BEE/MAE 453 Final Design Project Report

Photothermolysis Treatment of Acne
and the Effects on Healthy Surrounding Tissue

Karen Chin
Wilson Huang
David Peng
Jennifer Shum

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EXECUTIVE SUMMARY

Acne vulgaris, mostly known as pimple, is common among humans in various ages. Many treatments are available to treat acnes. With the current most effective treatment of ace, isotretinoin, having side effects, photothermolysis therapy, a process that uses absorption of light to produce thermal damages, offers a new solution for acne or skin scar removals. Many different types of lasers are available for this photothermolysis procedure. For the simulation of this study, we choose to use the 1450nm laser to model the heat transfer process for the skin layers and the acne region and examine the effects of the whole procedure to the acne region and the surrounding healthy skin tissues. The model of the acne treatment involves a total of five steps of cooling process using low temperature refrigerant and four steps of heating process using the1450nm laser. To simplify the complexity of the skin tissues for this model, we use 2-D axis symmetry for the skin layers, including epidermis, sebaceous glands (acne region), and dermis, and each layer's thickness is followed as closely as possible to human skin surfaces to make the model more realistic. With the diffusion approximation finite element analysis, we are able to evaluate the temperature profiles in different skin layers and the target acne region and gain insights on the potential acne and healthy skin thermal damages with the 1450nm laser.

Key words: photothermolysis, acne, skin

INTRODUCTION AND DESIGN OBJECTIVES

Acne vulgaris is a highly prevalent skin disorder that affects all ages to varying degrees. The majority of people affected are teenagers, and the consequences include physical and emotional scarring. The cause of acne vulgaris is unknown but it is characterized as a follicular disorder. The follicular opening, or pore, is obstructed, causing an increase in sebum (oil) production by the sebaceous glands (Figure 1). The sebum, which normally drains to the surface, is blocked, causing the proliferation of the bacteria, *Propionibacterium acnes*. This leads to inflammation and many other symptoms associated with *acne vulgaris*. [Lloyd, et. al]

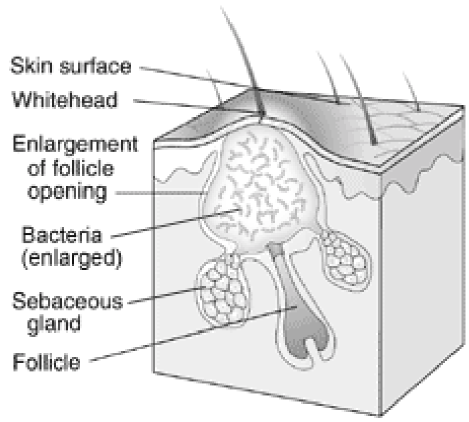


Figure 1. Acne (www.acne.org)

There are many treatments developed to treat acne. The most effective treatment thus far is isotretinoin, a drug that acts on the sebaceous glands. It has a 95% cure rate in the treatment of acne, but is also associated with many adverse side effects, including dryness of skin and mucous membranes, myalgia, arthalgia, benign intracranial hypertension, hepatitis, hyperlipidemia, acne fulminans, and visual disturbances. Isotretinoin also places users at risk for depression, suicide, psychoisis, and violent behavior [Charakida, et. al].

An alternative treatment with less severe side effects is needed, and a promising idea is light therapy. Laser light can be used to destroy the sebaceous glands located 100 – 1000 μm below the surface while sparing the overlying epidermis [Dierickx].The mechanisms by which this is possible is through photothermolysis, the absorption of high intensity light to produce thermal damage. Thermal damage of the sebaceous gland will stop sebum production, and thereby decrease *P. acnes* growth.

Typically near-infrared wavelengths are used because they can reach deeper depths where the sebaceous glands are located. Furthermore, the combination of the heating with surface cooling can spare the epidermis, overlying the sebaceous gland, from severe thermal injury.

Treatment consists of alternate heating and cooling of the skin. The whole procedure will involve five steps of cooling with a very low temperature refrigerant and four steps of heating with a 1450 nm laser. Each cooling step has an exposure time of 0.015 seconds and each heating step has an exposure time of 0.043 seconds (Fig. 2).

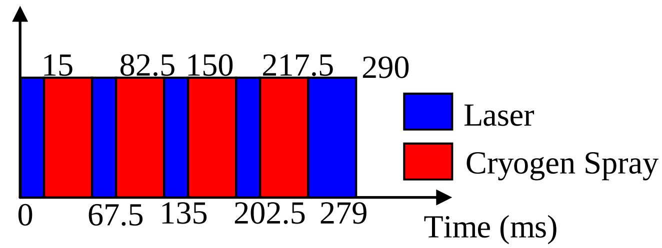


Figure 2. Cooling and heating procedure during acne treatment.

This light therapy shows great promise as an alternative treatment for acne, however more information is needed on the temperature changes within the treatment volume to determine whether the therapy is safe and effective. The design objectives we are considering are:

1. For an effective therapy, the temperatures in the sebaceous gland should reach above 70ºC, which is the temperature at which necrosis occurs.
2. For a safe therapy, the temperatures in the epidermis should not reach above 60ºC-70ºC, the temperature at which structural proteins begin to denature.

In order to satisfy our design objectives, we will model heat transfer in the acne region and surrounding skin during light therapy to determine what the laser power that would result in a safe and effective treatment. We will model the acne region with a 2D axisymmetric geometry, and the sebaceous gland located 100 um below the epidermal surface (Fig. 3)

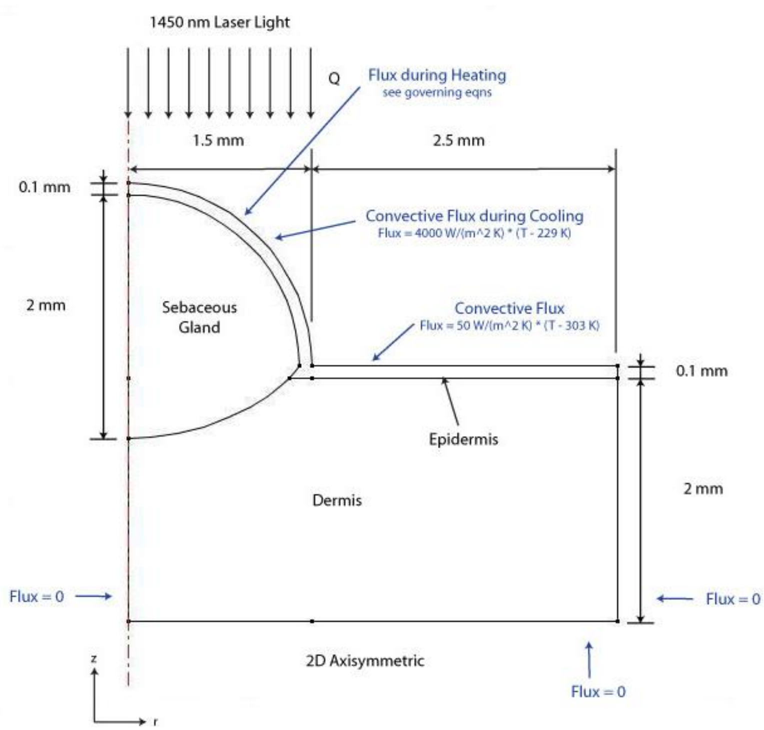


Figure 3. Schematic of acne region showing dimensions and boundary conditions.

Results and Discussion

Methods

The simulation was run on COMSOL Multiphysics to simulate both heat transfer and light diffusion into the acne-skin region using the model schematic above. Since the objective of this simulation was to determine the heating effects of the acne laser on the acne region and surrounding healthy tissue, the results outputted the temperature profile in the region of the schematic. The program we used in COMSOL was a transient analysis for heat conduction in the skin region above. This was coupled with a diffusion simulation to model laser behavior. However, the results outputted the final temperature gradient of the skin.

The company that developed this procedure originally used a Monte Carlo simulation to model the laser behavior in the skin [Paithankar et al]. Our project's simulation used the diffusion approximation model, which is similar to the Monte Carlo simulation but requires an improved scaling factor (ISF) to account for the discrepancies in accuracy between the Monte Carlo and diffusion approximation simulation [Zhang]. The heat transfer equation governing equation used was the one listed in the appendix. To model the laser behavior in the skin, the diffusion approximation equation listed in Appendix A was used as the mass transfer governing equation in COMSOL. The calculated value of fluence rate (Φ) was incorporated into the heat transfer governing equation as the heat generation source (Q).

Since the procedure involves alternating cooling and heating steps, an interpolation time function was entered into the program to account for the change from laser heating to rapid cooling. The cooling step was a convective flux at the surface of the acne. The time function was called heatfn(t) and coolfn(t) and was complementary to each other to model the alternating types of heat transfer. The time functions were modeled after the time steps in the procedure [Paithankar et al]. All parameters required in both equations were supplied (Appendix A) and inputted in the subdomain physics and boundary conditions in COMSOL with heat generation, laser flux, and convective flux being affected by the interpolated alternating time function. The geometry was modeled as 2-D axial-symmetric to simplify the simulation where the flux at all boundaries except the epidermal layers were zero. Flux at the epidermal layer was the heat flux in and out of the skin due to the laser and the cooling spray, respectively.

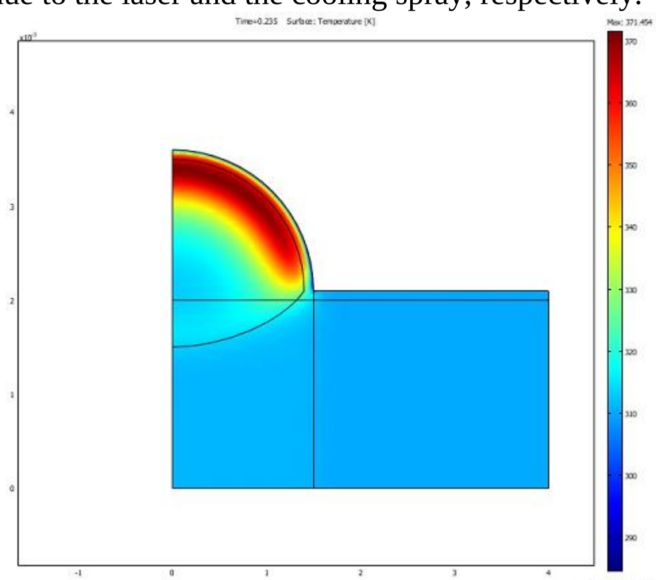


Figure 3. Contour plot of simulation at final time step, 235 milliseconds.

The simulation was run at 8665 mesh elements, which was the optimal mesh element number based on the mesh convergence (Appendix B) for accuracy and speed. The simulation followed the published procedure shown in the introduction and lasted for 235 milliseconds.

Results

Once all parameters were entered, the simulation was run and the temperature contour plot was given in Figure 3. Based on the contour plot, it is clear that the laser treatment penetrates the epidermis layer and heats up the sebaceous gland, where the acne bacteria reside. The maximum temperature reached in this area is 371.454 K, which is 98.304˚C. The average overall temperature in the sebaceous gland calculated from COMSOL is 343.38 K, which is 70.23˚C. The temperature required to kill the acne bacteria is around 60˚C [Anderson and Parrish]. This means that based on the model, the laser treatment successfully eliminates the acne bacteria. However, the simulation was also used to determine if there was significant damage to the epidermal layer.

The results indicated that the highest temperature in the epidermis reached around 360 K, or 86.85^{o}C. The average temperature calculated in COMSOL was 62.818^{o}C. The highest temperature was between on the boundary between the epidermis and sebaceous gland. The results show that the outer tissue of the epidermis remains undamaged. However, the inner layers of the epidermis and top layers of the sebaceous gland will experience thermal damage from the laser treatment. In order to quantitatively analyze the entire procedure, two points in the middle of the epidermis and sebaceous gland were plotted for temperature change over time. The points were directly in the middle of the axial-symmetric model because that is most likely the region of greatest temperature change.

Figure 4 shows that in both the sebaceous gland and the epidermis the temperature change is consistent with the alternating spray cooling and laser heating steps. The graphs show that there is a larger variation in temperature when cooling takes place due to its close approximation to the spray. The sebaceous gland temperatures do not drop as much due to the cooling. However, at the highest temperature the epidermis layer will still suffer thermal damage.

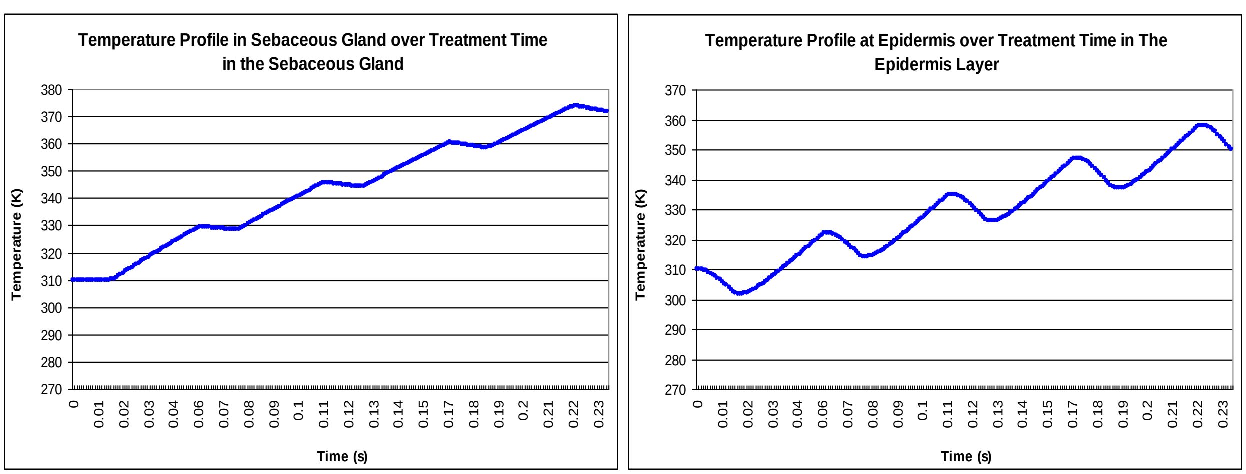


Figure 4. Temperature profile in sebaceous gland and epidermis over treatment time.

Sensitivity Analysis

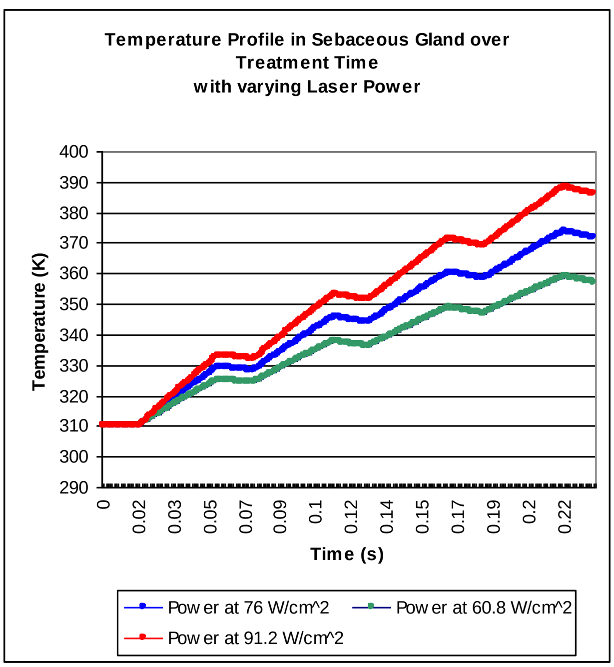
Due to the natural variations of properties in nature as well as the inconsistencies and minor but significant variations in machinery, a sensitivity analysis was performed to determine the effect of such variations on our results. Our sensitivity analysis focuses on temperature in two regions, the epidermis and the sebaceous gland. These two regions are chosen because they are the target areas of this whole model. With our goal of determining the effects of the heat transfer on acne and surrounding health tissues, it is important for us to know sensitive changes in epidermis (healthy region) and sebaceous gland (acne region) with the varying parameters. The parameters were varied by 20%. Varying 20% increase or decrease is chosen because it seems to be a reasonable change for the four parameters we are examining, and reflect numbers found in literature. It is not too great of a change that will dramatically change the results, but it is also not small enough to have no impact at all. These parameters include:

I. Laser Power
II. Coolant Temperature
III. Skin-Coolant H Value
IV. Thermal conductivities of Epidermis and Sebaceous Gland

We choose to vary these parameters to perform sensitivity analysis because they play important role in our governing equations, so we want to see any changes of these parameters can actually affect the model's result greatly.

Additionally, we graphed the maximum and minimum temperatures in the tissue at the end of the treatment after varying the parameters.

I. Laser Power



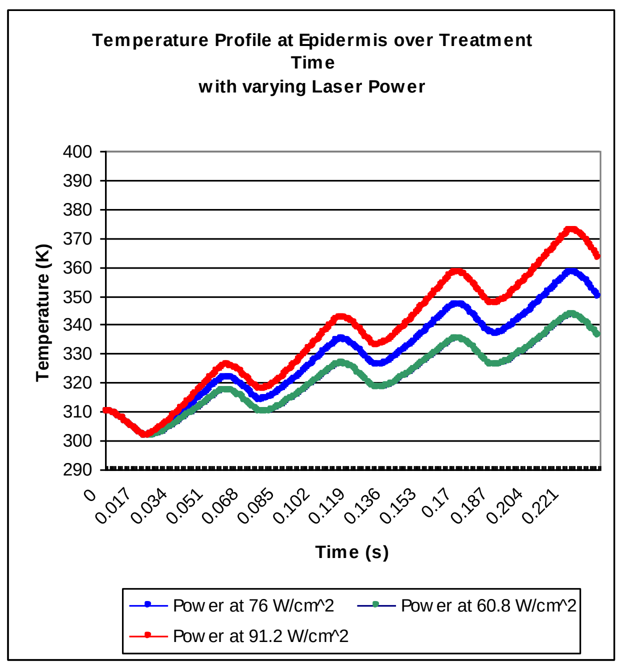


Figure 5. Sensitivity analysis of varying laser power, temperature profile in sebaceous gland and epidermis over time of treatment.

We varied the power by a 20% increase and decrease on the original laser power of 76 W/cm^2. From Figure 5, we can observe a noticeable change of temperature profile in each region. For the epidermis region, we can see that the total difference between maximum and minimum temperatures is around 25K, and the discrepancy between different power supplies grows larger as time goes on. As for the sebaceous gland region, the discrepancy is even bigger compared to the epidermis region. The difference between the maximum and minimum temperature is around 29K or 30K. It follows the pattern as seen from the epidermis region as well: larger changes as time goes on. This sensitivity analysis shows that power is a very sensitive parameter to our model because changes in power can cause significant changes in the temperature profile. We need to use and check with the experimental values for the power for this specific 1450nm laser to have an accurate results for our simulation.

II. Coolant Temperature

For the cooling temperature change, we apply the 20 % increase and decrease to the cooling temperatures. From Figure 6, we can observe that in both epidermis region and sebaceous gland region, there are no significant changes even as the time goes on. Therefore, we can conclude that varying cooling temperature is not very sensitive and will not affect the outcome or the simulation greatly.

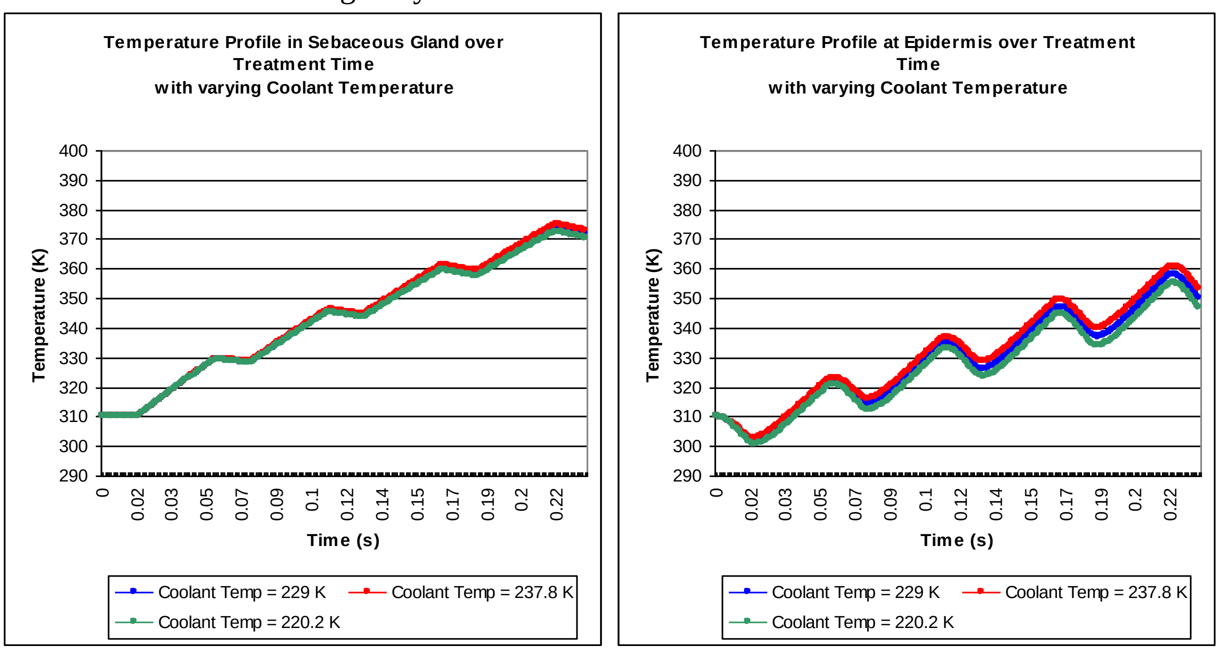


Figure 5. Sensitivity analysis of varying coolant temperature, temperature profile in sebaceous gland and epidermis over time of treatment.

III. Skin-Coolant H Value

For the skin-coolant H value, we can observe that varying the coolant heat coefficient does not create much difference. In the epidermis region, the difference between the maximum temperature and minimum temperate profile at the end of the simulation is approximately 10 K.

For the sebaceous gland, the three curves are almost identical. It is not that significant of a change increasing or decreasing the value by 20%.

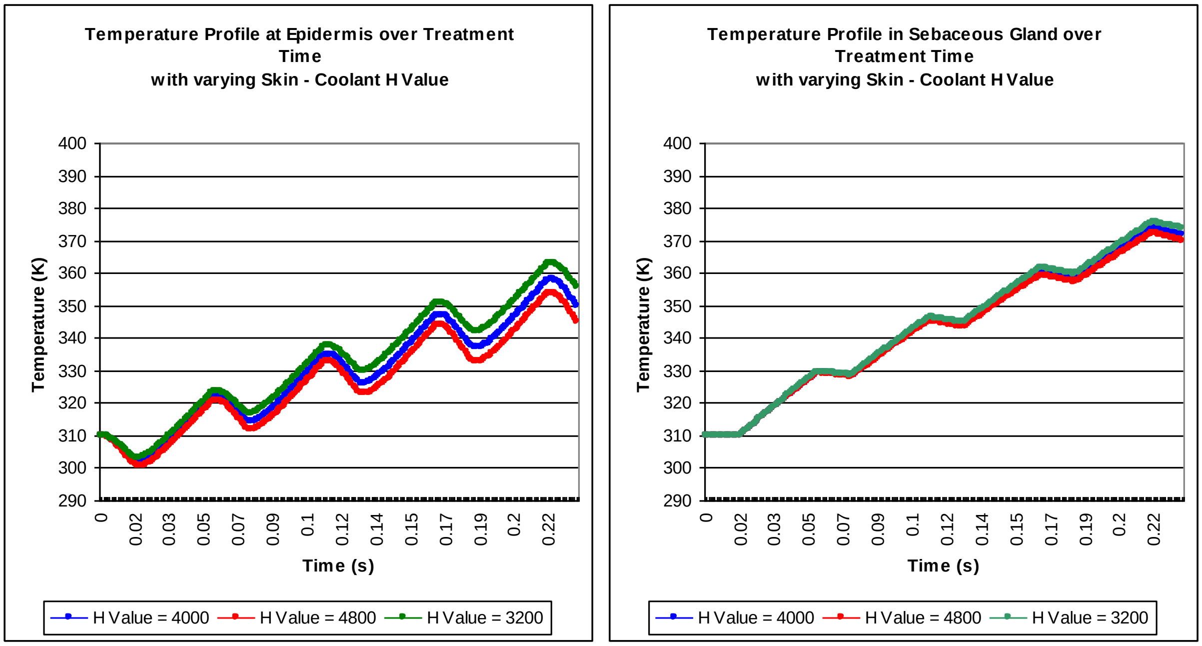


Figure 6. Sensitivity analysis of varying coolant temperature, temperature profile in sebaceous gland and epidermis over time of treatment.

V. Thermal conductivities of Epidermis, Sebaceous Gland, and Dermis

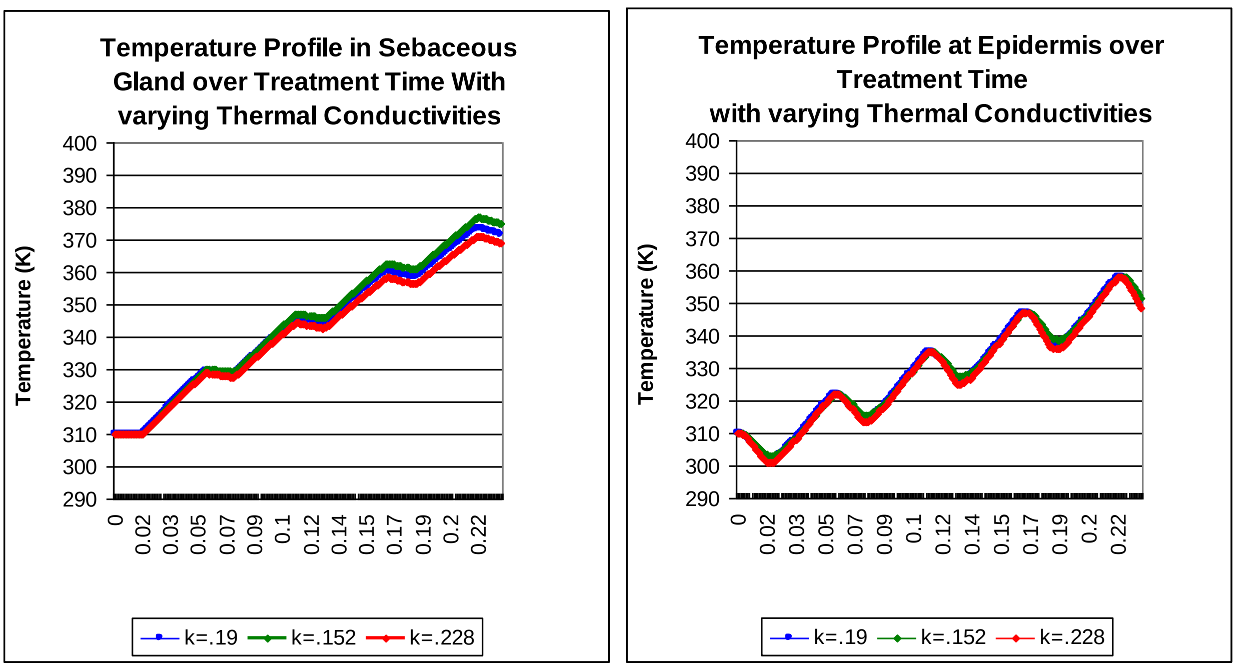


Figure 7. Sensitivity analysis of different thermal conductivities, temperature profile in sebaceous gland and epidermis over time of treatment.

For the thermal conductivity parameter, Figure 7 demonstrates that having a 20% change on the thermal conductivities does not create significant changes to our model. The curves for both the epidermis region and sebaceous region are almost the same. Therefore, this analysis suggests that thermal conductivity is not a crucial parameter to change our model.

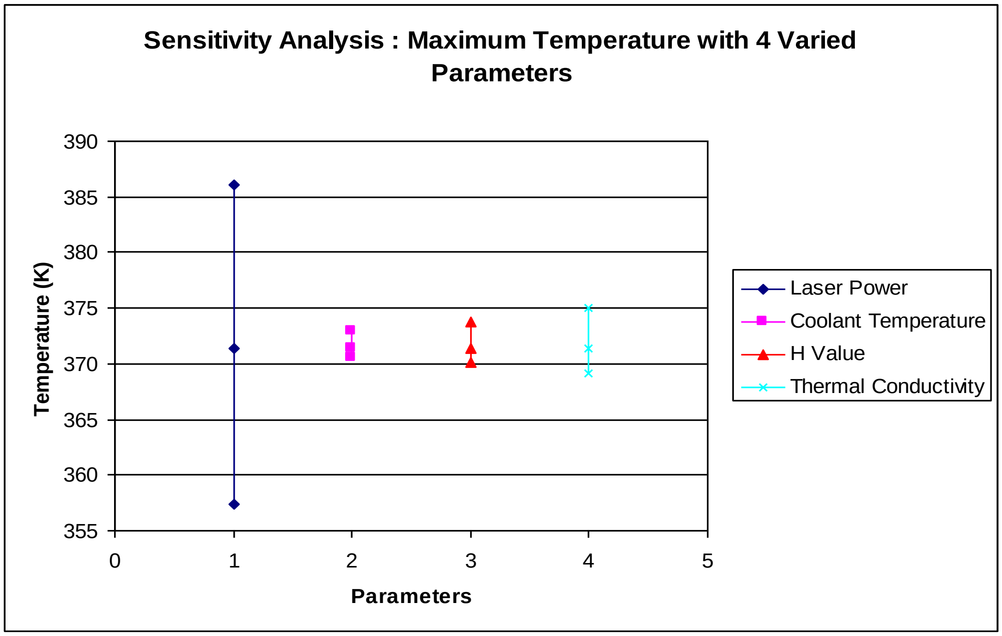


Figure 8. Maximum and minimum temperatures in tissue after treatment.

Figure 8 demonstrates the difference in maximum temperatures when the properties listed are increased and decreased by a factor of 20% from the original value. Varying the laser power causes the largest change in maximum temperature, whereas changing the other values does not cause a very significant change. This is because the maximum temperature occurs deep inside the epidermis and sebaceous gland. Thus, the convective cooling properties will not affect the temperature. Thermal conductivity needs to vary by orders of magnitude for a significant change.

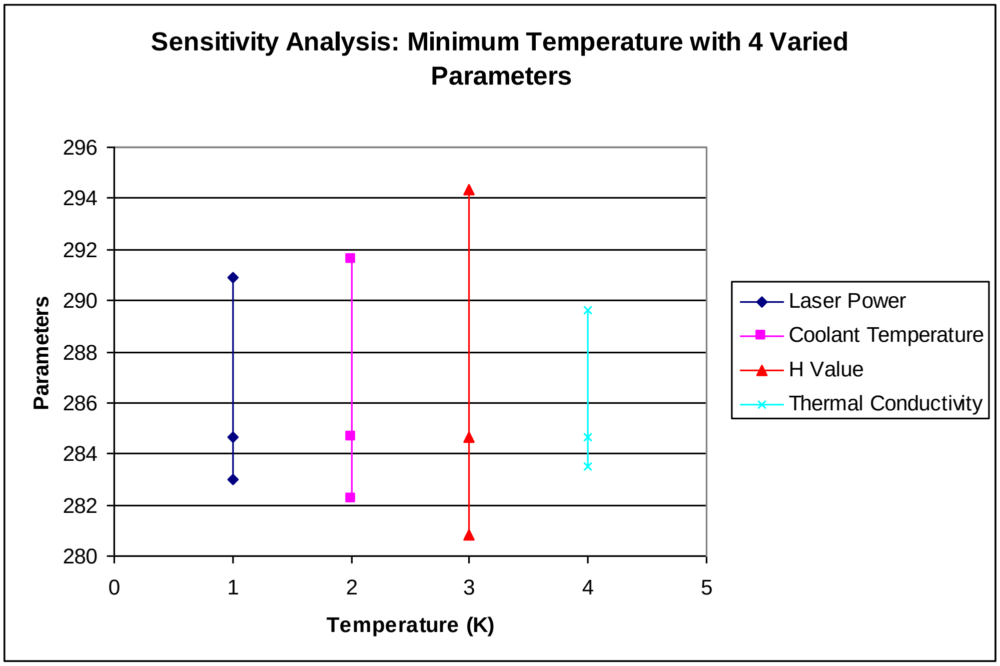


Figure 9. Minimum temperatures in tissue after treatment.

Figure 9 demonstrates the change in minimum temperatures in the skin when the properties are increased and decreased by a factor of 20%. There is a much more significant change for all the values than in the maximum temperatures. The most significant value is the heat transfer coefficient (H). This makes sense because the minimum temperature is at the surface where the coolant convection plays a large role in the temperature change. This is also the reason why the coolant temperature plays a significant role as well.

Accuracy Check

Our project was based upon published research done on this laser treatment procedure for acne. This made it easy for us to perform an accuracy check on our solution. The skin, laser, and time properties were all based on the paper "Acne Treatment with a 1,450 nm Wavelength Laser and Cryogen Spray Cooling" by Paithankar et al. The only difference was that the geometry in this publication was greatly simplified relative to ours (Figure 10). The geometry used in the publication was a slab with only one layer of a combination between the epidermis and sebaceous gland. We redesigned our geometry to fit the paper's geometry along with their parameters for the epidermis/sebaceous gland combination (Figure 11). Below is the comparison between the publication's contour plot and our simulated contour plot on COMSOL.

The results from the publication match the results from our simulation very well. The maximum temperature towards the end of the 235 millisecond treatment is 90^{o}C in the publication. The COMSOL simulation had a max temperature of 86.85^{o}C. This is only 4^{o}C off.

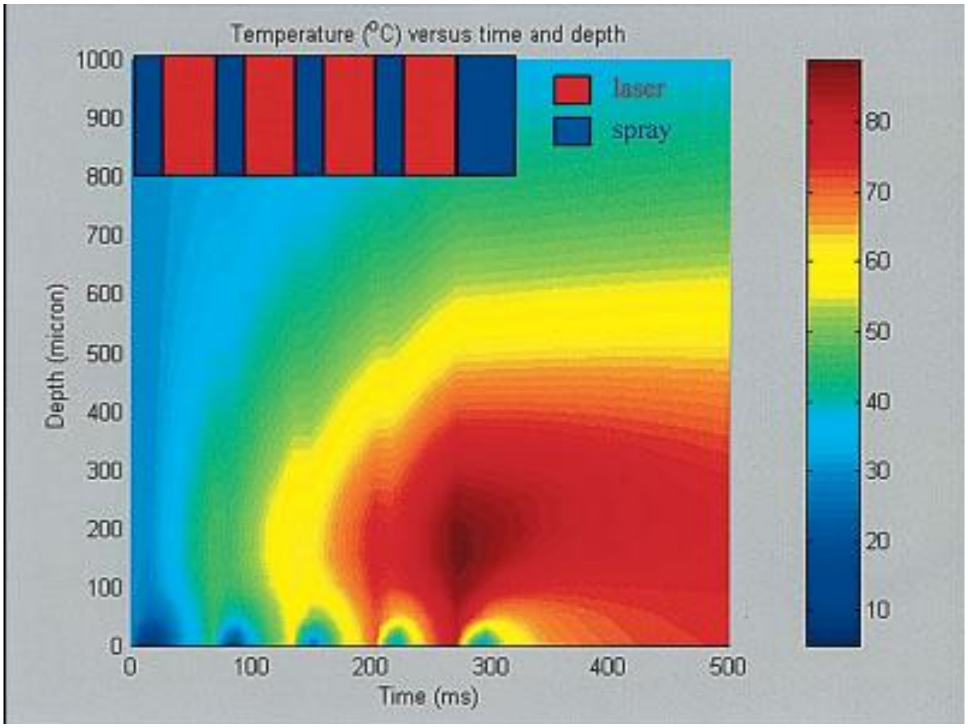


Figure 10. Slab geometry and results from Paithankar et al.

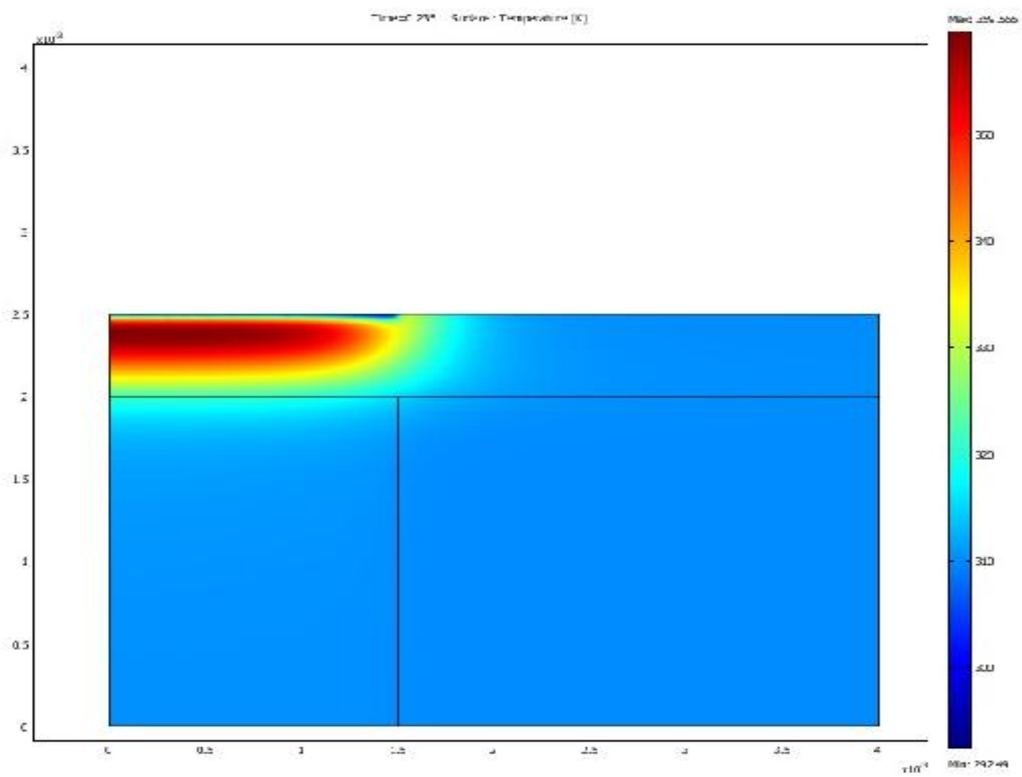


Figure 11. Redesigned geometry to match Paithhankar et al.

The small discrepancy in temperature may be due to the fact that the publication used the Monte Carlo simulation whereas our COMSOL simulation used the diffusion approximation to model laser behavior. The ISF factor is also merely an approximation. However, the difference is not significant enough. Furthermore, the publication also shows a cooling effect near the surface of the skin where the coolant spray is applied at the correct intervals. Other than the geometry, the parameters and properties in the slab simulation were equivalent to the parameters and properties in our more geometrically complicated simulation. This means that every property and parameter in our COMSOL simulation is fairly correct and accurate. Keeping all parameters the same, we can then use our more complex geometry.

When we rerun our simulation again, it gives a temperature profile that is similar to the publication's data. However, the temperatures are around 10^{o}C higher in the complicated geometry than they are in the slab. This discrepancy in temperature is due to the differences in the geometry. The epidermis layer thickness is reduced and the acne is clearly defined as the sebaceous gland that extends the skin into a quarter circle shape. Furthermore, there is now a sebaceous gland.

Even though the parameters for the diffusion approximation equation (Appendix A), such as absorption and scattering coefficient, in the sebaceous gland are equivalent to that of the epidermis, the thermal conductivity, density, and specific heat are different. This will alter the temperature profile as well. By making the geometry more complicated and closer to a real-life simulation, the temperature increases in the skin layer that receives the laser treatment.

Conclusion and Design Recommendation

Photothermolysis treatment allows the acne region to be treated at high temperatures with out harming the surrounding healthy tissue. We modeled this treatment in COMSOL to find the laser power that would allow for optimum treatment. We looked at a range of laser powers between 60 and 91 W/cm^2. We found that with a laser power of 60 W/cm^2, we were able to reach a temperature of 85° C. This temperature is above 70°C which is high enough to injure the sebaceous gland and stop sebum production, thus slowing down bacteria growth. Using the 60 W/cm^2 laser, the outer epidermis layer was heated to 70° C. Anderson et al have shown that temperatures above 60° or 70°C are when structural proteins become denatured. Our temperature is fairly close to this, but any temperature above will cause serious damage and necrosis. This problem, however, seems unavoidable. Many studies have shown histological slides of acne treated with photothermolysis that contain necrosis due to thermal damage.

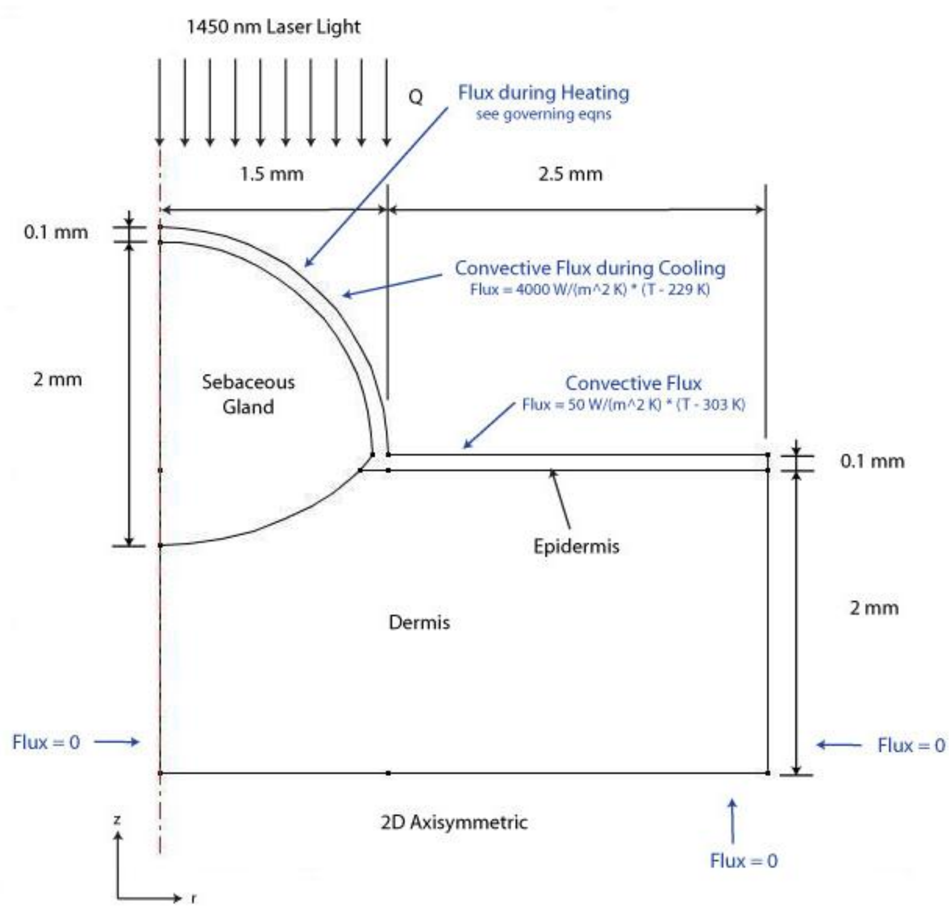
From our simulation of photothermolysis treatment of acne in COMSOL, we have determined an optimum laser power that will allow for heating of the sebaceous gland with out causing necrosis of the surrounding epidermis. We recommend that this form of treatment be entered into clinical trials, either lower model organisms or on willing human models. Although our simulation takes into account many factors such as more realistic geometry, changes in material properties, and changes in cooling parameter; many factors that may be unknown to us may still exist. Some of these factors may include different concentration of melanin in skin, different skin types, and other design constraints.

Our design to choose the optimum laser may be constrained by the type of laser used. There are many types of lasers; such as gas, chemical, dye, and semiconductor lasers. The laser medium types differ in each laser, which allows the laser to operate at a specific wavelength. Some of these lasers contain hazardous chemicals. Using these lasers in a setting where a client may be exposed to hazardous chemicals if the laser breaks, may cause health and safety problems and liability issues.

Our design may also be constrained by ethical issues that may occur during clinical trials. Our design is idealized and can not encompass all random variations. Some factors affecting the results of the acne treatment include the ethnicity of the person which affects the amount of melanin present in the skin, and the thickness of the skin. During clinical trials some people may receive 3rd degree burns of other injuries that may lead to scarring. We can not guarantee that people who join the study will receive the correct outcome.

APPENDICES

APPENDIX A: MATHEMATICAL STATEMENT OF THE PROBLEM



Governing Equations

Heat Transfer through conduction is modeled by the following equation:

$$\frac{\partial T}{\partial t} = \frac{k}{\rho c_p}\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial T}{\partial r}\right) + \frac{\partial^2 T}{dz}\right) + Q$$

where T is temperature (K), ρ is density (kg m^{-3}), k is thermal conductivity (W m^{-1} K^{-1}), c_p is specific heat capacity (J kg^{-1} K^{-1}) and Q is energy deposition through light absorption (W m^{-3}) in the tissue.

$$Q = \mu_a \varphi E_f$$

where φ is the fluence rate (W m^{-2}) of the incident laser light, μ_a is the absorption coefficienent (m^{-1}) of the tissue, and E_f is an improved scaling factor for the epidermis or sebaceous gland

The fluence rate, φ, is calculated using the diffusion approximation model [Zhang] and simulates the light distribution in multilayered skin. The diffusion approximation model describes light transport using the following differential equation:

$$\frac{\partial \varphi}{\partial t} = D\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial \varphi}{\partial r}\right) + \frac{\partial^2 \varphi}{dz}\right) + c_{e,sg,d}\,\mu_a \varphi$$

where $D = c_{e,sg,d}\left[3\left(\mu_a + (1-g)\mu_s\right)\right]^{-1}$

is the optical diffusion coefficient ($m^2\,s^{-1}$) of tissue, $c_{e,sg,d}$ is the speed of light in the epidermis, sebaceous gland, or dermis ($m\,s^{-1}$), μ_s is the scattering coefficient (m^{-1}) of the tissue, and g is the anisotropy factor

The boundary condition of the tissue during laser irradiation is a flux given by:

$$P(t)_{laser} c_o = -D\frac{\partial \varphi}{\partial r}$$

where $P(t)_{laser}$ is the laser irradiance ($W\,m^{-2}$), c_0 is the speed of light

Initial Conditions:
The temperature in the tissue is initially at 37ºC

$$T_o(t_o) = 37°C$$

Material Properties and Parameters

	Epidermis	Dermis	Sebaceous Gland
Thermal Conductivity, k	$0.21\ W\,m^{-1}\,K^{-1}$	$0.37\ W\,m^{-1}\,K^{-1}$	$0.2\ W\,m^{-1}\,K^{-1}$
Density, ρ	$1000\ kg\,m^{-3}$	$1000\ kg\,m^{-3}$	$900\ kg\,m^{-3}$
Specific Heat, c_p	$3181.82\ J\,kg^{-1}\,K^{-1}$	$2846.15\ J\,kg^{-1}\,K^{-1}$	$2000\ J\,kg^{-1}\,K^{-1}$
Absorption Coefficient, μ_a	20 cm-1	$.236mm^{-1}$	$20cm^{-1}$
Scattering Coefficient, μ_s	120 cm-1	$14.6mm^{-1}$	$120\ cm^{-1}$
Speed of Light, $c_{e,sg,d}$	2.19e-8m/s	2.19e-8m/s	2.19e-8m/s
Optical Anisotropy Factor, g	0.9	0.79	0.9

$P_{laser} = 76\ W\,cm^{-2}$
$h_{skin\text{-}coolant} = 4000\ W\,m^{-2}\,k^{-1}$
$h_{skin\text{-}air} = 50\ W\,m^{-2}\,k^{-1}$
$T_{coolant} = -44$ ºC = 229 K
$T_{air} = 30$ ºC = 303 K
$E_f = 0.4$
All properties were obtained from Zhang el al and Paithankar et al.

Assumptions:
The transport of light through tissue was calculated using the Diffusion Approximation, which assumes light to be a particle. E_f is an improved scaling factor that increases the accuracy of this model and makes the results more similar to the Monte Carlo Model. These values were approximated from the ISF values of 595 nm light [Zhang].

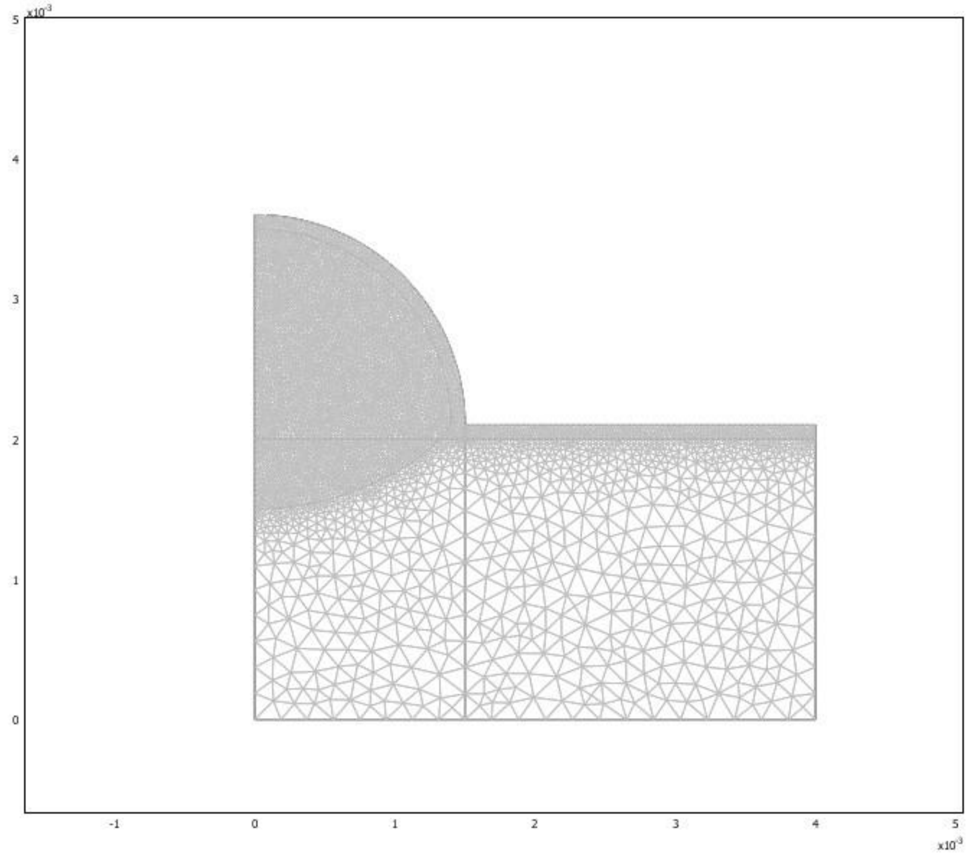
The absorption and scattering coefficient for epidermis and sebaceous gland were assumed to be the same. The thermal conductivity, density, and specific heat of the sebaceous gland were assumed to be subcutaneous fat.

For the geometry, we assumed the sebaceous gland is located at a depth of 100µm and is a spherical shape.

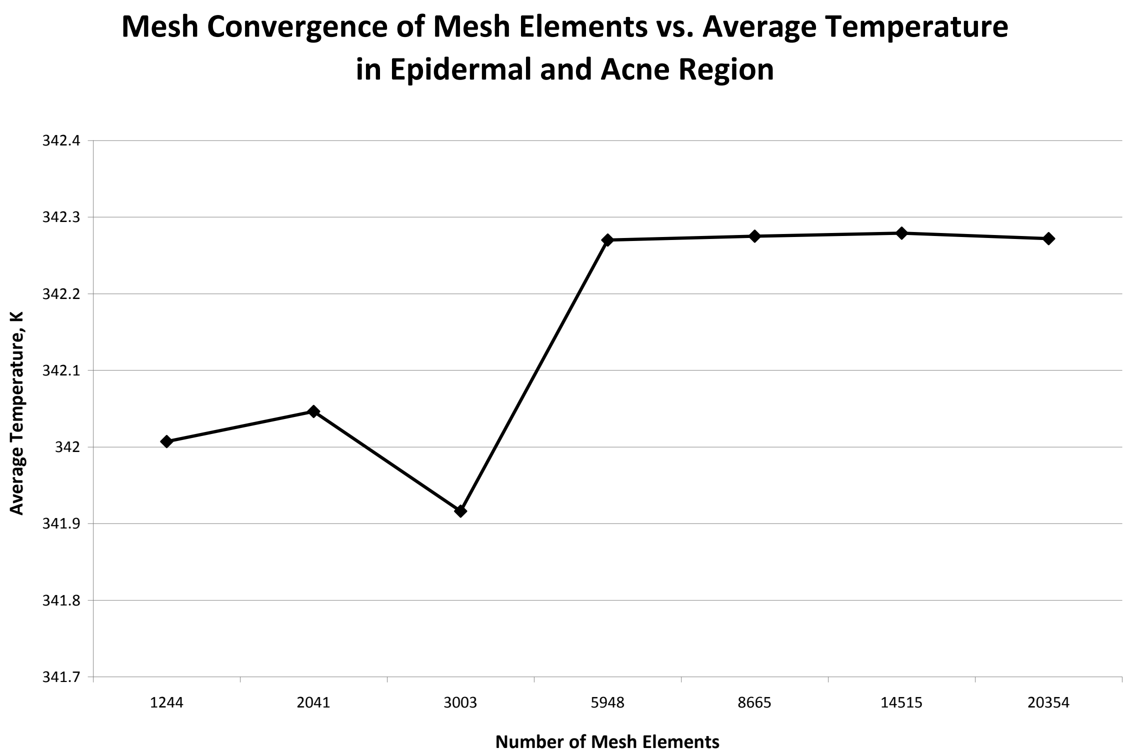
APPENDIX B:

The heat transfer, transient convection and conduction solver was used to solve the heat equation. The convection-diffusion, transient diffusion solver was used to solve the light diffusion equation which was then linked to the heat equation.

Element Mesh:



Mesh convergence:



From the plot above we can observe that our solution has converged to a average temperature of 342.2 K after 5948 elements. We used 8665 elements during our sensitivity analysis.

APPENDIX C: REFERENCES

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