Modeling Temperature in a Breast Cancer Tumor for Ultrasound-Based Hyperthermia Treatment

Brian Ho

Kanmani Kannayiram

Ryan Tam

Harrison Yang

Introduction

Hyperthermia, also called thermal therapy or thermotherapy, is a type of cancer treatment in which body tissue is exposed to high temperatures of up to 113 ºF to damage and/or kill cancer cells. Research has shown that high temperatures can damage and kill cancer cells with minimal injury to the surrounding tissue, making it much safer than traditional treatment therapies. Hyperthermia is most commonly used in conjunction with other forms of cancer therapy, such as radiation and chemotherapy. Furthermore, many clinical studies show that high temperature hyperthermia alone can be used for selective tissue destruction as an alternative to conventional invasive surgery. Due to the heterogeneous and dynamic properties of tissues, including blood perfusion and metabolic heat generation, it is important to present models of the temperature change during the treatment of tumors. The method of hyperthermia we will be looking at is local hyperthermia, in which heat is applied to a small area using a focused ultrasound beam. This will be an external approach where the applicator is positioned around the appropriate region.

The effectiveness of hyperthermia depends greatly on the temperature achieved during the treatment. Another important factor is the duration of the treatment and temperature of the surrounding tissue. This application can easily be done, but monitoring of the temperature requires invasive needles with tiny thermometers to be inserted in the treatment area to ensure that the desired temperature is reached and the surrounding tissue will not be damaged. Imaging techniques such as CT scans are also required and can be expensive to use for clinical study purposes. Thus, a mathematical model is better used for understanding the temperature profile of the tumor.

Problem Formulation, Assumptions and Values

In this study, we will be modeling the heat transfer of an ultrasound beam on a breast cancer tumor. This is more commonly known as a hyperthermia treatment for cancer. Literature has described that in order to have an effective treatment, resulting in a reduction of tumor size, the tumor must reach a temperature of approximately 45 ºC. To simply our model, we will be analyzing the tumor as a perfect sphere with radius R = 1 cm = 0.01 m. We will also be simplifying the ultrasound beam to be perfectly focused, in other words, the beam only applies heat at a point in the center tumor and any other heat energy from the beam is negligible.

For the purposes of this model we will be utilizing the Pennes bioheat equation (which is the general heat diffusion equation with additional terms for perfusion of blood and metabolic heat), in spherical coordinates, as follows:

$$\frac{\rho Cp}{k}\frac{\partial T}{\partial t}=\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T}{\partial r}\right)+q_p+\frac{q_m}{k}$$

Where ρ is density of the tumor, Cp is the heat capacity of the tissue, k is thermal conductivity of tissue and q_m is the metabolic heat term (or heat that the tumor generates from its metabolic processes). q_p is defined as heat perfusion or the heat that is carried away from the tumor site by arterial blood flow and is defined as: $\frac{\omega * \rho b * Cpb}{k}(T_\infty - \mathrm{T})$ where ω = perfusion rate of blood, T_∞ = arterial temperature, T = local tissue temperature, ρ_b = density of blood and C_{pb} = heat capacity of blood. This means that the temperature profile with respect to time is dependent on the diffusivity of heat through the tumor as well as how much heat is exchanged through the arteries and metabolic heat generation.

In this situation, we will be neglecting the q_p (the heat perfusion term) in an attempt to simplify the model. This means that we will be modeling the two remaining scenarios: the basic scenario without considering metabolic heat (Scenario 1) and then one considering the metabolic heat term (Scenario 2). This means that the equation to be modeled is reduced to (after dividing by $\frac{\rho Cp}{k}$ on both sides and simplifying):

$\frac{\partial T}{\partial t}$= D($\frac{\partial^2 T}{\partial r2}$) [Scenario 1]

$\frac{\partial T}{\partial t}$= D($\frac{\partial^2 T}{\partial r2}$) + $\frac{q_m}{k}$ [Scenario 2]

Where D = $\frac{k}{\rho Cp}$

We will analytically solve these equations to get the two respective temperature profiles. The boundary conditions applied are:

$T_H(0,t)$= 45 C [Temperature at the center of the tumor, applied point source temperature]

$T_H(R,t)$= 37 C [Temperature at the boundary of the tumor, physiological temperature]

And the initial condition used is:

$T_{SS}(r,0) =$ 37 C [Initial temperature of tumor at time t = 0, physiological temperature]

The physiological constant values used in the model (derived from literature) are:

k = 0.42 $\frac{\mathrm{W}}{\mathrm{m}*^\circ\mathrm{C}}$ [Thermal conductivity of tumor]

ρ = 920 $\frac{\mathrm{kg}}{m^3}$ [Density of tumor]

C_p = 3600 $\frac{J}{\mathrm{kg}*^\circ\mathrm{C}}$ [Heat capacity of tumor]

q_m = 29000 $\frac{W}{m^3}$ [Metabolic heat generation of tumor]

Analytical Solution

Scenario 1:

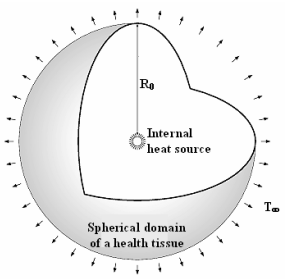
$$\boldsymbol{U(r,t) = \frac{-8r}{R} + 45 + \sum_{n=0}^{\infty} (\frac{-8}{n\pi}) \times sin\,(\frac{n\pi r}{R})\, e^{-(\frac{n\pi}{R})^2 Dt}}$$

Scenario 2:

$$\boldsymbol{U(r,t) = \frac{-q_m r^2}{2k} + \frac{(-8 + \frac{q_m r^2}{2k})r}{R} + 45 + \sum_{n=0}^{\infty} \frac{2}{R}[\left(\frac{8R}{n\pi}\right)(\cos(n\pi) - 1) + \frac{q_m}{2k}\left(\frac{-R^3}{n\pi}\cos(n\pi) + \frac{2R^3}{(n\pi)^3}(\cos(n\pi) - 1)\right) - \frac{R(8 - q_m R^2)}{2kn\pi}\cos(n\pi)\,] \times sin\,(\frac{n\pi r}{R})\, e^{-(\frac{n\pi}{R})^2 Dt}}$$

For derivation of the analytical solution, please refer to Appendix A & B.

Two models (and three attempted models) are presented, derived analytically, and modeled to approximate the effects of heating the center of an early stage breast cancer tumor. The models here presume that the ultrasound beam only focuses on the center of the tumor. As stated before, the tumor is approximated to be a perfect sphere of uniform density. This means that heat diffusion outwards from the center for all angles phi and theta of the sphere is the same. In this sense, it is very similar to modeling the heat diffusion through a slab where distance 'x' is now replaced by a distance 'r' away from the center. Since the sphere is 2 cm in diameter, our model would run for the radius of 1 cm with the ultrasound beam heating the center to a constant 45 degrees Celsius and the outside surface staying a constant 37 degrees Celsius. We chose a time to model of 100 seconds of exposure or 1.67 minutes.



First Model

The first model shows the heating profile of a tumor in an isolated system, which means there are no external factors to consider. This is to show the diffusion of heat through the tumor if no means of heat loss were present.

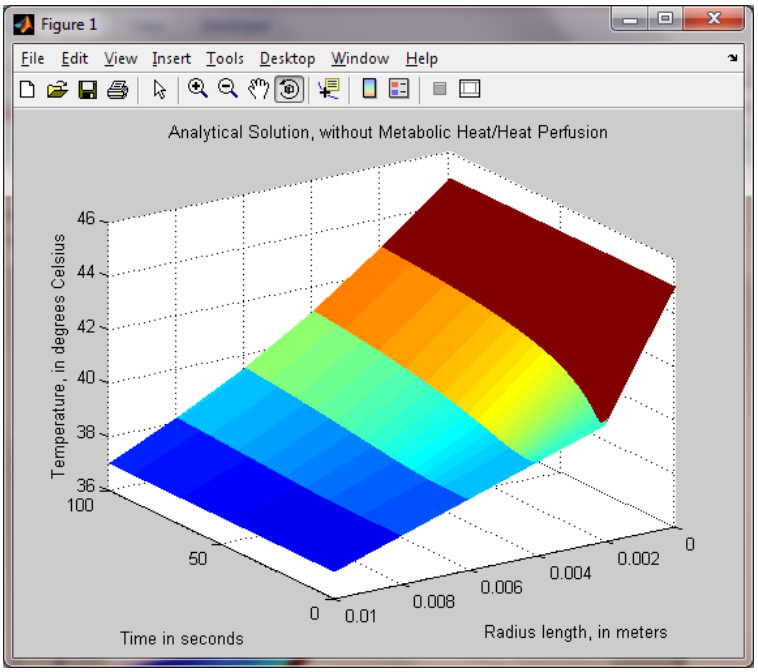


Figure 1: Temperature profile for a tumor isolated from the body, for 100 seconds.

The temperature at the center of the tumor is a constant 45˚C. Overtime the temperature of the tumor gradually increases.

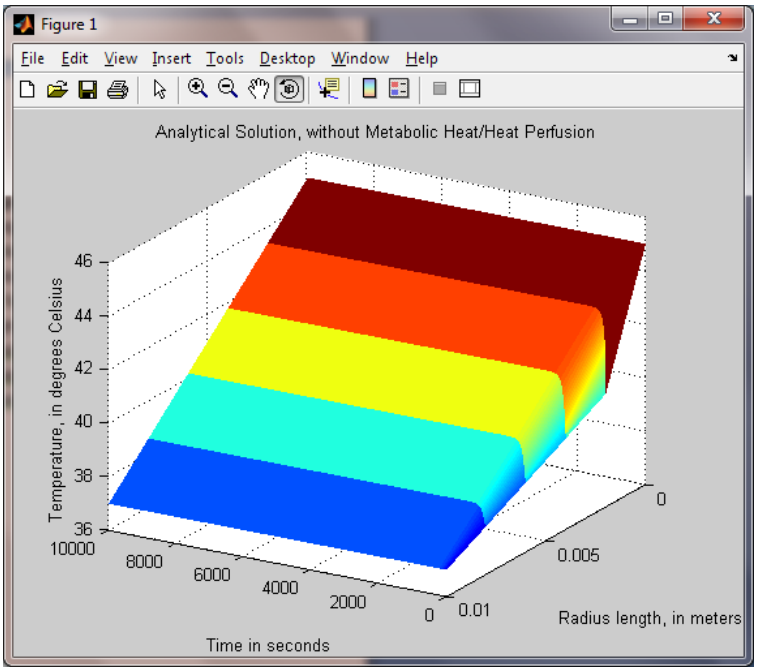


Figure 2: Temperature profile for a tumor isolated from the body, for 10000 seconds.

The temperature throughout the tumor is higher than the previous model which makes sense since a longer time is allotted for the tumor to heat.

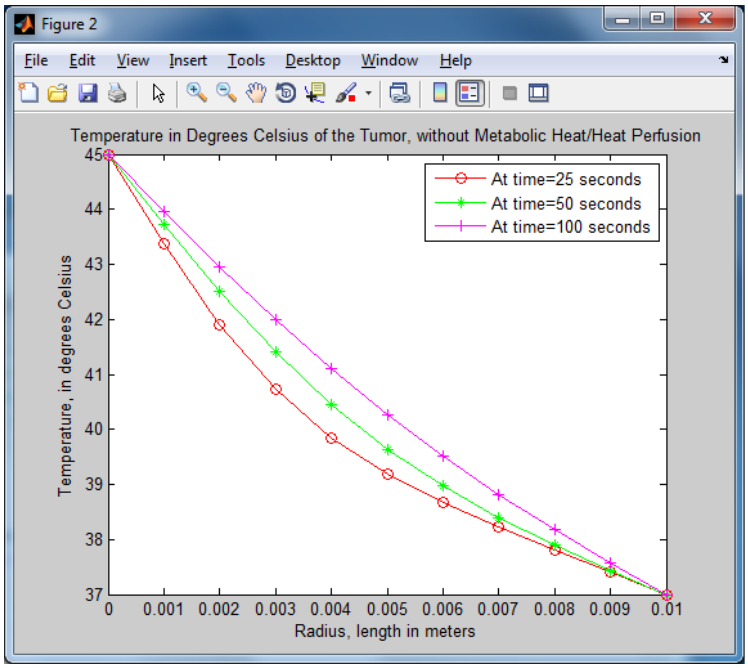


Figure 3: Effect of time on the analytical solution.

Confirms that as time goes on, the temperature of the tumor increases gradually with time.

Second Model

The second model is the same as the first but takes into account the metabolic heat generated by the cells themselves. The metabolic heat constant we used is $29000\frac{W}{m^3}$. The expectation is that the heat generated by the living tissue would have an additive effect to the external heat generated by the ultrasound. So the hypothesis would be that the tumor would reach an overall higher temperature and also heat at a faster rate.

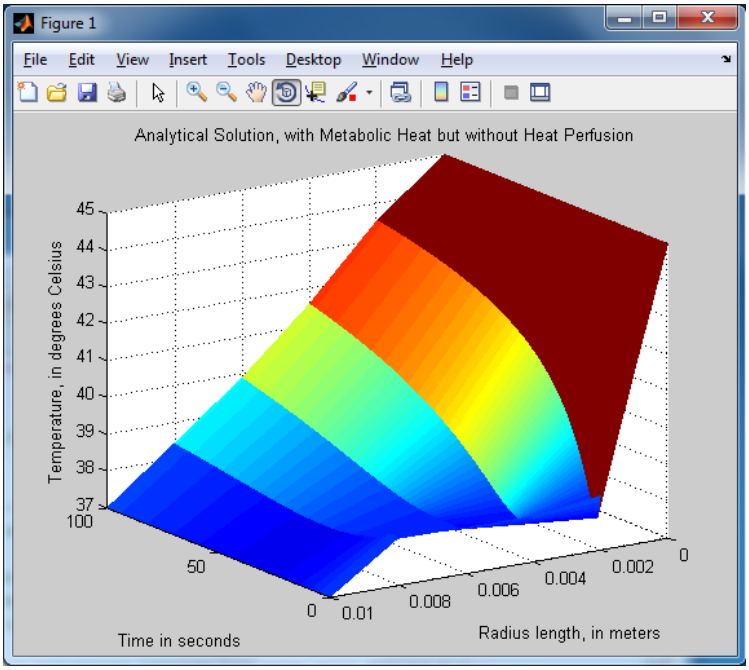


Figure 4: Temperature profile for a tumor in the body, taking into account metabolic heat generated, for 100 seconds.

The heat source at 45˚C is heats the tumor to a different gradient as the isolated tumor, but still increases the overall temperature.

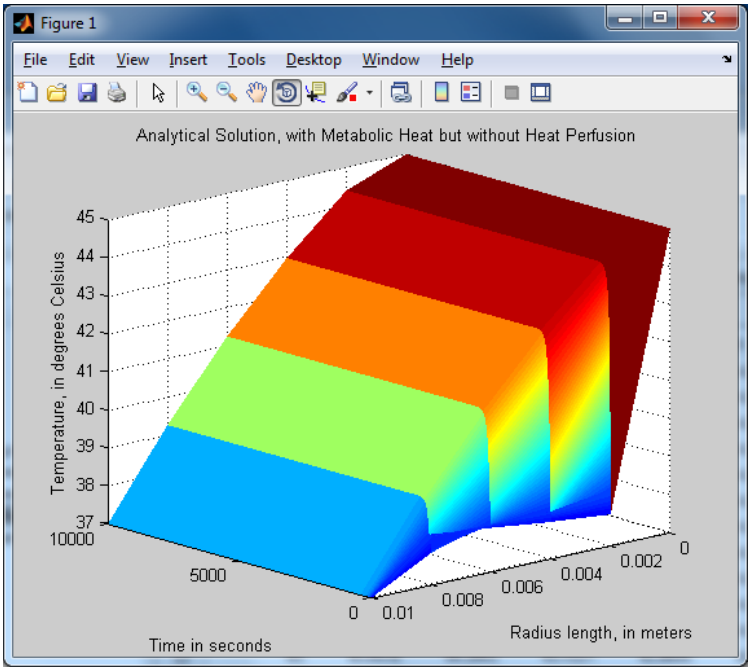


Figure 5: Temperature profile for a tumor in the body, taking into account metabolic heat generated, for 10000 seconds.

The overall temperature of the tumor improves with an increased duration of treatment, as observed by the final temperature profile compared to the previous figure.

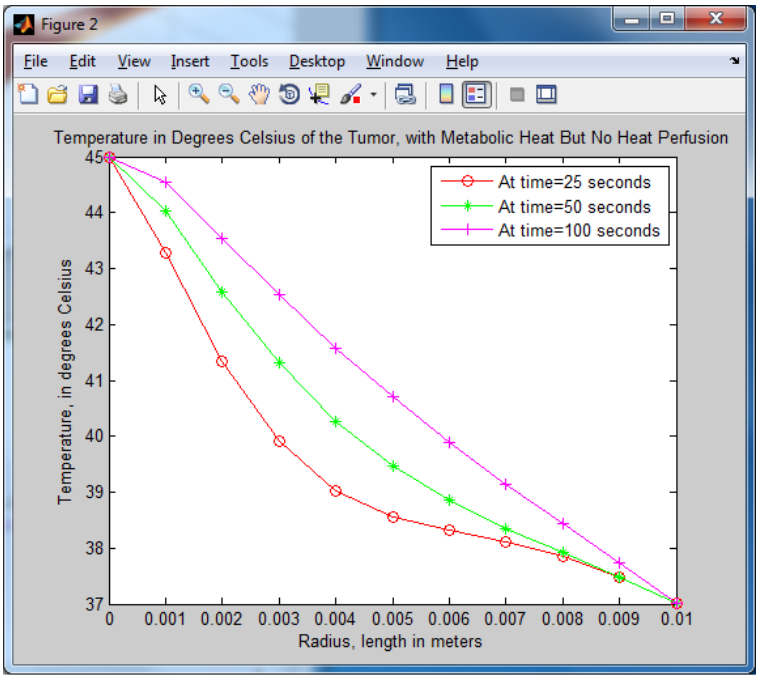


Figure 6: Effect of varying exposure times on the analytical solution.

As expected, at time = 100 seconds, it can be seen that the temperature is higher at all points throughout the radius of the spherical tumor model. Although for lower time models this is not always the case.

Comparing Figure 3 to Figure 6, perhaps the most unusual observation from these plots is that with the metabolic heat term introduced into the system, the temperature is lower for shorter exposure periods to the ultrasound. We originally expected a uniform shift upwards but this is only seen at the final time point of 100 seconds. We can only observe that the introduction of

metabolic heat affects the effectiveness of the ultrasound beam in some way that the temperature is lower than without the additional heat generation.

Conclusion

Ultrasound presents a new way to treat cancerous tumors by hyperthermia, or heating the tumor, with minimal damage to surrounding tissues. Most normal tissues are not damaged during hyperthermia if the temperature remains under 43.9 ºC, however, due to regional differences in tissue characteristics, higher temperatures may occur in various spots that result in burns, blisters, discomfort, or pain. Ultrasound reduces the damage to surrounding tissue by having a less pronounced effect on less dense tissue.

Our model shows that for a relatively small tumor (2 cm in diameter) and a point heat source set at 45 ºC, only a small part in the interior of the tumor would be damaged and/or destroyed within a period of approximately 100 seconds. However, it is good to note that this is a simplified model that is not taking into account arterial heat perfusion. The selected heat source temperature is a relatively low and to achieve better results, a point heat source at a higher temperature would be more effective at generating a sufficient temperature throughout the tumor faster. However, this comes at the risk of damaging the surrounding tissue even with the relative safety of ultrasound.

In conclusion, the results of this very simplified model form a basic foundation for a better understanding for the use of ultrasound for hyperthermia treatment and how heat diffusion works in tumors in general. To further our understanding of the effect of ultrasound, more complex and extensive analytical methods including all aspects of heat conduction, perfusion and metabolic heat terms should be considered to form a more complete picture of the phenomena that occurs in vivo when ultrasound is applied.

References

Gutierrez, Gustavo. "Study of the Bioheat Equation with a Spherical Heat Source for Local Magnetic Hyperthermia." XVI Congress on Numerical Methods and Their Applications (2007): n. pag. Web. 17 Oct. 2012.

"National Cancer Institute." Hyperthermia in Cancer Treatment -. N.p., n.d. Web. 17 Oct. 2012. <http://www.cancer.gov/cancertopics/factsheet/Therapy/hyperthermia>.

Hassan, Osama et. al. "Modeling of Ultrasound Hyperthermia Treatment of Breast Tumors." 26th National Radio Science Conference (2009): n. pag. 17 Mar. 2009. Web. 17 Oct. 2012.

Shih, Tzu-Ching et. al. "Analytical Analysis of the Pennes Bioheat Transfer Equation with Sinusoidal Heat flux Condition on Skin Surface." Medical Engineering & Physics (2007): n. pag. Web. 17 Oct. 2012.

Umadevi, V. et. al "Framework for Estimating Tumour Parameters Using Thermal Imaging." Indian Journal of Medical Research (2011): n. pag. Web. 17 Oct. 2012.

Special Thanks to:

Dr. Jakob Nebeker for providing the inspiration for this project

Dr. Guy Cohen for assistance with analytical methods

Appendix A: Analytical Solution For Model Without External Heat Sources

Assuming no perfusion of heat from the tumor and blood (q_p), and no metabolic heat released (q_m), the simplified diffusion equation is attained, where u is temperature (in degrees Celsius) and t is time (in seconds) and r is the distance (in meters):

$$\frac{du}{dt} = D\frac{d^2u}{dr^2} + \cancel{Dq_p} + \frac{\cancel{q_m}}{\cancel{c\rho}}$$

The complete solution is based on the summation of the homogeneous (U_H) and steady state terms (U_p):

$$U(r,t) = U_H(r,t) + U_p(r) \quad (0)$$

The boundary conditions are determined to be:

Initial Condition #1: U(r,0) = 37 ˚C

Boundary Condition #1: U(0,t) = 45 ˚C

Boundary Condition #2: U(R,t) = 37 ˚C

These boundary conditions reflect the fact that the tumor temperature is initially at physiological body temperature, which is 37 ˚C. The ultrasound laser heats the center of the tumor, at r=0, to 45 ˚C, and that comprises our first boundary condition. The edge of the tumor at r=R is modeled to be at body temperature, 37 ˚C.

Solve the steady state term (U_p) and plug boundary conditions to it:

$$\frac{du}{dt} = 0 = \frac{d^2u}{dr^2}; U_p(r,t) = \frac{-8r}{R} + 45 \quad (1)$$

Rescale to homogeneous initial and boundary conditions:

$$U_H(r,t) = U(r,t) - U_p(r)$$

New IC: $U_H(r,0) = 8(-1 + \frac{r}{R})$ (2)

New BCs: $U_H(0,t) = 0 \; and \; U_H(R,t) = 0$

Use separation of variables:

$U_H(r,t) = \psi(r)G(t)$ (3)

Upon solving, this gets $G = Ce^{-\lambda Dt}$ (4)

And for cases of $\lambda > 0$ (other cases proven to be trivial solutions) the characteristic equation of $\psi(r) = Acos\sqrt{\lambda}r + Bsin\sqrt{\lambda}r$ is attained. Plugging in the boundary conditions yields $\lambda = (\frac{n\pi}{R})^2$ and

$\psi(r) = Bsin(\frac{n\pi r}{R})$ (5)

Plug (5) and (4) to (3) yields

$U_H(r,t) = \sum_{n=0}^{\infty} B \times sin(\frac{n\pi r}{R})\, e^{-(\frac{n\pi}{R})^2 Dt}$ (6)

Where $B = \frac{2}{R}\int_0^R U_H(r,0)\ sin(\frac{n\pi r}{R})dr$ (7)

Plug in (2) to (7) and integrate the term, and replug B to (6) to get the final

$U_H(r,t) = \sum_{n=0}^{\infty}(\frac{-8}{n\pi}) \times sin(\frac{n\pi r}{R})\, e^{-(\frac{n\pi}{R})^2 Dt}$ (8)

And replug (8) and (1) to (0) to get the complete temperature profile:

$$\boldsymbol{U(r,t) = \frac{-8r}{R} + 45 + \sum_{n=0}^{\infty}(\frac{-8}{n\pi}) \times sin(\frac{n\pi r}{R})\, e^{-(\frac{n\pi}{R})^2 Dt}}$$

Appendix B: Analytical Solution For Model with Addition of Metabolic Heat Term

Assuming no perfusion of heat from the tumor and blood (q_p), and no metabolic heat released (q_m), the simplified diffusion equation is attained, where u is temperature (in degrees Celsius) and t is time (in seconds) and r is the distance (in meters):

$$\frac{du}{dt} = D\frac{d^2u}{dr^2} + \cancel{Dq_p} + \frac{q_m}{c\rho}$$

The complete solution is based on the summation of the homogeneous (U_H) and steady state terms (U_p):

$$U(r,t) = U_H(r,t) + U_p(r) \quad (0)$$

The boundary conditions, as in Appendix A, are determined to be:

Initial Condition #1: U(r,0) = 37 ˚C

Boundary Condition #1: U(0,t) = 45 ˚C

Boundary Condition #2: U(R,t) = 37 ˚C

Solve the steady state term (U_p) and plug boundary conditions to it:

$\frac{du}{dt} = 0 = \frac{d^2u}{dr^2} + \frac{q_m}{c\rho}$; know $D = \frac{k}{c\rho}$, so solve:

$$U_p(r,t) = \frac{-q_m r^2}{2k} + \frac{(-8+\frac{q_m r^2}{2k})r}{R} + 45 \quad (1)$$

Rescale to homogeneous initial and boundary conditions:

$$U_H(r,t) = U(r,t) - U_p(r)$$

New IC: $U_H(r,0) = -8 + \frac{q_m r^2}{2k} - \frac{\left(-8+\frac{q_m r^2}{2k}\right)r}{R}$ (2)

New BCs: $U_H(0,t) = 0 \; and \; U_H(R,t) = 0$

Use separation of variables:

$U_H(r,t) = \psi(r)G(t)$ (3)

Upon solving, this gets $G = Ce^{-\lambda Dt}$ (4)

And for cases of $\lambda > 0$ (other cases proven to be trivial solutions) the characteristic equation of $\psi(r) = Acos\sqrt{\lambda}r + Bsin\sqrt{\lambda}r$ is attained. Plugging in the boundary conditions yields $\lambda = (\frac{n\pi}{R})^2$ and

$\psi(r) = Bsin\,(\frac{n\pi r}{R})$ (5)

Plug (5) and (4) to (3) yields

$U_H(r,t) = \sum_{n=0}^{\infty} B \times sin\,(\frac{n\pi r}{R})\, e^{-(\frac{n\pi}{R})^2 Dt}$ (6)

Where $B = \frac{2}{R}\int_0^R U_H(r,0)\ sin\,(\frac{n\pi r}{R})dr$ (7)

Plug in (2) to (7) and integrate the term, and replug B to (6) to get the final

$U_H(r,t) = \sum_{n=0}^{\infty} \frac{2}{R}[\left(\frac{8R}{n\pi}\right)(\cos(n\pi) - 1) + \frac{q_m}{2k}\left(\frac{-R^3}{n\pi}\cos(n\pi) + \frac{2R^3}{(n\pi)^3}(\cos(n\pi) - 1)\right) - \frac{R(8 - q_m R^2)}{2kn\pi}\cos(n\pi)\,] \times sin\,(\frac{n\pi r}{R})\, e^{-(\frac{n\pi}{R})^2 Dt}$ (8)

And replug (8) and (1) to (0) to get the complete temperature profile:

$$\boldsymbol{U(r,t) = \frac{-q_m r^2}{2k} + \frac{(-8 + \frac{q_m r^2}{2k})r}{R} + 45 + \sum_{n=0}^{\infty} \frac{2}{R}[\left(\frac{8R}{n\pi}\right)(\cos(n\pi) - 1) + \frac{q_m}{2k}\left(\frac{-R^3}{n\pi}\cos(n\pi) + \frac{2R^3}{(n\pi)^3}(\cos(n\pi) - 1)\right) - \frac{R(8 - q_m R^2)}{2kn\pi}\cos(n\pi)\,] \times sin\,(\frac{n\pi r}{R})\, e^{-(\frac{n\pi}{R})^2 Dt}}$$

Appendix C: MATLAB Code

Part I: MATLAB Code For Model Without External Heat Sources

```
%Ryan Tam
%Ultrasound beam focused on center of spherical tumor
%Modeled outside of tumor (length R away from the tumor on all sides) at
%body temperature, 37 degrees Celsius
%Assume no heat generation or perfusion in idealized model, but ultrasound
beam
%heats the center of the tumor at 45 degrees. Initial temperature is 37
%degrees throughout sphere (only affected by the body temperature).

clear all
close all
clc

%tissue refers to the tumor; tissue constants
K_tissue= 0.42; %in W/m, thermal conductivity of the tissue
density_tissue = 920; %in kg/m^3, density of the tissue
specificheat_tissue= 3600; %in J/kg*degrees Celsius, specific heat of tissue,
3600 is another option from another source
diffusivity_tissue=K_tissue/(density_tissue*specificheat_tissue);

radius_tumor=0.01; %1 cm, converted to m; because tumor diameter is 2 cm,
which is a early stage 2 breast cancer tumor
r_distance=radius_tumor*2;

time_total=100; %100 seconds
dr=r_distance/10; %step size in for r distance (along radius of tumor)
dt=0.1; %step size in the t direction (time in seconds)

rmesh=0:dr:r_distance; %iterates to 2X the radius of the tumor, past the
tumor's surface and a distance r from the tumor surface
tmesh=0:dt:time_total; %iterates up to 100 seconds
rskip=2;
tskip=2;

number_iterations=10;

nr=length(rmesh);
nt=length(tmesh);

V=zeros(nt,nr);

for i=1:nr
    for j=1:nt
```

```
        for k=1:number_iterations %first ten terms of series (starts from zero
below)
            Z(k)=(-
16/(k*pi))*sin((k*pi*rmesh(i))/(2*radius_tumor))*exp(diffusivity_tissue*tmesh(
j)*(-((k*pi)/(2*radius_tumor))^2));
                %for each radius and time iteration gets Z value
        end

    steady_state(j,i)=((-4*rmesh(i))/radius_tumor)+45;

    V(j,i)=sum(Z)+steady_state(j,i);
    %sums up the homogeneous summation (left) and the steady state
    %response (right) and stores it into array
    end
end

temperature=V';

figure(1)
surf(tmesh(1:tskip:end),rmesh(1:rskip:end),temperature(1:rskip:end,1:tskip:end
), 'EdgeColor', 'none') %transpose of each array
title('Analytical Solution')
xlabel('Time in seconds')
ylabel('Radius length, in meters')
zlabel('Temperature, in degrees Celsius') %throughout the homogeneous cell
suspension


%-------------------------------------------------------------------------
%Plots temperature throughout the radius of the tumor at specific times listed
below (2D)

temperature_twentyfive_seconds=temperature(:,251); %because t_total=100
seconds and step size for is 0.1,
%so 250 steps to reach 25 seconds, but add 1 to it because it starts at t=0.
%the analysis is done in the columns because the mesh is (t,x)

temperature_fifty_seconds=temperature(:,501); %because t_total=100 seconds and
step size for is 0.1,
%so 500 steps to reach 50 seconds, but add 1 to it because it starts at t=0.
%the analysis is done in the columns because the mesh is (t,x)

temperature_hundred_seconds=temperature(:,1000);

figure(2)
plot(rmesh, temperature_twentyfive_seconds, 'ro-', rmesh,
temperature_fifty_seconds, 'g*-',rmesh,temperature_hundred_seconds,'m+-');
title('Temperature in Degrees Celsius of the Tumor');
xlabel('Radius, length in meters')
ylabel('Temperature, in degrees Celsius')
legend('At time=25 seconds', 'At time=50 seconds','At time=100 seconds');

%-------------------------------------------------------------------------
```

Part II: MATLAB Code For Model with Addition of Metabolic Heat Term

```
 %Ryan Tam
%Ultrasound beam focused on center of spherical tumor
%Modeled outside of tumor (length R away from the tumor on all sides) at
%body temperature, 37 degrees Celsius
%Assume no heat generation or perfusion in idealized model, but ultrasound
beam
%heats the center of the tumor at 45 degrees. Initial temperature is 37
%degrees throughout sphere (only affected by the body temperature).

clear all
close all
clc

%tissue refers to the tumor; tissue constants
K_tissue= 0.42; %in W/m, thermal conductivity of the tissue
density_tissue = 920; %in kg/m^3, density of the tissue
specificheat_tissue= 3600; %in J/kg*degrees Celsius, specific heat of tissue,
3600 is another option from another source
diffusivity_tissue=K_tissue/(density_tissue*specificheat_tissue);

%blood constants
perfusion_blood=9*10^-6; %tumor perfusion rate, in L/s
density_blood=1000; %1000 kg/m^3
specificheat_blood=3000; %in J/kg*degrees Celsius,
blood_constant=(perfusion_blood*density_blood*specificheat_blood)/K_tissue;

temperature_arteries=37; %given arterial temperature, degrees Celsius

radius_tumor=0.01; %1 cm, converted to m; because tumor diameter is 2 cm,
which is a early stage 2 breast cancer tumor
r_distance=radius_tumor*2;

time_total=100; %100 seconds
dr=r_distance/10; %step size in for r distance (along radius of tumor)
dt=0.1; %step size in the t direction (time in seconds)

rmesh=0:dr:r_distance; %iterates to 2X the radius of the tumor, past the
tumor's surface and a distance r from the tumor surface
tmesh=0:dt:time_total; %iterates up to 100 seconds
rskip=2;
tskip=2;

number_iterations=10;

nr=length(rmesh);
nt=length(tmesh);

V=zeros(nt,nr);
```

```
for i=1:nr
    for j=1:nt
        for k=1:number_iterations %first ten terms of series (starts from zero
below)

            first_term=(-8+temperature_arteries)*((-
2*radius_tumor)/(k*pi))*(cos(k*pi)-1);


second_term_one=(1/(2*sqrt(blood_constant))*sin((k*pi*sqrt(blood_constant))/(2
*radius_tumor))*cosint((k*pi*(2*radius_tumor-
sqrt(blood_constant)))/(2*radius_tumor)));

second_term_two=sin((k*pi*sqrt(blood_constant))/(2*radius_tumor))*cosint((k*pi
*(2*radius_tumor+sqrt(blood_constant)))/(2*radius_tumor));

second_term_three=cos((k*pi*sqrt(blood_constant))/(2*radius_tumor))*(sinint((k
*pi*(sqrt(blood_constant)-
2*radius_tumor))/(2*radius_tumor))+sinint((k*pi*(2*radius_tumor+sqrt(blood_con
stant)))/(2*radius_tumor)));

second_term_four=(1/(2*sqrt(blood_constant))*sin((k*pi*sqrt(blood_constant))/(
2*radius_tumor))*cosint((k*pi*(-sqrt(blood_constant)))/(2*radius_tumor)));

second_term_five=sin((k*pi*sqrt(blood_constant))/(2*radius_tumor))*cosint((k*p
i*(sqrt(blood_constant)))/(2*radius_tumor));

second_term_six=cos((k*pi*sqrt(blood_constant))/(2*radius_tumor))*(sinint((k*p
i*(sqrt(blood_constant)))/(2*radius_tumor))+sinint((k*pi*(sqrt(blood_constant)
))/(2*radius_tumor)));


second_term=(blood_constant*temperature_arteries)*(second_term_one+second_term
_two-second_term_three-second_term_four-second_term_five+second_term_six);

            third_term=((8-temperature_arteries-
((blood_constant*temperature_arteries)/((4*radius_tumor^2)-
blood_constant)))/(2*radius_tumor))*((-4*cos(k*pi)*radius_tumor^2)/(k*pi));

            b_term=(1/radius_tumor)*(first_term+second_term+third_term);


Z(k)=b_term*sin((k*pi*rmesh(i))/(2*radius_tumor))*exp(diffusivity_tissue*tmesh
(j)*(-((k*pi)/(2*radius_tumor))^2));
                %for each radius and time iteration gets Z value
        end

    steady_state(j,i)=(45-temperature_arteries)+((-
blood_constant*temperature_arteries)/(((rmesh(i))^2)-
blood_constant))+(rmesh(i)/(2*radius_tumor))*(-
8+temperature_arteries+((blood_constant*temperature_arteries)/((4*radius_tumor
^2)-blood_constant)));

    V(j,i)=sum(Z)+steady_state(j,i);
```

```
    %sums up the homogeneous summation (left) and the steady state
    %response (right) and stores it into array
    end
end

temperature=V';

figure(1)
surf(tmesh(1:tskip:end),rmesh(1:rskip:end),temperature(1:rskip:end,1:tskip:end
), 'EdgeColor', 'none') %transpose of each array
title('Analytical Solution, with Heat Perfusion to Arteries')
xlabel('Time in seconds')
ylabel('Radius length, in meters')
zlabel('Temperature, in degrees Celsius') %throughout the homogeneous cell
suspension


%-------------------------------------------------------------------------
%Plots temperature throughout the radius of the tumor at specific times listed
below (2D)

temperature_twentyfive_seconds=temperature(:,251); %because t_total=100
seconds and step size for is 0.1,
%so 250 steps to reach 25 seconds, but add 1 to it because it starts at t=0.
%the analysis is done in the columns because the mesh is (t,x)

temperature_fifty_seconds=temperature(:,501); %because t_total=100 seconds and
step size for is 0.1,
%so 500 steps to reach 50 seconds, but add 1 to it because it starts at t=0.
%the analysis is done in the columns because the mesh is (t,x)

temperature_hundred_seconds=temperature(:,1000);

figure(2)
plot(rmesh, temperature_twentyfive_seconds, 'ro-', rmesh,
temperature_fifty_seconds, 'g*-',rmesh,temperature_hundred_seconds,'m+-');
title('Temperature in Degrees Celsius of the Tumor');
xlabel('Radius, length in meters')
ylabel('Temperature, in degrees Celsius')
legend('At time=5 seconds', 'At time=25 seconds', 'At time=50 seconds','At
time=100 seconds');

%-------------------------------------------------------------------------
```