasi homogeneous temperature distribution is expected at 470 nm (treatment time: 30s).

In order to induce a photocoagulation result, it is important to induce a temperature above the coagulation temperature threshold (i.e. ~ 55-60°C for protein coagulation in blood) [11]. To avoid thermal damage to the surrounding tissues it is important that this temperature value is reached only in the target tissue. The model results evidenced that the 405 nm induced a higher temperature enhancement inside the blood content. By the use of an irradiation time of about 30 s and putting the LED source in close contact with the abraded skin, we could reach the necessary photocoagulation temperature in the blood layer, without inducing irreversible thermal damage in the deep tissue.

4. Conclusions

Comsol Multiphysics was used to design preliminary tests and optimization of a device for selective photocoagulation of skin abrasions. The results were used to test the best light source and configuration design of a LED based photocoagulator, to be used as a support tool in laser facial skin treatments. The use of this computer based technology enabled to reduce the number of animals in experimental and preclinical research and to test a device that was safe for the use in living animals and in human subjects.

5. References

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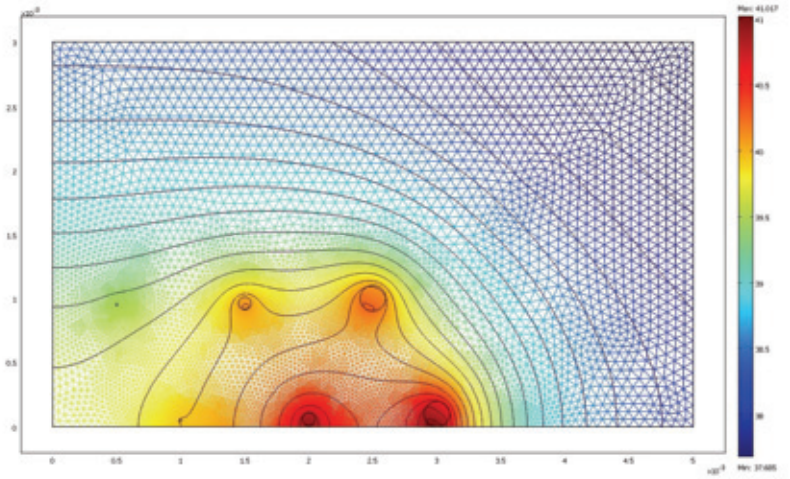

Figure 3. Temperature distribution inside the dermis and capillaries, after 30 s irradiation of a 405 nm LED, put in close contact with an abraded melaninless rat skin model.

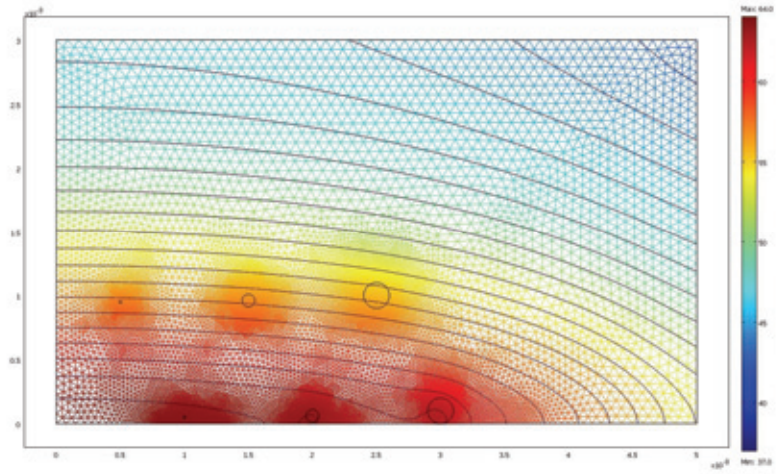

Figure 4. Temperature distribution inside the dermis and capillaries, after 30 s irradiation of a 475 nm LED, put in close contact with abraded melaninless rat skin model.

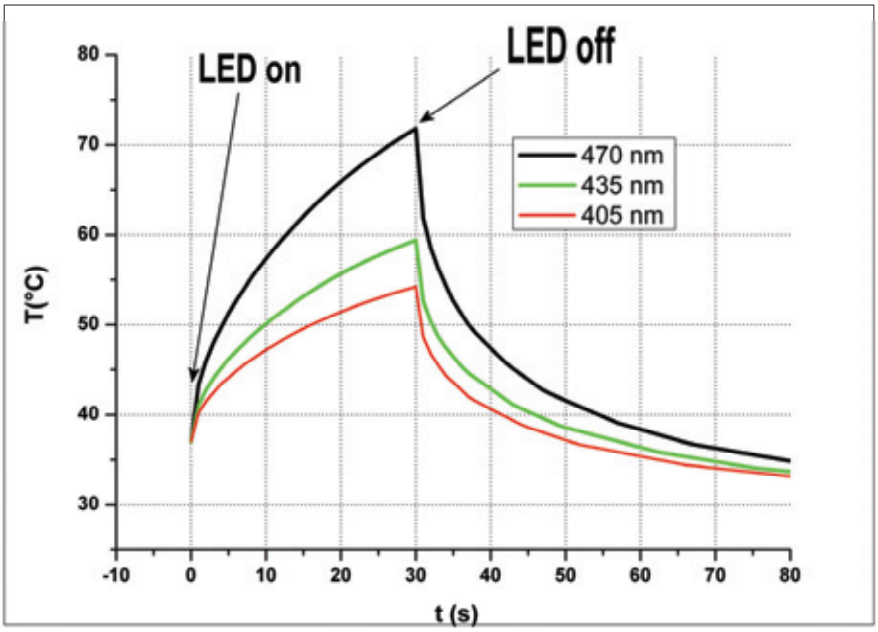

Figure 5. Temperature dynamics for three different wavelength during and soon after LED irradiation of a skin abrasion (at z=0)