Journal of
Lasers
in Medical Sciences

J Lasers Med Sci 2024;15:e63

Original Article

http://journals.sbmu.ac.ir/jlms

doi 10.34172/jlms.2024.63

CO2 Fractional Laser Induced Skin Micro-Tunnel Thermal Damage Patterns: A Simulation Study

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Received: July 17, 2024
Accepted: November 6, 2024
ePublished: December 21, 2024

Abstract

Introduction: The heat distribution and the resulting thermal damage pattern following the light absorption in tissue can be used for treatment optimization. Besides rejuvenating effects, CO2 fractional-induced microtunnels have recently become a tool for drug delivery. To minimize the unwanted thermal damage in this latter use and to optimize the laser program, we simulated the heat distribution and thermal damage models of CO2 fractional lasers of different sizes, pulse durations, and powers.

Methods: COMSOL software is used for simulation. The skin is modeled as three homogeneous layers of epidermis/dermis/hypodermis. The photothermal coefficient of the tissue model and the irradiation laser system (CO2, 10600 nm) are defined as 0.07 mm spot size, 10, 12 and 15 W power range, and 0.5, 10 and 15 ms pulse durations, respectively.

Results: Our results show that the power of 10 W with different time pulses creates a better micro-tunnel in the tissue while preventing unwanted injuries. At a power higher than 15 W and 5 pulses, the tissue will be damaged inconsiderably. The fractional laser creates heat only at the desired point of the treatment, and this heat is absorbed through the tissue, and micro-tunnels in it form the tissue. Also, 10 W power with a shorter pulse duration did not have a good effect on the tissue. Instead, by increasing the pulse duration, less damage to the surroundings resulted.

Conclusion: Due to the absorbed laser light in tissue and the creation of heat, skin damage as micro-tunnels are caused. The greater distance between the created micro-tunnels indicates better tissue preservation. Also, COMSOL seems to be promising software for preclinical investigations and optimizing laser treatment plans.

Keywords: Simulation; COMSOL; Thermal distribution; Thermal damage; Fractional laser.

Introduction

Lasers have been used successfully in medicine as a safe and effective method since they were approved by the FDA in 1995.[1] To achieve effective thermal effects by laser therapy and prevent damage to neighboring tissues, the correct selection of the radiation parameters of the laser is essential for sufficient thermal damage to the tissue target.[2,3] According to the original selective photothermolysis theory, proper wavelength, fluence, and pulse duration should be selected for the optimized treatment response.[4-6]

Laser fractional photothermolysis (LFP) seems to be a novel approach based on selective photothermolysis whereby controlled width, depth, and density of the micro-thermal zones are made. The concept of FP was proposed to address the inadequacies of conventional ablative and non-ablative modalities. The term fractional might be correlated with source energy that delivers high fluence within a small spot size, creating pixels of damage while sparing the surrounding epidermis and dermis leading to fast repair.[7] Laser skin resurfacing (LSR) is one of the most influential developments in cosmetic dermatology. LSR seems to be an art and science in this field.[8] For the last two decades, LSR has evolved from a traditional to a Fractional Non-ablative method. The non-ablative LSR technique targets chromophores in the epidermis and dermis, producing dermal thermal lesions without damaging the epidermis. Fractional CO2 lasers for LSR create microscopic tunnels in the skin. Although non-ablative laser therapy has been shown to be very safe, with less recovery time and fewer complications, its efficacy might not be optimized for a special case.[9] This micro-tunnel allows dermatologists to control the width, spacing and depth of these bars. This selective skin care promotes healing and increases comfort.[8-10] Skin damage using a laser is controllable and the skin responds to a predictable repair process.

Modeling of the thermal damage alterations for the fractional laser with various pulse durations and energy densities may be useful for understanding how to choose

Please cite this article as follows: Shorakaie A, Nahvifard E, Shirkavand A, Ataie Fashtami L, Mohajerani E. CO2 fractional laser induced skin micro-tunnel thermal damage patterns: a simulation study. *J Lasers Med Sci.* 2024;15:e63. doi:10.34172/jlms.2024.63

the right irradiation parameters. In addition, it is crucial to find out tissue optics' principles, to increase the efficiency of the process of light delivery to the tissue, heat generation and its subsequent thermal damage.[11] The best laser treatment may be proposed based on modeling analysis of light propagation in human skin using the thermal and optical properties of tissue components. Various approaches have been developed to simulate laser-tissue interactions, including diffusion solutions.

In this simulation, we can model the propagation of light in different tissue layers and calculate the distribution of absorbed light and generated heat in the tissue during laser irradiation. There are some numerical and modeling studies which have proposed mathematical models for simulating the effect of laser and tissue parameter variations on the thermal effects of ablative and non-ablative treatment scenarios.[2,3,11-14] The aim of our study was to investigate the effects of changes in pulse duration and power of the CO2 (10 600 nm) fractional laser on skin thermal distribution and thermal damage patterns using Multiphysics COMSOL software. This study aimed to explore the optimized parameters of the laser to achieve better treatment results and reduced side effects.

Materials and Methods

Model of Tissue

Three layers of the skin, consisting of the epidermis, dermis, and subdermis, are selected to simulate the heat distribution and thermal damage at the target. The modeling is based on existing knowledge of the differences in optical properties of the skin, each determined by criteria and standards according to various factors such as thickness, location, shape, refractive index, anisotropy factor, content, absorption and scattering coefficients, and thermal energy.[2,15]

We assumed a smooth, semi-infinite three-layer skin surface geometry, which consisted of a top 0.1-mm-thick epidermis, 1-mm-thick dermis, and a 5-mm overlying fat layer.[2,3,16-20]

The tissue volume was decomposed into a 3D Cartesian grid, where the volumetric heat generation and thermal damage were calculated.[3] The ablation area at the target was viewed as a columnar microtunnel. This geometry is shown in Figure 1.

Physical Properties and Simulation

We used COMSOL Multiphysics (version 6). The validation of the software was done based on the reference which was a 3-D temperature distribution simulation study had been compared by experimental data. In other words, we selected a previously evaluated modeling study for assessing the result of our data at the first step.[21] At this reference, the distribution of the 805 nm laser energy which came with a diameter of 1.5 cm was modeled. In addition to the light energy distribution affected by biological tissue, ICG in tissue modeling was implemented to contribute some more laser light absorption to the modeled tumor.[21]

The Bioheat module program calculates and displays the heat distribution and thermal damage patterns in biological tissues during superficial and interstitial thermal treatments. The software consists of three main components, which will be discussed below. The structure of COMSOL combines these components through an algorithm to calculate the energy and heat distribution of the laser radiation in addition to the thermal damage.[19,20]

The propagation of the laser light in biological tissue and its transformation into thermal energy due to the absorption of the photons is governed by optical properties such as the absorption coefficient μ_a(mm^{-1}), the scattering coefficient μ_s(mm^{-1}), the anisotropy factor g, and the refractive index n.[2,3,17-25] Here, it was assumed that the modeled skin has a uniform refractive index, and hence, there is no refraction or reflection as light transmits from layers. Table 1 summarizes the optical properties of the skin model in this study.

Calculation of the Heat Conduction

In COMSOL Multiphysics , the heat deposition is individually calculated for each voxel after each time interval. The temperature rise $\Delta T(x,t,z)$ (in Celsius

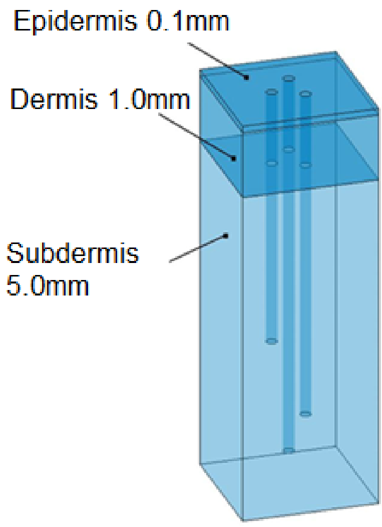

Figure 1. The 3D-Geometry of the Modeled Three-Layer Skin Containing Epidermis, Dermis and Sub-dermis

Table 1. Optical Properties of the Modeled Skin Layers in the Infrared Wavelength Range

	Thickness (mm)	μ_a (mm^{-1})	μ_s (mm^{-1})	g	n
Epidermis	0.1	0.007	1.66	0.8	1.56
Dermis	1	0.013	16.3	0.9	1.4
Subdermis	5	0.0125	10.8	0.9	1.45

μ_a: Absorption coefficient; μ_s: Scattering coefficient; g: Anisotropy factor; n: real refractive index.

degree or Kevin degree) in a special voxel volume of the tissue V_{voxel} is determined by the amount of converted energy $\Delta E(x,t,z)$:

$$\Delta T(x,y,z) = \frac{\Delta E(x,y,z)}{\rho . C_p . V_{voxel}} \tag{1}$$

Where ρ and C_p, the thermal properties of the tissue, are density and specific heat capacity, respectively.

The basis of heat transfer calculations is a numerical solution of the corresponding differential equation which is solved using the Finite Differences Elements (FDM) method. All the calculations are run automatically by the software. From physical references, the thermal properties of tissue can be calculated approximately depending on the water content of the tissue (w), in which w = 50% for the epidermis, w = 75% for the dermis, and approximately 10% for subdermal fat (18, 19). The calculated thermal coefficients based on the water content formulation[2] are presented in Table 2. The surface and the bottom temperatures of the skin model were set at 30 °C and 37 °C, respectively.

Tissue Damage Formulation

While the temperature rises above 60 °C, undesired thermal effects like coagulation and cell death happen immediately or after some time.[18] As an approximation, the temperature behavior of the cells can be described by a damage integral $\Omega(T,t)$ based on the Arrhenius formulae. This integral calculates the state of protein denaturation as a rate equation[7]:

$$\Omega(T,t) = A \int_{t_i}^{t_f} \exp(\frac{-E}{RT})dt \tag{2}$$

This integral defines the extent of tissue damage. If thermal damage is greater than 63%, the skin tissue is considered undamaged.[8]

In this integral, R is the universal gas constant $(8.314 \, {}^{J}\!/_{mol.K})$, t is the irradiation time, and A and E are the Arrhenius constants and the values of $(3.1 \times 10^{98}\ s^{-1})$ and $(6.3 \times 10^5\ J/mol)$, respectively.[2,18,20]

Laser Systems

In this study, we modeled the SmartXide Deka CO2 laser systems (Germany). One system had a 0.07 mm spot size, a power of (10, 12, and 15 W) and pulse durations of 0.5, 10, and 15 ms. we modeled the laser beam in terms of the number of pulses.[1-5] We also assumed that the laser light was perpendicular to the skin.

Table 2. Thermal Properties of Various Skin Components Used in Our Study

Components	$\kappa({}^{W}\!/_{cmK})$	$\rho({}^{g}\!/_{cm^3})$	$C_P({}^{J}\!/_{gK})$
Epidermis	0.0034	1.1497	2.789
Dermis	0.0048	1.075	3.488
Subdermis	0.00113	1.27	1.8143

k: Thermal conductivity
P: Density
Cp: Specific heat capacity

Results

Validation Results

To validate the applied software, the problem conditions of reference[21] for heat production and temperature changes were our input. The result of our COMSOL Multiphysics software is presented in Figure 2. The obtained result depicts our outcome has a trend similar to experimental results obtained in the modeled reference.[21]

Heat Change Due to Various Parameters

In the first part, we consider one pulse, a power of 12 W, and changed the pulse width (0.5, 10, and 15 ms) for investigating the effect of heat production and temperature rise. The results presented in Figure 3 are for temperature changes along the y-axis.

For a constant power of 12 W and one pulse, we changed the pulse duration (0.5, 10 and 15 seconds) for the effect of the pulse duration on the heat distribution modeling. In this section, temperature changes were checked radially.

As shown in Figure 4, in the axial orientation of the modeled tissue, the tissue heat change at a pulse duration of 0.5 ms seems not to be considerable in comparison with the pulse durations of 10 ms, and with a pulse duration of 15 ms, there is a rise in temperature. Referring to this information, a pulse duration as long as 15 ms seems more appropriate to lead to the thermal damage zone in the tissue. Data quantities alongside the z-axis, by the depth of 1.5 mm which is considered in the third layer of the modeled tissue, showed that with a pulse duration of 15 ms in comparison with 0.5 ms, causes more increase in temperature as they obtained 96 °C, and 55 °C respectively.

We also set the pulse duration of 15 ms for one pulse and then changed the power for 10 and 12 and 15 W. The temperature changes in the y-axis of the modeled tissue are presented in Figure 5.

Tissue Thermal Damage Due to Various Parameters

After all, the effect of various parameters was tested on the thermal damage pattern of tissue using simulations. In thermal damage modeling graphs, the color bar of the graphs indicates the scale of tissue damage from 0 to 100% which 100% indicates complete irreversible thermal damage.

To simulate the pulse duration effect on thermal damage, the number of pulses and power were kept constant, while the pulse duration of the pulse was changed to 5, 10, and 15 ms (Figure 6). We used the power of 12 W and some pulse durations of 5, 10 and 15 ms.

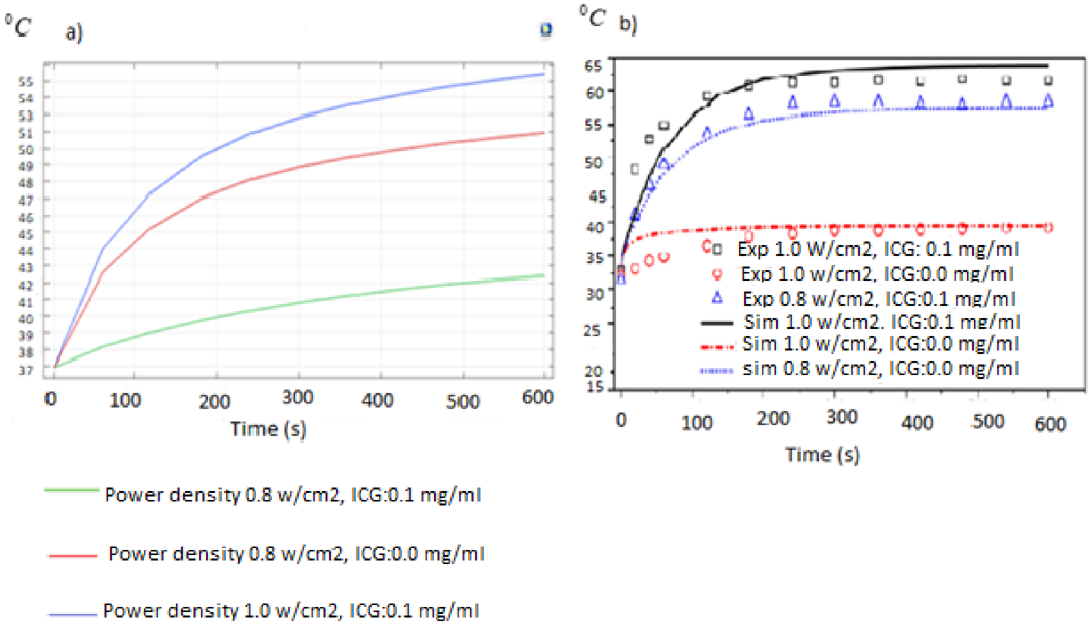

Figure 2. Comparison of the temperature in Celsius Degree calculated in (a) our simulated and (b) reference results[21]

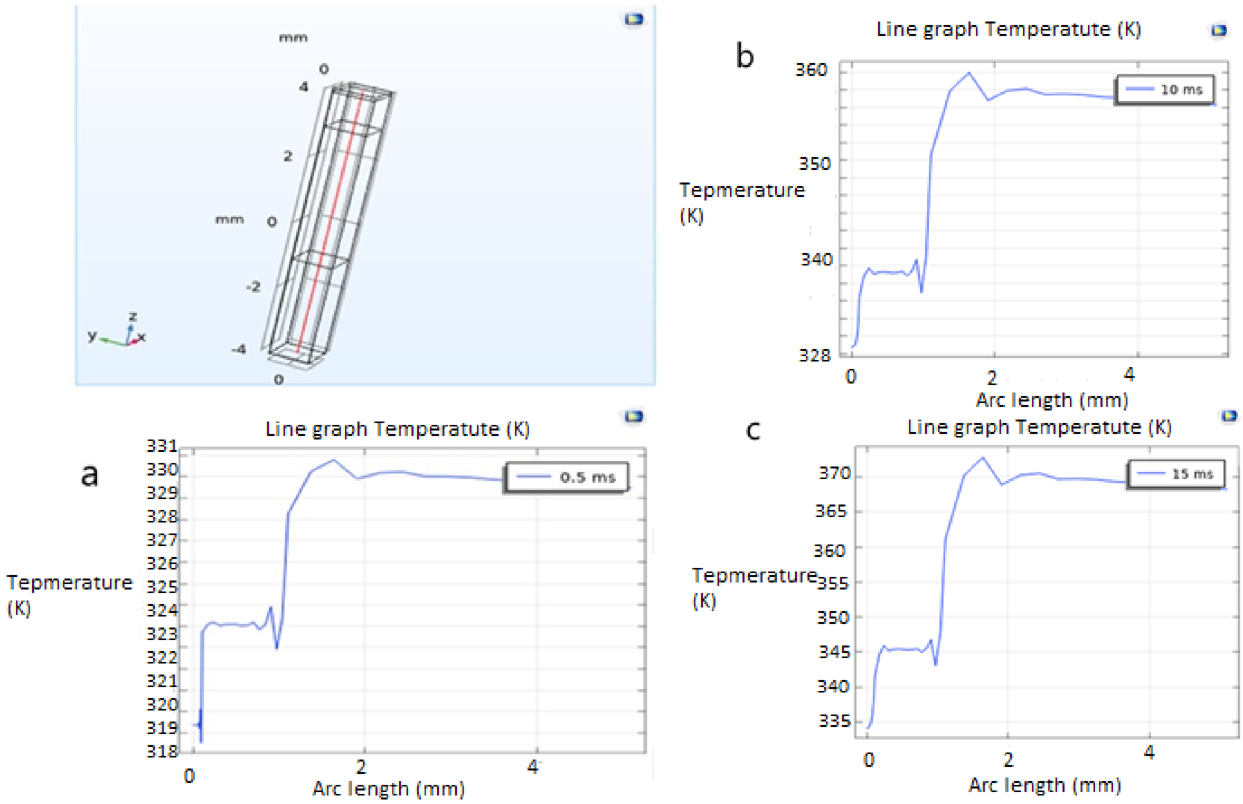

Figure 3. Temperature Changes in the Y-Axis with a Power of 12 W, One Pulse Number for Different Pulse Durations: a) 0.5 ms, b) 10 ms c)15 ms

As shown in Figure 6, the diameter and depth of the irreversible thermal damage of the cones were quantitatively calculated. Based on the quantified data of the thermal damage patterns, the pulse durations of 5, 10 and 15 ms caused different tissue damaged zones with diameters of 0.21, 0.24, and 0.27 mm and depths of 0.32, 0.54, and 0.92 mm, respectively. This achievement indicates that the longer the pulse duration, the larger the volume of damaged micro-tunnels. The thermal damage patterns of the micro-tunnel due to the changes of power

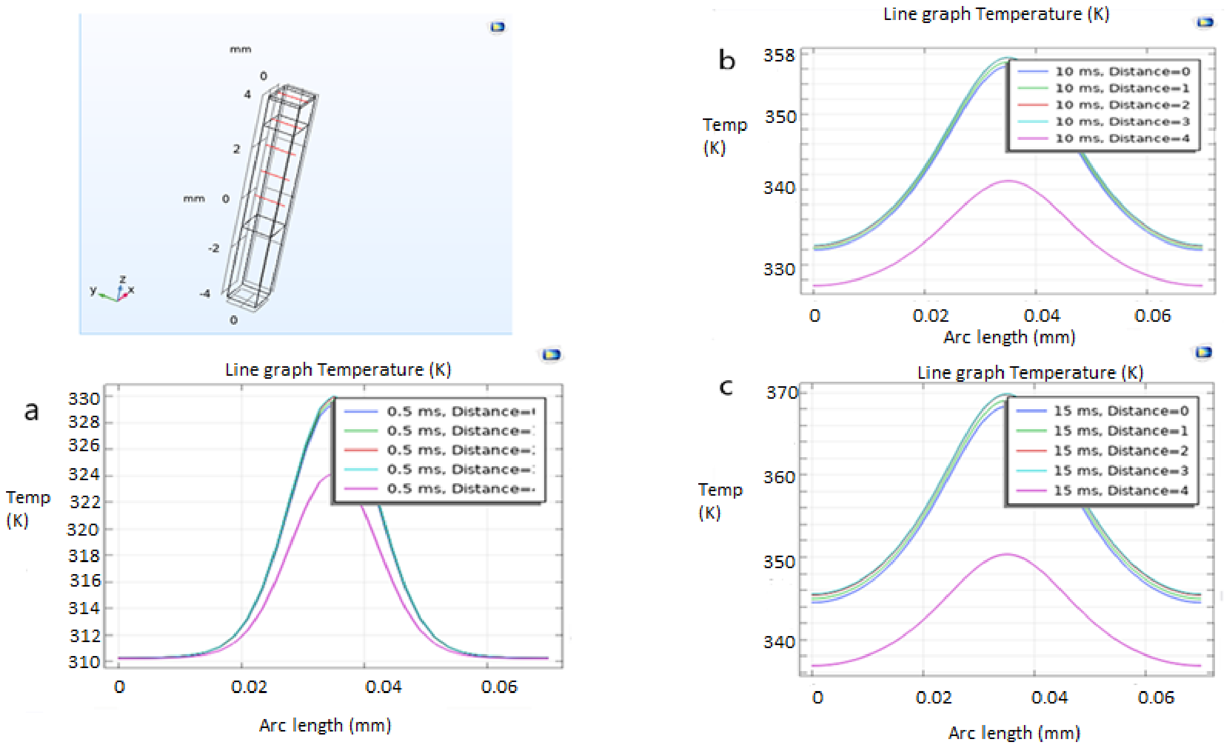

Figure 4. Temperature Changes Through the Radial Axis of the Tissue (X-Y Axis or Arc Length) Distances from the Surface by the Power of 12 W, One Pulse, and Different Pulse Durations: a) 0.5, b) 10, c) 15 ms

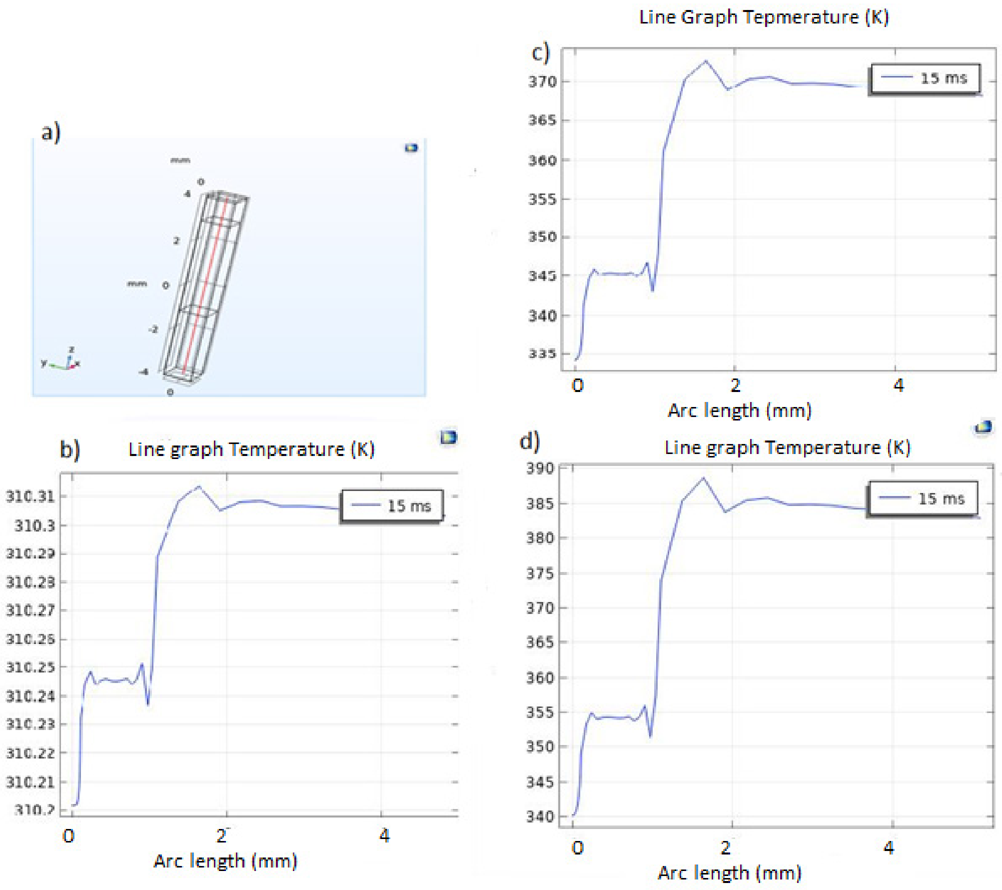

Figure 5. Temperature Changes in the Y-Axis with a Pulse Duration of 15 ms, One Pulse Number for Different Powers: a) 10 W, b) 12 W, c)15 W

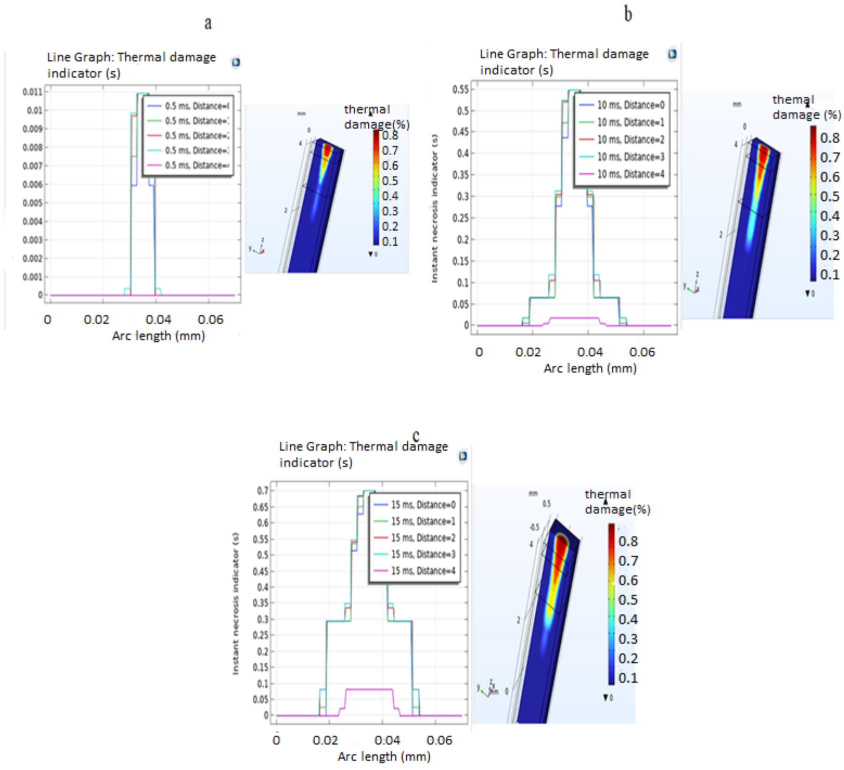

Figure 6. Tissue Damage Versus Pulse Duration for the Power of 12 W, One Pulse, and Pulse Duration of: (a) 5, (b) 10, and (c) 15 ms

for a constant pulse duration of 15 ms and various powers of 10, 12 and 15 W are depicted in Figure 7.

Figure 7 presents that using more the power, the volume of created microzones due to the thermal damage becomes higher.

Based on the quantitative information of the damaged cones by changing the pulse numbers in Figure 8, the diameters of the micro-tunnel damaged volumes for different pulse numbers of 1, 3 and 5 were estimated at 0.24, 0.27, and 0.3 mm while their depths were calculated at 0.54, 1.13, and 1.16 mm, respectively. It can be deduced that by increasing the pulse number the damaged zone volume increases.

Discussion

With the growing trend in medical laser applications, various medical practices take advantage of physical models to ensure safety and optimize the side effects for a successful treatment. Fundamental laser interactions with biological tissues and thermal effects are of special importance for a better understanding of heat transfer in the tissues following light irradiation and absorption, which leads to the destruction of the tissue.[22-25]

This research was conducted to model the pattern of thermal damage due to the heat distribution in the skin tissue and to investigate the effect of changing laser radiation parameters such as pulse duration and power to determine optimal radiation parameters for the treatment protocol. The simulations were done for a typical fractional CO2 laser system with a radiation wavelength of 10 600 nm.

For the power effect on the heat distribution and thermal damage, the highest selected power of 15 W for modeling produces more heat compared to 10 W, and hence, its thermal damage in the tissue can be achieved with a greater temperature rise in the tissue and more penetration depth of micro-tunnels (Figures 5 and 7). As it can be quantitatively achieved, the power of 15 W causes more damage and heat in radial lines than the powers of 10 W and 12 W.

Based on the reference, the histological information has shown that the CO2 fractional laser generates thermal damage patterns in the form of skin micro-tunnels surrounded by undamaged tissue. The ex-vivo human skin thermal damage patterns were confirmed as cones, which agrees with the modeled thermal damage patterns in this study.[26]

In recent years, the concept of tissue thermal damage time has been presented as the optimal time for tissue thermal damage and preservation of dermis and epidermis tissues. The results of this research showed that with different pulse durations, the depth of penetration increased by increasing the power. Also, due to delivering more energy by using more pulsed of laser, it causes more pain in the tissue. Hence, the patient's tolerance threshold is lost in this case; Then, for reducing the pain for applying a greater number of pulses, the power might be selected less. More pain in the tissue and the patient's tolerance

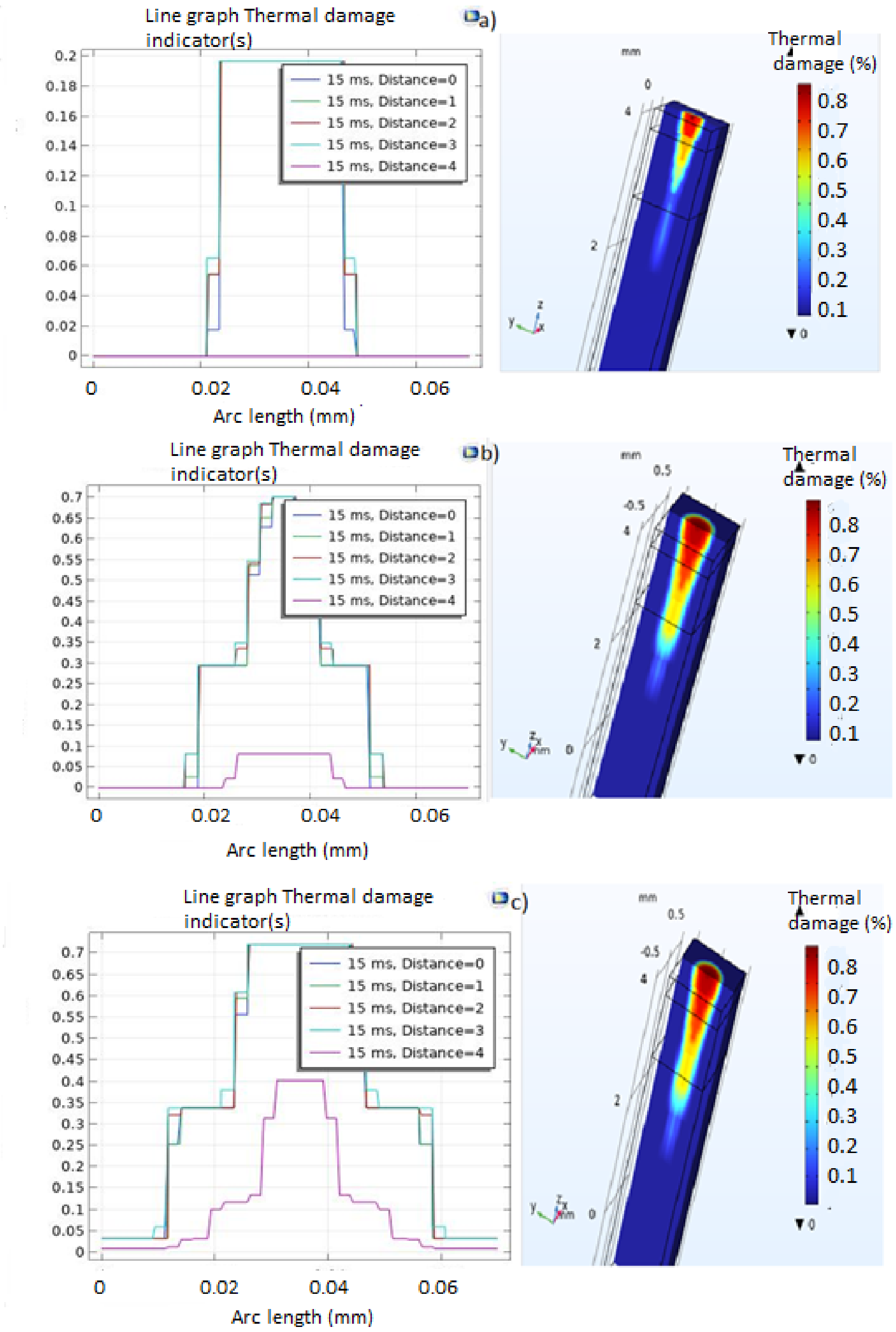

Figure 7. Tissue Damage Versus Power for the Pulse Duration of 15 ms, One Pulse, and Power of (a) 10, (b) 12, and (c) 15 W

threshold is lost in this case; therefore, for reducing this pain in a higher number of pulses, the power might be selected less.

Again, by an increase in the laser power, increased heat and tissue thermal damage resulted in tissue with the highest tested power of 15 W. This shows a greater damaged depth achieved in targeted tissues that can lead to the loss of the patient's tolerance threshold due to the severity of thermal damage.

Based on the results of this modeling study, we could reach applicable quantitative information regarding the diameter and depth of damaged micro-tunnels' volume by changing the laser irradiation parameters like power, pulse duration, or pulse numbers. This information sheds light on the designing of preferable micro-tunnel cones for drug delivery or rejuvenation by treatment modeling using the COMSOL Multiphysics software more than providing a skin biopsy and investigating the histology,

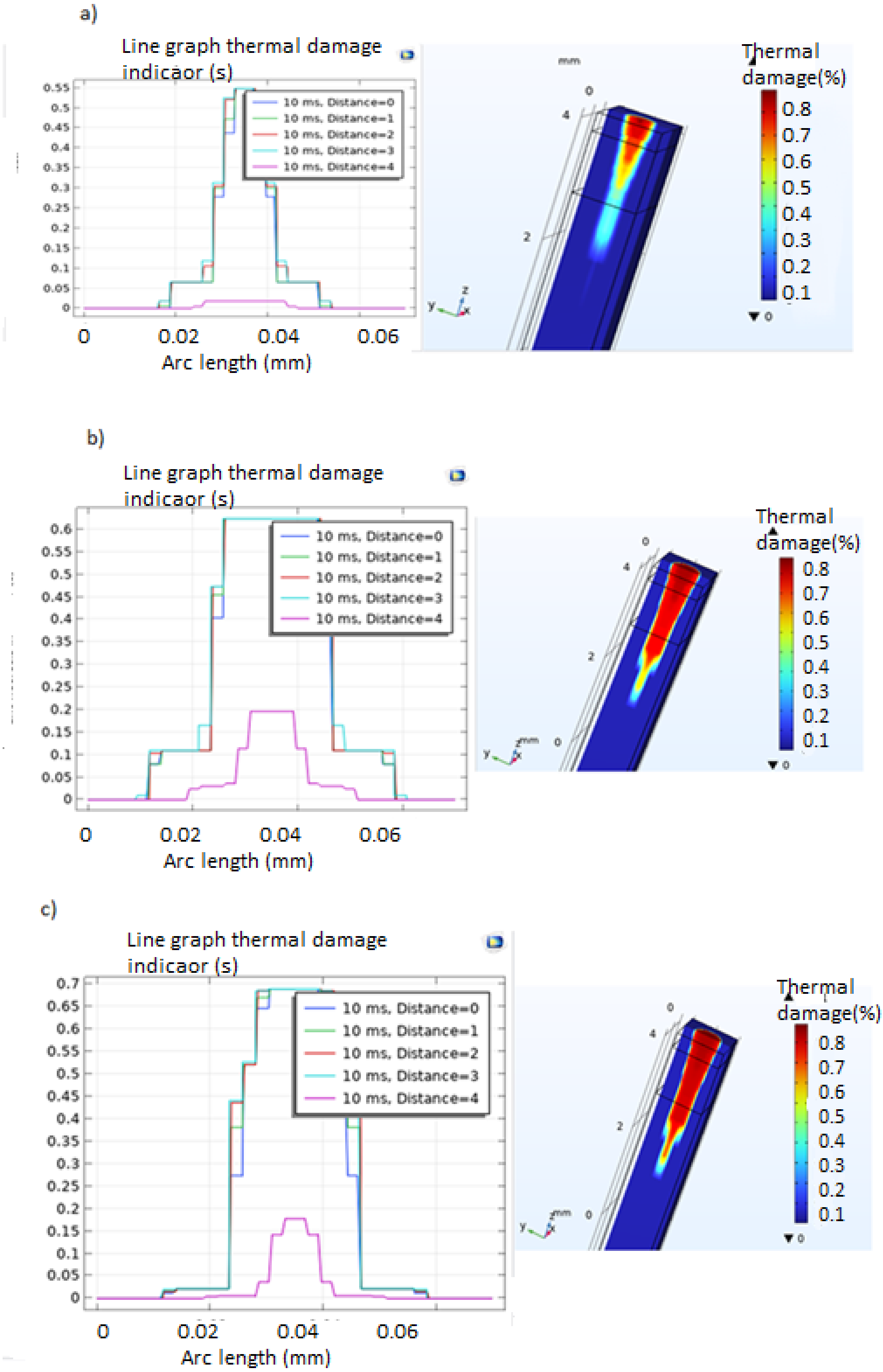

Figure 8. Tissue Damage Versus Pulse Numbers for the Power of 12 W, Pulse Duration of 10 ms, and Number of Pulses: (a) 1, (b) 3, and (c) 5

especially in cosmetic approaches which are undesirable. By doing this, we can plan for creating more suitable micro-tunnels in the skin layers by optimizing laser parameters based on the clinician's goals.

In conclusion, in case of the need for deeper micro-tunnels, for drug delivery and other purposes, a higher number of pulses, that is, 3 and more, might be more applicable. To prevent thermal changes, the more we increase the distance between the irradiated points, the less tissue damage is caused.

Furthermore, the more the number of points, the more energy would be transmitted.

This modeling suffers from some limitations. As a pilot study, we initiated the simulations for a selected laser CO2 fractional laser. In addition, the tissue model might be a standard referral skin model with defined optothermal parameters. However, more extended simulation research is recommended for more detailed understanding. Similar simulations can be done for other types of skin based on Fitzpatrick's classification. In addition, for other lasers like the Er: glass laser (1540 nm), similar modeling might shed light on the thermal damage effects and treatment optimizations. To achieve this goal, we aim to do more simulation studies for a more in-depth understanding. In this study, we applied a simplified three-layer skin model; while this is a common approach, it is considered to be somehow different from real human skin in terms of heterogeneity and optical properties. This is also considered a limitation, so it might be replaced by more realistic tissue models in future simulations.

Combining photothermal and chemical dynamics modules in COMSOL Multiphysics, it might be possible to evaluate the state of dynamic distribution and drug kinetics in fractional laser micro-tunnels.

Conclusion

A fractional laser is a promising approach for cosmetic and drug delivery goals. Modeling and theoretical study of heat distribution in tissues seems to be helpful for better understanding. In this study, COMSOL software was used for modeling. The bio-heat module of the software seems to be promising for theoretical preclinical studies in thermal damage evaluation of micro-tunnels. Such simulation studies might offer clinicians a better understanding of the applied treatment plan.

Acknowledgments

The authors would like to thank Danesh Skin and Laser Clinic for their kind help in providing the information of the CO2 fractional laser system.

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Validation: Afshan Shirkavand, Ezeddin Mohajerani.
Visualization: Ali Shorakaie.
Writing–original draft: Afshan Shirkavand, Ali Shorakaie.
Writing–review & editing: Leila Ataie Fashtami, Elaheh Nahvifard, Ezeddin Mohajerani.

Competing Interests

None declared.

Ethical Approval

This was just a theoretical numerical modeling with no need of ethical code.

Funding

None.

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