Heat Transfer Analysis for Breast Cancer Detection

By Yoni Danzig ([redacted])

& Maor Rosenberg([redacted])

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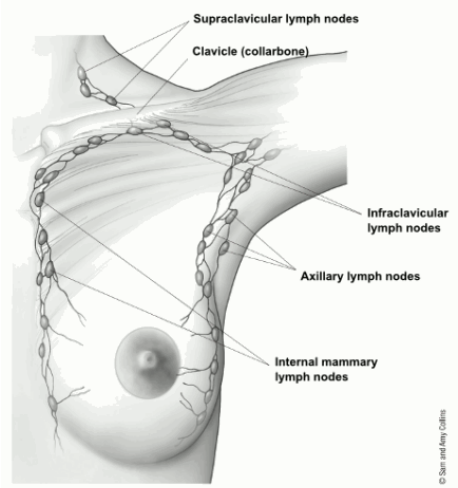
Introduction

Breast cancer is the most common cause of death in women and the second leading cause of cancer deaths worldwide. Primary prevention in the early stages of the disease becomes complex as the causes remain almost unknown.
However, there are several techniques to detect breast cancer at early stages:

- Mammography
- Ultrasound
- MRI
- Microwave Imaging
- Breast thermography



Lymph nodes in relation to the breast

In this paper we will give the background for breast cancer, detail the different applications for diagnosis of breast cancer with emphasis on the Thermography application and give Numerical simulation based on the governing equations of the heat transfer in the breast.

The breast cancer

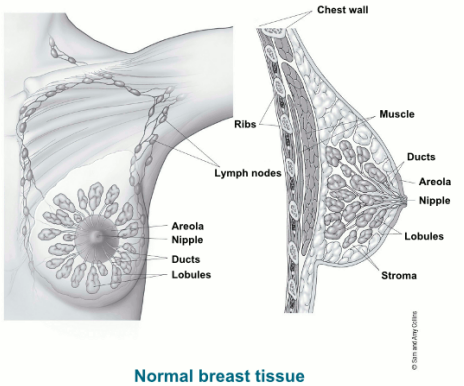
Breast cancer is a malignant tumor - a group of cancer cells that can invade surrounding tissues or spread to distant areas of the body. The disease occurs almost entirely in women, but men can get it, too.

The female breast is made up mainly of:

Lobules - milk producing glands.

Ducts – tiny tubes that carry the milk to the nipple.

Stroma – tissue surrounding the ducts and lobules, blood vessels and lymphatic vessels.



Normal breast tissue

Cancer can spread through tissue, the lymph system and the blood.

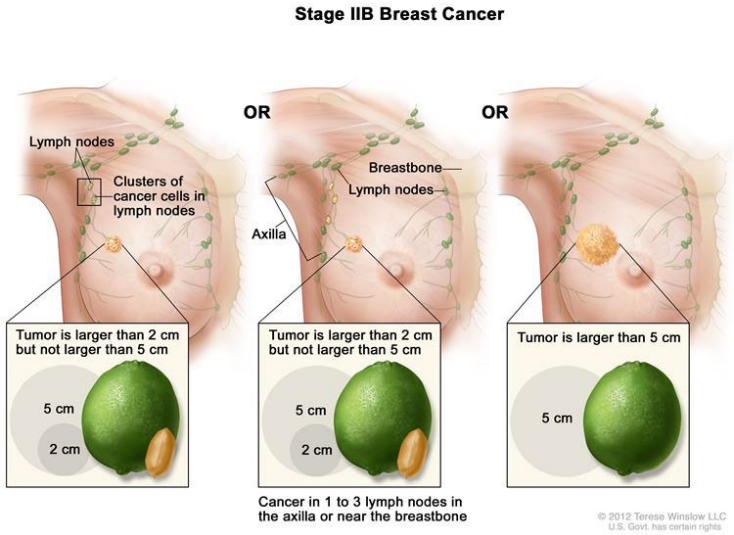
This lymph system has several parts:

Lymph nodes – small, bean shaped collections of immune system cells that are connected by lymphatic vessels.

Lymphatic vessels – small veins like, that carry a clear fluid called lymph (instead of blood) away from the breast.

Lymph – contains tissue fluid, waste product, immune system cells

Tumor grading is a system used to classify a malignant breast cancer tumor based upon the severity of the mutation and the likelihood that it will spread.



Stage 2 breast cancer:

- 5cm >tumor > 2 cm and small clusters of cancer cells in lymph node
- 5cm >tumor > 2 cm and cancer is found in 1 to 3 axillary lymph nodes or lymph nodes near the breastbone
- tumor > 5 cm and has not spread to the lymph nodes

Different applications for breast cancer diagnosis

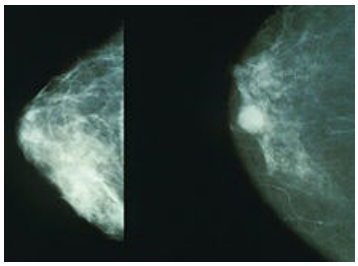
Mammography

Mammography is the process of using low-energy X-rays (usually around 30 kVp) to examine the human breast.

It has been the gold standard for screening breast cancer, though as a screening tool its sensitivity and specificity are limited.

The risks and challenges of Mammography:

The sensitivity of mammography in the general population is believed to reside between 75% to 90% with a positive predictive value of only 25%.



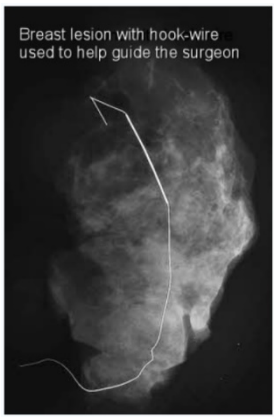
It may be influenced by age, breast density, and family history. The radiation exposure associated with mammography is a potential risk of screening. The risk of exposure appears to be greater in younger women.

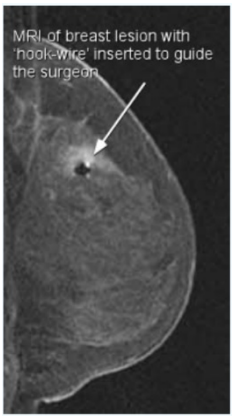
Ultrasound

Uses high-frequency sound waves to produce an image of the inside of breasts, showing any lumps or abnormalities. A transducer is placed on the skin and emits sound waves and picks up the echoes as they bounce off body tissues. The echoes are converted by computer into a black and white image on a computer screen.

MRI

Breast MRI is often used in women who already have been diagnosed with breast cancer, to help measure the size of the cancer, look for other tumors in the breast, and to check for tumors in the opposite breast.





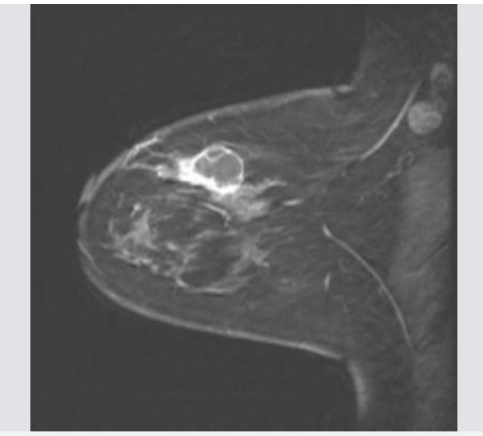
For certain women at high risk for breast cancer, a screening MRI is recommended along with an early mammogram. MRI is not recommended as a screening test by itself because it can miss some cancers that a mammogram would find.

Although MRI can find some cancers not seen on a mammogram, it's also more likely to find something that turns out not to be cancer (called a false positive). False-positive findings must be checked out to know that cancer isn't present. This can mean more tests and/or biopsies. This is why MRI is not recommended as a screening test for women at average risk of breast cancer, because it would result in unneeded biopsies and other tests for many of these women.

Microwave Imaging

Microwave imaging for medical applications has been of interest for many years. Microwave images are maps of the electrical property distributions in the body. The electrical properties of various tissues may be related to their physiological state. For example, the properties of tissues change with temperature.

One application of microwave imaging that has been proposed is monitoring hyperthermia, which is the application of heat to tissue. In this case, the changing electrical properties indicate the successful deposition of heat in the tissue of interest. Other changes in electrical properties may be caused by disease.



Microwave imaging can be used to monitor how well treatment for breast cancer is working.

There is some evidence of changes in the properties of cancerous tissues when compared to normal tissues. Cancer detection with microwave imaging is based on this contrast in electrical properties.

Breast Thermography

Thermography is the term used to describe the technique of mapping skin temperature patterns and the interpretation of that information to assess physiologic status.
The temperature map is typically obtained with a scanning infrared radiometer; a CRT typically provides a visual image of the map. Temperature levels may be displayed by various shades of grey or by colors representing discrete temperature levels.

The use of digital infrared imaging is based on the principle that metabolic activity and vascular circulation in both pre-cancerous tissue and the area surrounding a developing breast cancer is almost always higher than in normal breast tissue. In an ever-increasing need for nutrients, cancerous tumours increase circulation to their cells by holding open existing blood vessels, opening dormant vessels, and creating new ones (neoangiogenesis). This process frequently results in an increase in regional surface temperatures of the breast.

Infrared Radiation is emitted from objects with a temperature above absolute zero at wavelengths between 0.8 µm and 1.0 µm. Therefore, accurate temperature values can be recorded from measurements of the infrared radiation from the skin.
The procedure is carried out using an ultra-sensitive medical infrared cameras and sophisticated computers to detect, analyse, and produce high-resolution images of these temperature variations.

Thermography has the obvious advantage of being a non-invasive technique that provides the physician with a spatially coherent map of surface temperature.

The primary disadvantages of thermography are related to the lack of specificity of the examination and the careful control of environmental conditions and instrument calibration that are required.

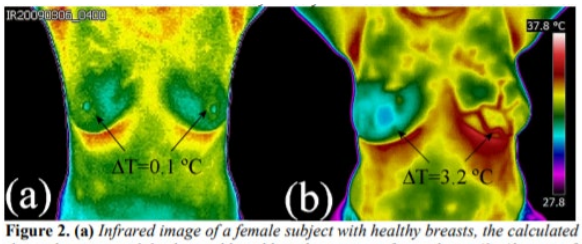
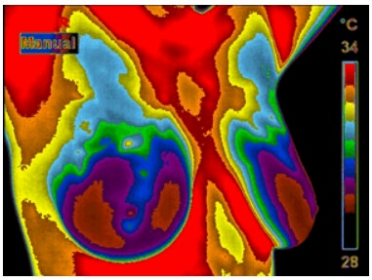
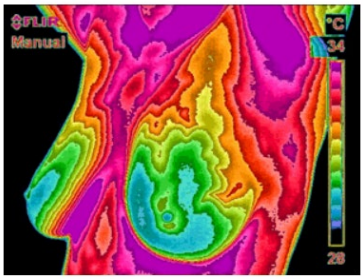
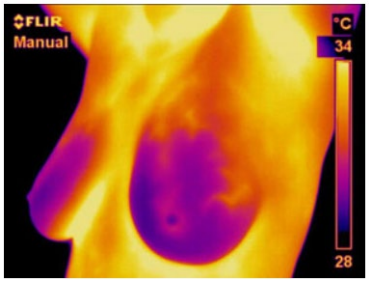


Figure 2. (a) *Infrared image of a female subject with healthy breasts, the calculated thermal score was 1.1, obtained by adding the amount of vascularity (1: Absence of vascular patterns) and 0.1 (difference in surface temperature, ΔT, at the lesion site compared to the contralateral breast).* **(b)** *Infrared image of a female subject with infiltrating ductal carcinoma in her left breast, mammography showed a 2 cm tumor at a depth of 1.2 cm from the skin surface, the calculated thermal score was 7.2, obtained by adding the amount of vascularity (4: Extended vascular asymmetry in at*







Governing equations and numerical simulation

In this paper we will examine and analyze the influence of breast tumor on the heat transfer of the whole breast tissue.
The above will be demonstrated by finding the surface temperature of the breast examined through simulation of 3 different cases:

1. A round ball of tissue (represent a healthy breast) in a room temperature and without prefusion and metabolic heat generation.
2. A round ball of tissue (represent a healthy breast) in a room temperature and with prefusion and metabolic heat generation.
3. A round ball that contains a smaller concentric ball (represent the tumor) inside of it, which has an increased prefusion and metabolic heat generation properties similar to a carcinogenic tissue.

To complete the analyses, we will present the influence of a different tumors properties (perfusion and metabolic heat generation) on the surface temperature of the breast.
By that we will provide the association between the size of the tumor and the breast surface temperature.

Case Number 1

A round ball of tissue (represent the breast) in a room temperature and without prefusion and metabolic heat generation.

$$T_a = T_\infty$$

Let us develop the second order differential equation using the control volume with a thickness of dr:

$$\rho C_p \frac{\partial T}{\partial t} \cdot 4\pi r^2 dr = \left[-k\frac{\partial T}{\partial r}4\pi r^2\right]_r - \left[-k\frac{\partial T}{\partial r}4\pi r^2\right]_{r+dr} /* \frac{1}{4\pi r^2 dr}$$

$$\rho C_p \frac{\partial T}{\partial t} = \frac{\left[k\frac{\partial T}{\partial r}r^2\right]_{r+dr} - \left[k\frac{\partial T}{\partial r}r^2\right]_r}{r^2 dr} = \frac{k}{r^2}\frac{\partial}{\partial r}\left[\frac{\partial T}{\partial r}r^2\right]$$

$$\boxed{\frac{1}{\alpha}\frac{\partial T}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\left[r^2\frac{\partial T}{\partial r}\right]} \; or \; \boxed{\frac{\partial T}{\partial t} = \alpha\left[\frac{\partial^2 T}{\partial r^2} + \frac{2}{r}\frac{\partial T}{\partial r}\right]}$$

When:

$$\frac{1}{\alpha} = \frac{\rho C_p}{k}$$

We obtained a second-order differential equation. this equation represents the heat transfer behavior inside the ball and the solution for this equation will demonstrate the heat distribution vs. the ball radius and time.

The initial condition:

$$T(\mathrm{r}, \mathrm{t} = 0) = T_0 = T_b$$

The 2 boundary conditions:

1. From the symmetry of the problem:

$$\left[\frac{\partial \mathrm{T}}{\partial r}\right]_{r=0} = 0$$

2. From Newton boundary condition on the surface:

$$\left[-k\frac{\partial \mathrm{T}}{\partial \mathrm{r}}\right]_{r=R} = h_r(T_{r=R} - T_a)$$

h_r – Is the radiation heat transfer coefficient that can be calculated using the approximation of a correlation of a small body in distant environment.

$$h_r = \epsilon_0\sigma(T_0^2 + T_a^2)(T_0 + T_a)$$

In order to solve this equation analytically we will have to normalize the equation and the boundary and initial conditions as well:

$$\tilde{T}(r,t) = T - T_a \Rightarrow T = \tilde{T} + T_a$$

$$\theta(r,t) = \tilde{T}(r,t) * r \Rightarrow \tilde{T}(r,t) = \frac{\theta(r,t)}{r} \Rightarrow T = \frac{\theta(r,t)}{r} + T_a$$

We will substitute T into the differential equation:

$$\frac{1}{\alpha r}\frac{\partial \theta}{\partial \mathrm{t}} = \frac{1}{\mathrm{r}^2}\frac{\partial}{\partial \mathrm{r}}\left[\mathrm{r}^2\frac{\partial}{\partial \mathrm{r}}\left[\underbrace{\frac{\theta(r,t)}{r}}_{u*v}\right]\right] = \frac{1}{\mathrm{r}^2}\frac{\partial}{\partial \mathrm{r}}\left[\mathrm{r}^2\left(\frac{\partial \theta}{\mathrm{r}\,\partial \mathrm{r}} - \frac{\theta}{r^2}\right)\right] = \frac{1}{\mathrm{r}^2}\frac{\partial}{\partial \mathrm{r}}\left[\frac{\partial \theta}{\partial \mathrm{r}}r - \theta\right] = \frac{1}{\mathrm{r}^2}\left[\frac{\partial}{\partial \mathrm{r}}\left(\underbrace{\frac{\partial \theta}{\partial \mathrm{r}}r}_{u*v}\right) - \frac{\partial \theta}{\partial \mathrm{r}}\right]$$

$$= \frac{1}{\mathrm{r}^2}\left[\frac{\partial^2 \theta}{\partial \mathrm{r}^2}r + \frac{\partial \theta}{\partial \mathrm{r}} - \frac{\partial \theta}{\partial \mathrm{r}}\right] = \frac{1}{\mathrm{r}^2}\left[\frac{\partial^2 \theta}{\partial \mathrm{r}^2}r\right] = \frac{1}{\mathrm{r}}\left[\frac{\partial^2 \theta}{\partial \mathrm{r}^2}\right]$$

So that:

$$\boxed{\frac{1}{\alpha}\frac{\partial \theta}{\partial \mathrm{t}} = \frac{\partial^2 \theta}{\partial \mathrm{r}^2}}$$

We will look to solve the equation by separating the variables:

$$\theta(r,t) = R(r) * \tau(t)$$

Substituting in the equation above:

$$\frac{1}{\alpha} R(r)\tau'(t) = R''(r)\tau(t) /* \frac{1}{R(r)\tau(t)}$$

$$\frac{1}{\alpha}\frac{\tau'(t)}{\tau(t)} = \frac{R''(r)}{R(r)} = -\lambda^2$$

Later, we will return to this relation we just received.

In the meanwhile, we will continue to convert the boundary and initial conditions.

from normalizing the initial and boundary condition we receive the equation bellow:

$$T(r,t) = \frac{\theta(r,t)}{r} + T_a$$

In order to convert the initial conditions, we'll substitute the above:

$$T(\mathrm{r,t} = 0) = T_0 => T_0 - T_a = \frac{\theta(r,0)}{r}$$

From the first boundary condition:

$$\left[\frac{\partial \mathrm{T}}{\partial r}\right]_{r=0} = 0 => \left[\frac{\partial\left(\frac{\theta(r,t)}{r} + T_a\right)}{\partial r}\right]_{r=0} = \left[\frac{\partial\theta}{\partial r}\cdot\frac{1}{r} - \frac{\theta}{r^2}\right]_{r=0} = 0$$

We will substitute the solution:

$$\theta(r,t) = R(r) * \tau(t)$$

Into the equation and we'll receive:

$$\left[R'(r) * \tau(t)\cdot\frac{1}{r} - \frac{R(r) * \tau(t)}{r^2}\right]_{r=0} = 0 /\cdot \frac{r^2}{\tau(t)} \qquad \tau(t) \neq 0$$

$$[R'(r) * r - R(r)]_{r=0} => R(r=0) = 0$$

For the second boundary condition we will substitute: $T = \frac{\theta(r,t)}{r} + T_a$

$$\left[-k\frac{\partial \mathrm{T}}{\partial \mathrm{r}}\right]_{r=R} = h_r(T_{r=R} - T_a) => \left[-k\frac{\partial\left(\frac{\theta(r,t)}{r} + T_a\right)}{\partial \mathrm{r}}\right]_{r=R} = h_r\left(\frac{\theta(R,t)}{R} + T_a - T_a\right) = h_r\frac{\theta(R,t)}{R}$$

$$\left[-k\left(\frac{\partial\theta(r,t)}{\mathrm{r}\,\partial r} - \frac{\theta(r,t)}{r^2}\right)\right]_{r=R} = h_r\frac{\theta(R,t)}{R}$$

We will substitute again the solution we are looking for:

$$\theta(r,t) = R(r) * \tau(t)$$

$$\left[\frac{R'(r)\tau(t)}{r} - \frac{R(r)\tau(t)}{r^2}\right]_{r=R} = -\frac{h_r}{k}\frac{R(R)*\tau(t)}{R}$$

$$\frac{R'(R)\cancel{\tau(t)}}{R} - \frac{R(R)\cancel{\tau(t)}}{R^2} = -\frac{h_r}{k}\frac{R(R)*\cancel{\tau(t)}}{R} /: \tau(t) \neq 0$$

$$\frac{R'(R)}{R} - \frac{R(R)}{R^2} = -\frac{h_r}{k}\frac{R(R)}{R} /* R$$

$$R'(R) - R(R)\left[\frac{1}{R} - \frac{h_r}{k}\right] = 0$$

We will now return to the relation we left above after substituting θ and develop 2 equations:

$$\frac{1}{\alpha}\frac{\tau'(t)}{\tau(t)} = \frac{R''(r)}{R(r)} = -\lambda^2 =>$$

$$I) R''(r) + \lambda^2 R(r) = 0 \qquad \text{II) } \tau'(t) + \alpha\lambda^2\tau(t) = 0$$

We will solve the first equation:

$$R''(r) + \lambda^2 R(r) = 0 => y^2 + \lambda^2 = 0 => y = \pm\lambda => \mathrm{R(r)} = \mathrm{Asin(\lambda r)} + \mathrm{Bcos(\lambda r)}$$

We'll find the constant by substitution in the first boundary condition:

$$R(r = 0) = 0 => \mathrm{Asin(\lambda r)} + \mathrm{B}\underbrace{\cos(\lambda * 0)}_{1} = 0 => B = 0$$

Hence:

$$\mathrm{R(r)} = \mathrm{Asin(\lambda r)}$$

A reminder from the mathematic development above:

$$R'(R) - R(R)\left[\frac{1}{R} - \frac{h_r}{k}\right] = 0$$

We'll substitute R(r) into it:

$$\lambda \mathrm{A}\cos(\lambda \mathrm{R}) = \mathrm{A}\sin(\lambda \mathrm{R})\left[\frac{1}{R} - \frac{h_r}{k}\right] /: \cos(\lambda R)$$

$$\lambda = \left[\frac{1}{R} - \frac{h_r}{k}\right]\tan(\lambda \mathrm{R}) => \lambda_n = \lambda_n|_{n=1,2,3\ldots,\infty}$$

The solution for this equation is an infinite values of Lambda.

Solving equation 2:

$$\text{II)}\ \tau'(t) + \alpha\lambda^2\tau(t) = 0 => \tau(t) = \mathrm{C}e^{-\alpha\lambda_n^2 t}$$

Hence the general solution for (r, t) :

$$\theta(r, t) = \mathrm{AC} * \mathrm{e}^{-\alpha\lambda_n^2 t}\sin(\lambda_\mathrm{n}\mathrm{r})$$

The equation is linear that's why any linear combination of the solution is also a decent solution:

$$\theta(r, t) = \sum_{n=1}^{\infty} \mathrm{C_n} * \mathrm{e}^{-\alpha\lambda_n^2 t}\sin(\lambda_\mathrm{n}\mathrm{r})$$

Based on the orthogonality properties and the initial conditions of θ we have left to find the constants $\mathrm{C_n}$.

from the initial condition:

$$T_0 - T_a = \frac{\theta(r, t=0)}{r} = \frac{1}{r}\sum_{n=1}^{\infty} \mathrm{C_n} * \sin(\lambda_\mathrm{n}\mathrm{r})$$

Now we will integrate from 0 to R and multiply both sides of the equation by $\sin(\lambda_\mathrm{m}\mathrm{r})$:

$$\int_{r=0}^{R}\sum_{n=1}^{\infty} \mathrm{C_n} * \sin(\lambda_\mathrm{n}\mathrm{r})\sin(\lambda_\mathrm{m}\mathrm{r})\,\mathrm{dr} = \int_0^R r(T_0 - T_a)\sin(\lambda_\mathrm{m}\mathrm{r})dr$$

$$\sum_{n=1}^{\infty} \mathrm{C_n} \underbrace{\int_{r=0}^{R} \sin(\lambda_\mathrm{n}\mathrm{r})\sin(\lambda_\mathrm{m}\mathrm{r})dr}_{X} = (T_0 - T_a)\underbrace{\int_0^R r\sin(\lambda_\mathrm{m}\mathrm{r})dr}_{Y}$$

For X, the inner sin() function are orthogonal hence the integral solution is:

$$X = \int_{r=0}^{R} \sin(\lambda_n r)\sin(\lambda_m r)dr = \begin{cases} 0, & m \neq n \\ \frac{R}{2} - \frac{\sin(2\lambda_m R)}{4\lambda_m}, & m = n \end{cases}$$

When $m = n$, the solution of X is:

$$X_{|m=n} = \int_{r=0}^{R} \sin^2(\lambda_m r)\, dr = \int_{r=0}^{R} \frac{1-\cos(2\lambda_m r)}{2} dr = \frac{1}{2}\int_{r=0}^{R} dr - \frac{1}{2}\int_{r=0}^{R} \cos(2\lambda_m r)\, dr = \frac{R}{2} - \frac{\sin(2\lambda_m R)}{4\lambda_m}$$

Or in other words:

$$X = \left(\frac{R}{2} - \frac{\sin(2\lambda_m R)}{4\lambda_m}\right) \cdot \delta_{mn}$$

Now we will calculate Y:

$$Y = \int_{0}^{R} r\sin(\lambda_m r)dr = \frac{\sin(\lambda_m R)}{\lambda_m^2} - \frac{R\cos(\lambda_m R)}{\lambda_m}$$

$$\boxed{C_n = \frac{Y(T_0 - T_a)}{X} = \frac{\left[\frac{\sin(\lambda_n R)}{\lambda_n^2} - \frac{R\cos(\lambda_n R)}{\lambda_n}\right](T_0 - T_a)}{\left(\frac{R}{2} - \frac{\sin(2\lambda_n R)}{4\lambda_n}\right)}}$$

And the solution is:

$$\theta(r,t) = \sum_{n=1}^{\infty} C_n * e^{-\alpha\lambda_n^2 t}\sin(\lambda_n r)$$

We will return to original parameter T and will write the final solution:

$$T(r,t) = \frac{\theta(r,t)}{r} + T_a$$

$$\boxed{T(r,t) = T_a + \sum_{n=1}^{\infty} C_n \cdot e^{-\alpha\lambda_n^2 t} \cdot \frac{\sin(\lambda_n r)}{r}} \quad \lambda = \left[\frac{1}{R} - \frac{h_r}{k}\right]\tan(\lambda R) => \lambda_n = \lambda_n|_{n=1,2,3\ldots,\infty}$$

To simulate our problem, we will choose the following parameters (3):

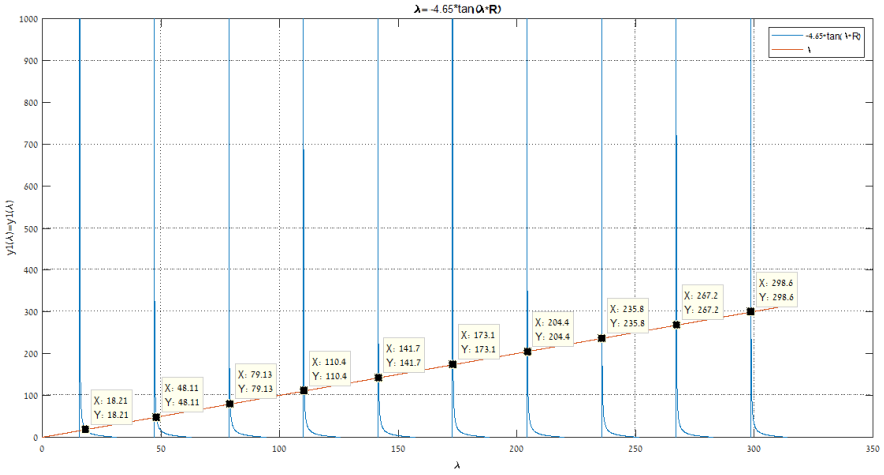
$$\mathrm{R} = 10cm,\quad T_a = 298°K[24℃],\quad T_0 = 310°K[37℃],\quad k_{tissue} = 0.42\left[\frac{W}{mk}\right],$$
$$\rho = 920\left[\frac{kg}{m^3}\right],\quad C_p = 3000\left[\frac{J}{kg\cdot K}\right]$$

For a small element in a remote environment the radiation can be proximate by the following:

$$h_r = \epsilon_0\sigma(T_0^2 + T_a^2)(T_0 + T_a) = 0.97 * 5.67 * 10^{-8} * (310^2 + 298^2)(310 + 298)$$
$$\cong 6.15\left[\frac{W}{m^2k}\right]$$

We will find now the 10th first values of λ_n:

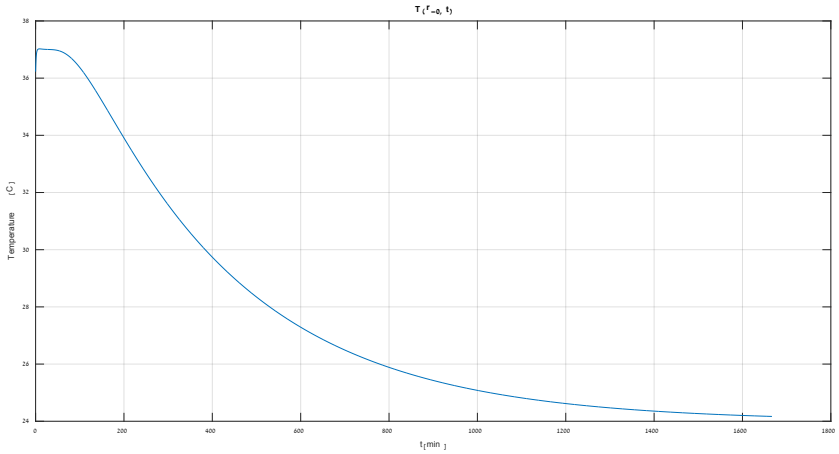
$$\lambda = \left[\frac{1}{R} - \frac{h_r}{k}\right]\tan(\lambda\mathrm{R}) = \left[\frac{1}{10cm} - \frac{6.15}{0.42}\right]\tan(\lambda\mathrm{R}) = -4.64\tan(\lambda\cdot 10 * 10^{-2})$$



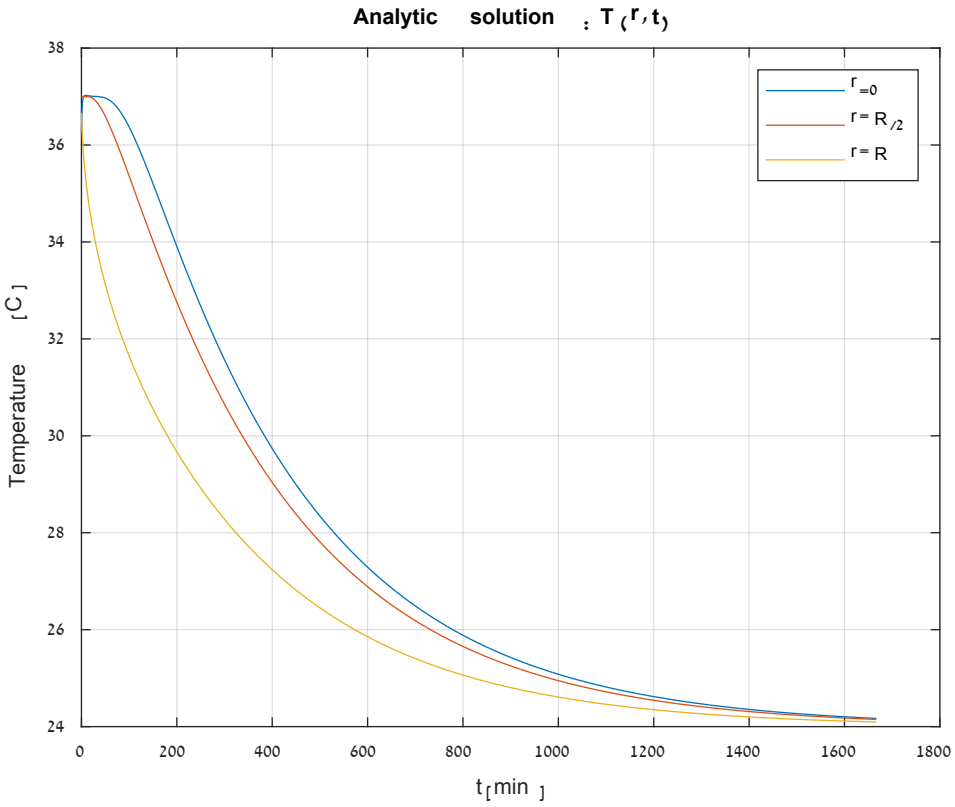
We calculated the following values:

$$\lambda_1 = 18.21, \lambda_2 = 48.11, \lambda_3 = 79.13, \ldots, \lambda_{10} = 298.6$$

The temperature change at the center of the breast:

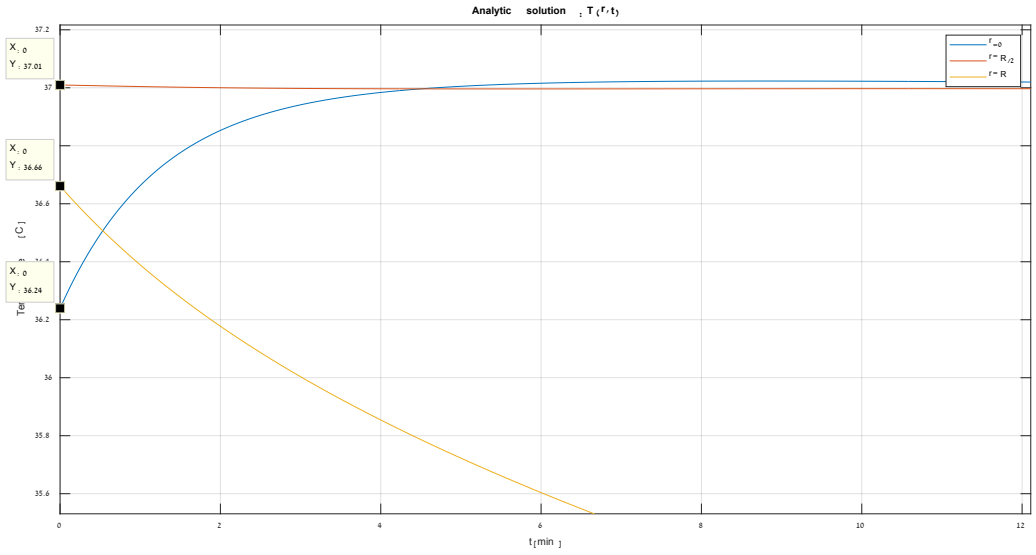


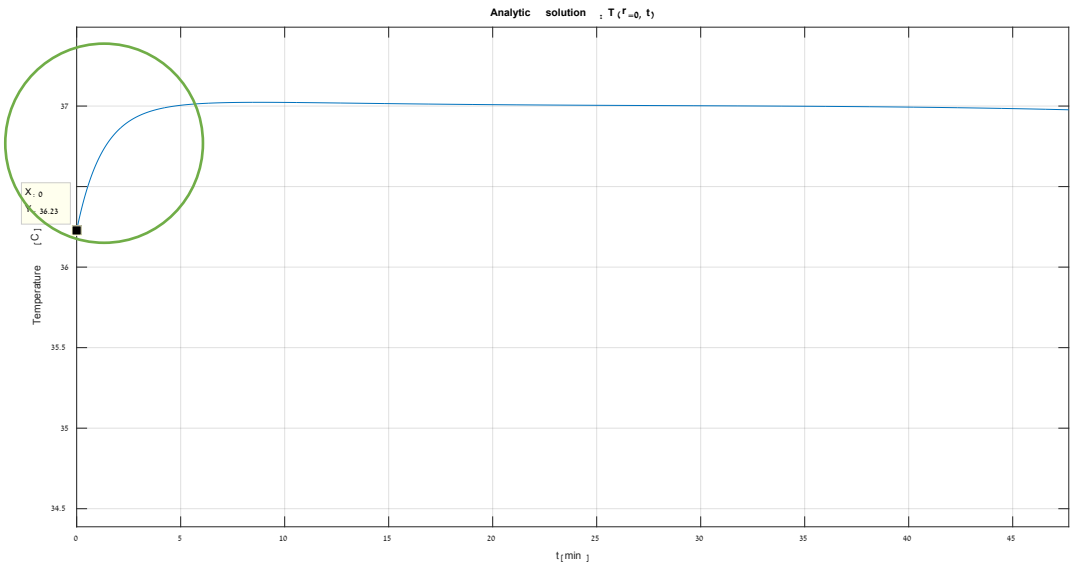
The temperature change in 3 different radiuses along the breast:



We can clearly see that the temperature decrease on the breast surface is the highest – A reasonable result caused by the fact, the surface directly exposed to the environment temperature. (24 °C)

We can notice the slight error in our solution:





At t=0, we notice a "jump" and the temperature did not start at 37°C as expected.

It is desired to choose an endless number of λ_n, but we took in consideration only 10 value due to the fact our solution is analytic and not numeric. That is the reason we received the "jump" above.

Now we will solve the same problem with a numerical simulation using the MATLAB built-in function pdepe (7).

This function parameters are as followed:

$$sol = pdepe(m, pdefun, icfun, bcfun, xmesh, tspan)$$

A short explanation of the function:

m - A parameter corresponding to the symmetry of the problem. m can be slab = 0, cylindrical = 1, or spherical = 2.

Pdefun - A handle to a function that defines the components of the differential equation

Icfun – A handle to a function that defines the initial conditions.

Bcfun - A handle to a function that defines the boundary conditions.

Xmesh - A vector [x0, x1, ..., xn] specifying the points at which a numerical solution is requested for every value in tspan.

Tspan - A vector [t0, t1, ..., tf] specifying the points at which a solution is requested for every value in xmesh.

The structure of the differential equation should be design as followed:

$$C(x,t,u,\frac{du}{dx})\cdot\frac{du}{dt}=x^{-m}\cdot\frac{d}{dx}\left[x^{m}\underbrace{f\left(x,t,u,\frac{du}{dx}\right)}_{\text{usually}=\frac{du}{dx}}\right]+s(x,t,u,\frac{du}{dx})$$

Our differential equation from the calculation above:

$$\frac{1}{\alpha}\frac{\partial T}{\partial t}=\frac{1}{r^2}\frac{\partial}{\partial r}\left[r^2\frac{\partial T}{\partial r}\right]$$

We will reshape it so it could be substitute in the MATLAB function:

$$\frac{1}{\alpha}\frac{\partial T}{\partial t}=r^{-2}\frac{\partial}{\partial r}\left[r^2\frac{\partial T}{\partial r}\right]+0$$

So the function arguments are:

$$C=\frac{1}{\alpha},m=2,x=r,u=T,s=0,f=\frac{du}{dx}$$

The main MATLAB function we built:

```
function  pde1
%PDE1 main function solving numerically
R = 10*10^-2; %[m]
m = 2;
x = linspace(0,R,20);         %we will see a change in radius range
t = linspace(0,1600*60,106); %we will see a change every ~15 min
sol = pdepe(m,@pdefun,@icfun,@bcfun,x,t);
% Extract the first solution component as u.
u = sol(:,:,1);

% A surface plot is often a good way to study a solution.
surf(x,t/60,u)
title('Numerical solution computed with 20 mesh points.')
xlabel('Distance r[m]');
ylabel('Time - t[min]');
zlabel('Temperature [C]');
```

The secondary functions are:

```
function [c,f,s] = pdefun(x,t,u,DuDx)
rho=920;          %[kg/m^3]
cp=3000;          %[J/kgK]
k=0.42;           %[W/m*k]
alpha=k/(rho*cp);%[m^2/s]
c = 1/alpha;
f = DuDx;
s = 0;
end
```

$C=\frac{1}{\alpha},m=2,x=r,u=T,s=0,f=\frac{du}{dx}$

The initial problem condition in the MATLAB will be define as:

Remainder: $T(\mathrm{r}, \mathrm{t}=0)=T_0$

```
function u0 = icfun(x)
%Initial condition function
T_0 = 37; %[C] initial temperature
u0 = T_0;
```

And for the 2 boundary conditions:

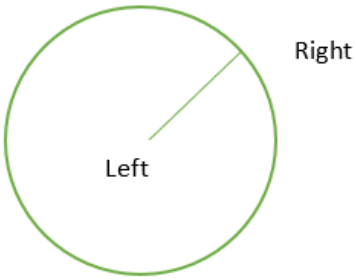
1. From the symmetry of the problem:

$$\left[\frac{\partial \mathrm{T}}{\partial r}\right]_{r=0}=0$$

2. From Newton boundary condition on the surface:

$$\left[-k\frac{\partial \mathrm{T}}{\partial \mathrm{r}}\right]_{r=R}=h_r(T_{r=R}-T_a)$$

We will describe the boundary line from the left to the right:



We shell reshape the boundary condition as well so it will fit the MATLAB structure:

$$\boxed{p+qf=0}$$

At the left side of the round ball we can state:

$$\frac{\partial \mathrm{T}}{\partial r}=\frac{\partial \mathrm{U}}{\partial x}=>\underbrace{0}_{P}+\underbrace{1}_{q}*\underbrace{\frac{\partial \mathrm{U}}{\partial x}}_{f}=0=>\boxed{p=0, q=1}$$

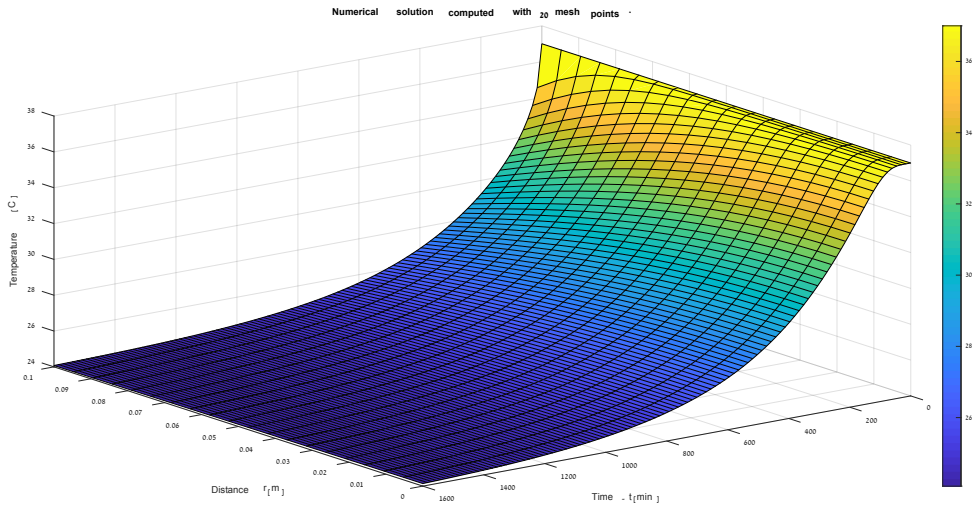
At the right side (on the surface) of the round ball we can state:

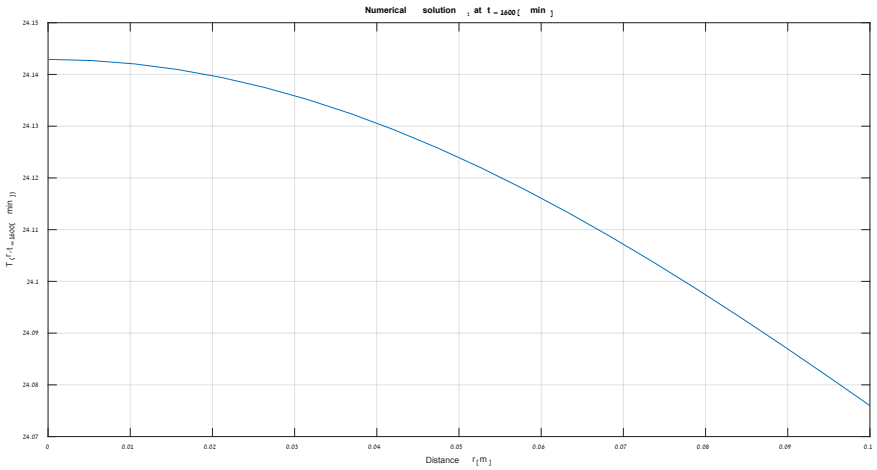
$$\underbrace{\frac{h_r}{k}(T_{r=R}-T_a)}_{p}+\underbrace{1}_{q}*\underbrace{\frac{\partial \mathrm{U}}{\partial \mathrm{x}}}_{f}=0=>\boxed{p=\frac{h_r}{k}(ur-T_a), q=1}$$

Hence the MATLAB function will be:

```
function [pl,ql,pr,qr] = pdex1bc(xl,ul,xr,ur,t)
%Boundary condition function
%r=right l=left, form is p + qf = 0
%Parameters calculation:
T_0=37;                     %[C]
T_a=24;                     %[C]
rho=920;                    %[kg/m^3]
cp=3000;                    %[J/kgK]
k=0.42;                     %[W/m*k]
eps=0.97;                   %skin emissivity
sigma=5.67*10^-8;           %[W*m^-2*K^-4] Boltzmann constant
                            %hr=6.1530;%[W*m^-2*K^-1]
hr=eps*sigma*((T_0+273)^2+(T_a+273)^2)*(T_0+T_a+2*273);%[W*m^-2*K^-1]
%function form: p + qf = 0 for right and left
pl = 0;
ql = 1;
pr = (hr/k)*(ur-T_a);
qr = 1;
end
```

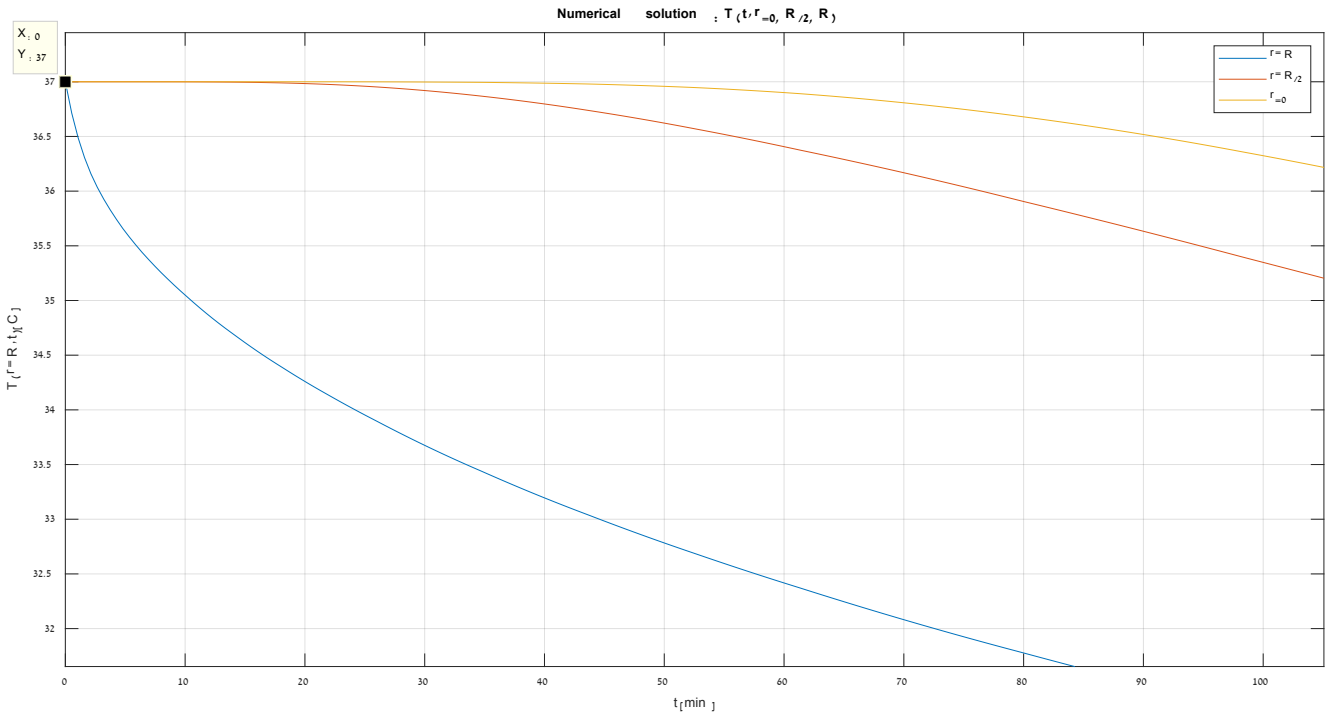
The plotted graph from the main function is as followed:





As we mentioned earlier, the analytic solution consists an error that the numerical solution doesn't, thanks to the fact that the numerical solution is more accurate.

All the graphs, now starts from 37°C as expected:



Case Number 2

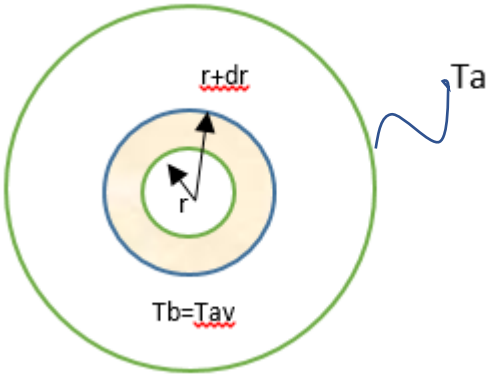
For a round ball with profusion and metabolic heat generation – Healthy Tissue

Prefusion parameters – $\rho_b, \omega_b, c_{p_b}, T_{av}$

Tissue parameters – ρ, C_p, k, T_b

Meatabolic heat generation – q_m

Arterial blood temperature -- T_{av}



Analyzing the control volume, gives us the following equation:

$$\rho C_p \frac{\partial T}{\partial t} \cdot 4\pi r^2 dr = \left[-k\frac{\partial T}{\partial r}4\pi r^2\right]_r - \left[-k\frac{\partial T}{\partial r}4\pi r^2\right]_{r+dr} - \rho\omega c_p(T - T_{av})4\pi r^2 dr + q_m 4\pi r^2 dr / * \frac{1}{4\pi r^2 dr}$$

$$\rho C_p \frac{\partial T}{\partial t} = \frac{\left[k\frac{\partial T}{\partial r}r^2\right]_{r+dr} - \left[k\frac{\partial T}{\partial r}r^2\right]_r}{r^2 dr} - \rho\omega c_p(T - T_{av}) + q_m$$

$$= \frac{k}{r^2}\frac{\partial}{\partial r}\left[\frac{\partial T}{\partial r}r^2\right] - \rho\omega c_p(T - T_{av}) + q_m$$

$$\boxed{\frac{1}{\alpha}\frac{\partial T}{\partial t} = \frac{1}{r^2}\frac{\partial}{\partial r}\left[r^2\frac{\partial T}{\partial r}\right] - \rho_b\omega_b c_{p_b}(T - T_{av}) + q_m}$$

While:

$$\frac{1}{\alpha} = \frac{\rho C_p}{k}$$

As before, the initial condition:

$$T(r, t = 0) = T_0 = T_b$$

And the 2 boundary conditions:

1. From the symmetry of the problem:

$$\left[\frac{\partial \mathrm{T}}{\partial r}\right]_{r=0} = 0$$

2. Newton boundary condition on the surface:

$$\left[-k\frac{\partial \mathrm{T}}{\partial \mathrm{r}}\right]_{r=R} = h_r(T_{r=R} - T_a)$$

Remainder about the MATLAB structure we need to follow:

$$\mathrm{C}\left(x,t,u,\frac{du}{dx}\right)\cdot\frac{du}{dt} = x^{-m}\cdot\frac{d}{dx}\left[x^m \underbrace{f\left(x,t,u,\frac{du}{dx}\right)}_{\text{usually}=\frac{du}{dx}}\right] + s\left(x,t,u,\frac{du}{dx}\right)$$

So our equation will be in the form of:

$$\frac{1}{\alpha}\frac{\partial \mathrm{T}}{\partial \mathrm{t}} = r^{-2}\frac{\partial}{\partial \mathrm{r}}\left[\mathrm{r}^2\frac{\partial \mathrm{T}}{\partial \mathrm{r}}\right] - \rho_b\omega_b c_{p_b}(T - T_{av}) + q_m$$

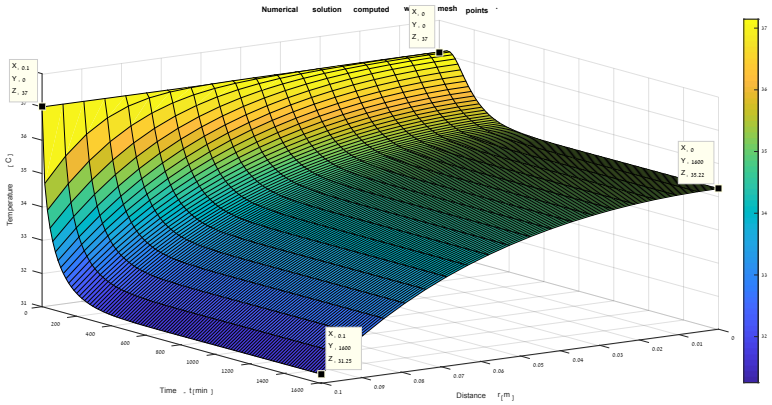
$$\mathrm{C} = \frac{1}{\alpha}, \mathrm{m} = 2, \mathrm{x} = \mathrm{r}, \mathrm{u} = \mathrm{T}, f = \frac{du}{dx}, s = q_m - \rho_b\omega_b c_{p_b}(u - T_{av})$$

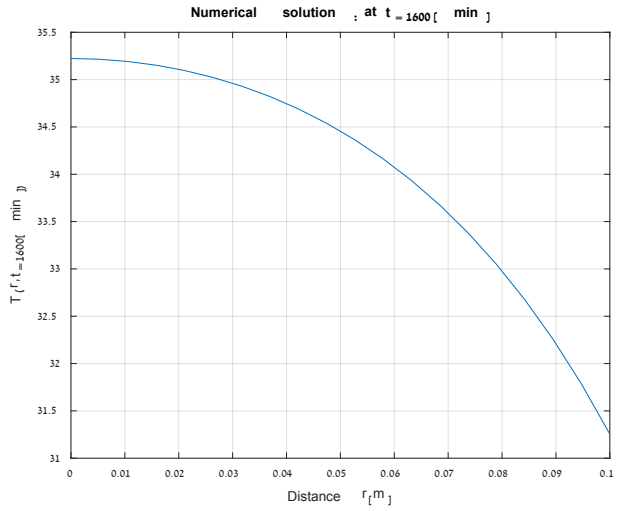
We will modify the MATLAB function we built as shown below:

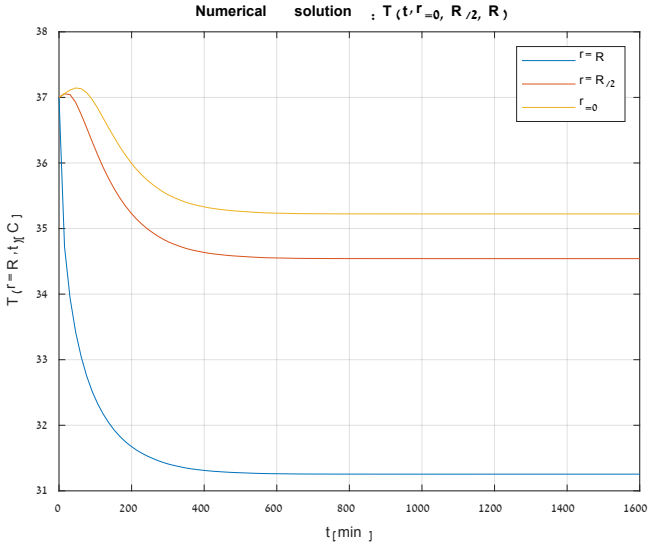
```
function [c,f,s] = pdex2pde(x,t,u,DuDx)
rho=920;          %[kg/m^3]
cp=3000;          %[J/kgK]
k=0.42;           %[W/m*k]
alpha=k/(rho*cp);%[m^2/s]
qm=450;           %Metabolic heat generation rate of healthy tissue[W/m^3]
rho_b=1055;       %Blood density [kg/m^3]
omega_b=0.00018; %Blood perfusion rate [ml/s/ml]
cp_b=3660;        %Heat capacity at constant pressure [J/kgK]
T_av=37;          %Arterial blood temperature [C]

c = 1/alpha;
f = DuDx;
s = qm-rho_b*omega_b*cp_b*(u-T_av); %with prefusion and qm
%s=0; %%with perfusion and qm
```

The plotted graphs from the main function is as followed:



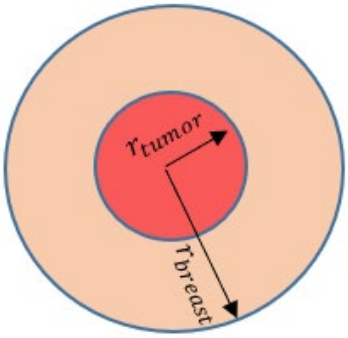




It is clear, that the main influence of the prefusion and the internal heat generation is the preservation of the tissue temperature – even at the breast surface, all that in comparison to the simulation we ran without the prefusion and heat generation.

Case Number 3

For a round ball with profusion and metabolic heat generation and a tumor inside (cancer tissue)



Prefusion parameters – $\rho_b, \omega_b, c_{p_b}, T_{av}$

Tissue parameters – ρ, C_p, k, T_b

Meatabolic heat generation – q_m

Arterial blood temperature -- T_{av}

We'll define the system parameters using the table below (3):

Parameter	Units	Cancer Tissue	Healthy Tissue
Radius size	$r[cm]$	$0 < r < 2cm$	$2cm < r < 10cm$
Thermal Conductivity	$k\left[\frac{W}{mk}\right]$	0.42	0.42
Tissue Density	$\rho\left[\frac{kg}{m^3}\right]$	920	920
Heat capacity at constant pressure	$C_p\left[\frac{j}{kg \cdot K}\right]$	3000	3000
Specific heat of the blood	$C_{p_b}\left[\frac{j}{kg \cdot K}\right]$	3660	3660
Blood density	$\rho_b\left[\frac{kg}{m^3}\right]$	1055	1055
Blood perfusion rate	$\omega_b\left[\frac{1}{s}\right]$	**0.009**	**0.00018**
Arterial blood temperature	$T_{av}[K]$	$310.15[K] = 37[C]$	$310.15[K] = 37[C]$
Metabolic heat generation rate	$q_m\left[\frac{W}{m^3}\right]$	***29,000***	**450**

Table 1- system parameters

Additional systems parameters:

$$T_a = T_\infty = 298°K[24°C], \quad T_0 = T_{body} = 310.15°K[37°C]$$

A remainder of the differential equation that we developed:

$$\frac{1}{\alpha}\frac{\partial \mathrm{T}}{\partial \mathrm{t}} = \frac{1}{\mathrm{r}^2}\frac{\partial}{\partial \mathrm{r}}\left[\mathrm{r}^2\frac{\partial \mathrm{T}}{\partial \mathrm{r}}\right] - \rho_b\omega_b c_{p_b}(T - T_{av}) + q_m$$

After understanding the different tissue properties, we split the added prefusion and internal heat generation in to 2 sections depending on the radius of the tumor.

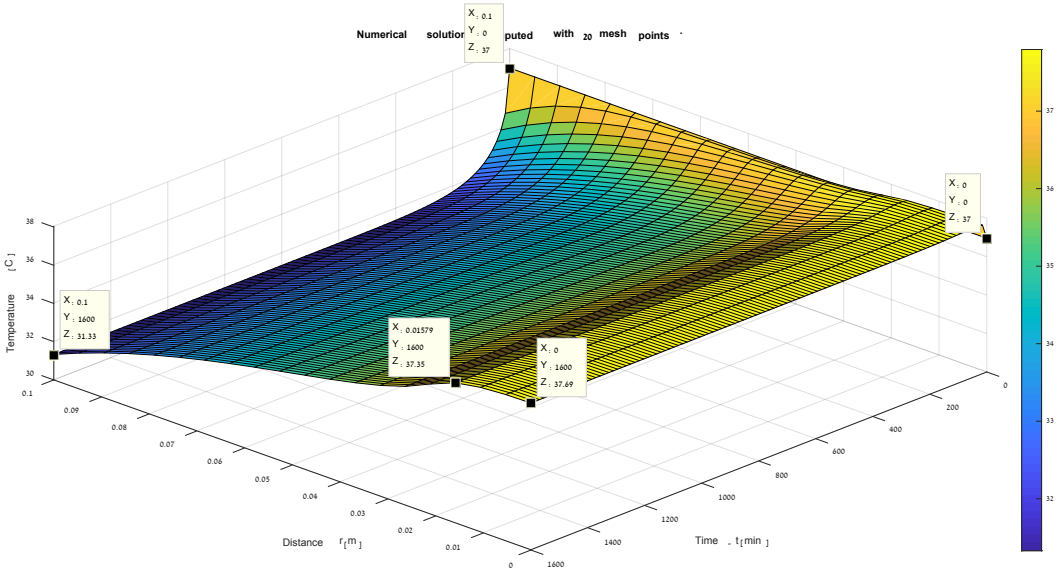
$$s = \rho_b\omega_{b_{Tumor}}c_{p_b}(T - T_{av}) + q_{m_{Tumor}} \quad | \, 0 < r < 2cm$$

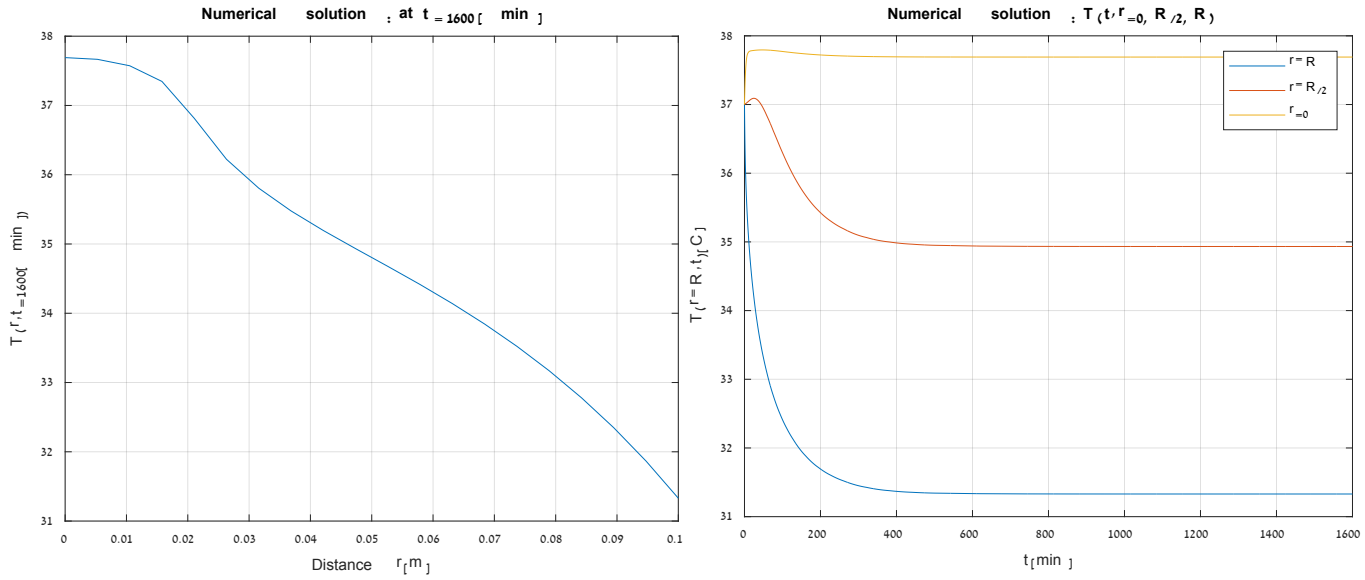
$$s = \rho_b\omega_{b_{Tissue}}c_{p_b}(T - T_{av}) + q_{m_{Tissue}} \quad | \, 2\mathrm{cm} < r < 10cm$$

The change in s will take place using a Boolean term on the radius:

```
% --------------------------------------------------------------
function [c,f,s] = pdex2pde(x,t,u,DuDx)
rho=920;                    %[kg/m^3]
cp=3000;                    %[J/kgK]
k=0.42;                     %[W/m*k]
alpha=k/(rho*cp);           %[m^2/s]
qm_normal=450;    %Metabolic heat generation rate in normal tissue [W/m^3]
qm_tumor=29000;   %Metabolic heat generation rate in cancer tissue [W/m^3]
rho_b=1055;                 %Blood density [kg/m^3]
omega_b_normal=0.00018;     %Blood perfusion rate in normal tissue [ml/s/ml]
omega_b_tumor=0.009;        %Blood perfusion rate in cancer tissue [ml/s/ml]
cp_b=3660;                  %Heat capacity at constant pressure [J/kgK]
T_av=37;                    %Arterial blood temperature [C]
r1= 2*10^-2;                %Tumor size[m]
c = 1/alpha;
f = DuDx;
s = (qm_tumor-rho_b*omega_b_tumor*cp_b*(u-T_av)).*(x<=r1) + (qm_normal-
rho_b*omega_b_normal*cp_b*(u-T_av)).*(x>r1); %Tumor inside a normal tissue
both with perfusion and qm
%s = qm_normal-rho_b*omega_b_normal*cp_b*(u-T_av); %with perfusion and qm
%s = 0; %%with prefusion and qm
% --------------------------------------------------------------
```

The plotted graph from the main function is as followed:





We can notice that the main difference between the simulation we ran earlier (breast without a tumor) and a breast with a concentric tumor (size of 4cm) is the raise of temperature in the center of the breast and less on the surface.

We need to remember that our equation is one dimension and depends only on r (just to simplify the problem)

If the tumor was located near the surface of the breast, we would clearly see an increase of the surface temperature.

Let us examine the parameter that were found in the work of Francisco Javier González (3)

Patient #	Age (years)	Tumor Size (cm)	Tumor Depth (cm)	Measured Delta-T (°C)	Thermal Score	Metabolic Heat Production (mW/cm^3)
1	53	4	2.5	2.6	4.7	1371
2	58	2	2.6	1.2	4.2	1096
3	55	1.2	1	1.5	5.5	272
4	42	5	1.05	1.5	5.5	96
5	55	5	2	1.5	5.5	376
6	35	3	1.5	1.5	5.5	272
7	65	3	1.1	0.3	3.3	29
8	69	2.5	1.5	1.9	4.9	399
9	44	1.2	2.1	1.5	4.5	1312
10	63	1.2	1	1.2	4.2	205
11	55	5	2	1.2	5.2	295
12	53	1.88	2.1	3	7	1645
13	52	3.1	0.95	0.6	3.6	8
14	56	1.85	0.95	0.7	4.7	44
15	73	10	0.5	4.1	8.1	75
16	53	4	2.5	2.6	6.6	1272
17	36	1.8	2.01	0.4	4.4	454
18	49	1	1.95	1.6	5.6	1464
19	81	1.9	2.25	0.7	4.7	448
20	36	4	0.85	2.1	6.1	116

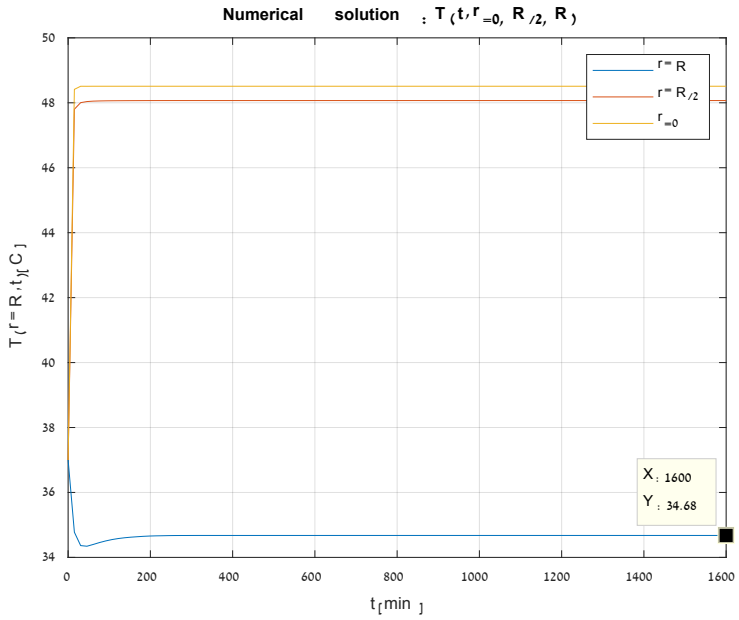
Table I. *Tumor parameters obtained from X-ray mammography, digital infrared imaging and finite element simulations.*

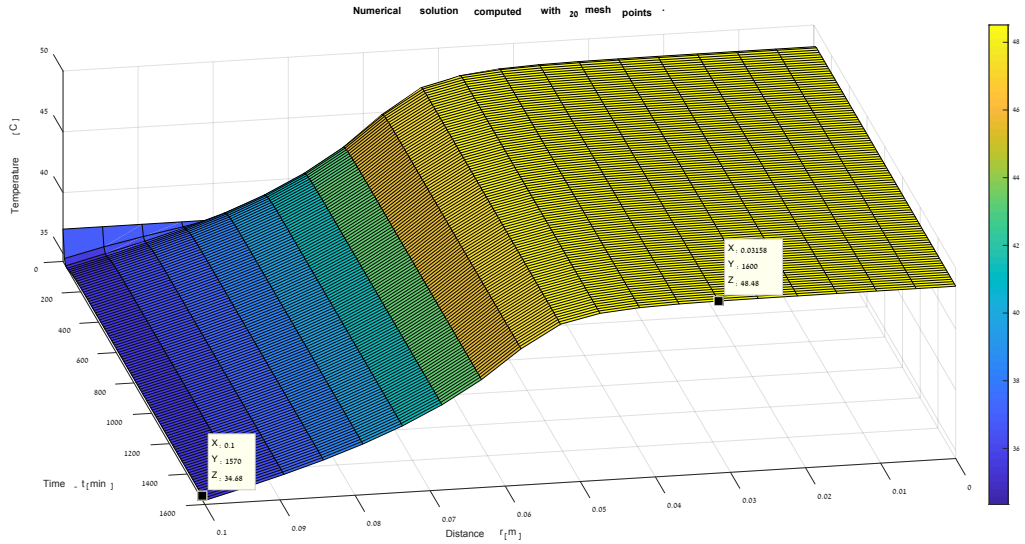
It is obvious that a tumor size was found to vary between 1.2-10cm, and the internal heat generation from $q_m = 8\left[\frac{kW}{m^3}\right]$ to $q_m = 1645\left[\frac{kW}{m^3}\right]$.

Hence, we would like to run our simulation using more extreme parameters so we choose the following:

$$q_m = 400\left[\frac{kW}{m^3}\right] \ , r = 6cm$$

The plotted graph from the main function is as followed:





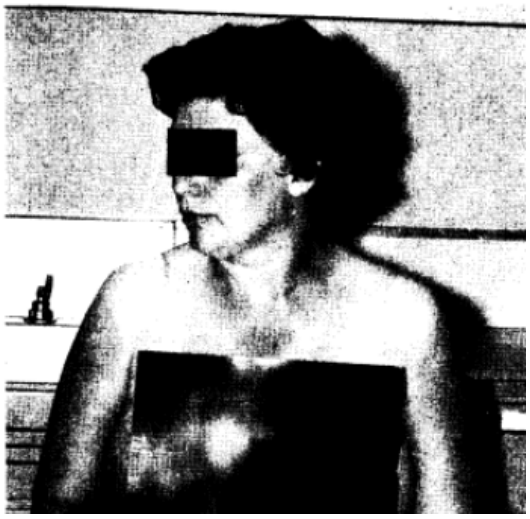
We noticed that the tumor temperature under the new parameters we used is 48.48 °C, clearly it is an extremely harmful temperature for the surrounding tissue.

We can also see that the surface temperature raised by 10% - a difference that can be more easily identify from a breast that contains an healthy tissue.

Reviewing another article by Jama – "Breast Cancer and Body Temperature" (4) shows a table with different patient breast surface temperature.

TABLE I.

Case No.	Tumour temp. (°C.)	Temp. of identical area opposite breast (°C.)	Temperature difference (°C.)	Room temp. (°C.)	Pathology
221190	37.5	33.0	3.5	21.0	Cancer
212363	36.2	35.0	1.2	21.0	"
213205	36.2	35.0	1.2	21.0	"
213369	36.8	35.8	1.0	21.0	"
214566	36.5	35.0	1.5	21.0	"
215866	36.0	34.25	1.75	21.0	"
216803	36.7	34.2	2.5	21.0	"
216994	37.7	36.0	1.7	21.0	"
217301	36.0	34.0	2.0	21.0	"
217653	36.75	34.5	2.25	21.0	"
218179	36.6	35.5	1.1	21.0	"
220325	37.0	Previous mastectomy		21.0	"
216588	35.8	Previous mastectomy		21.0	"
218368	35.7	34.8	0.9	21.0	"
219954	37.0	35.4	1.6	21.0	"
218344	35.6	35.0	0.6	21.0	"
218716	37.0	36.4	0.6	21.0	"
219007	36.6	36.6	0.0	21.0	"
219646	35.7	35.7	0.0	21.0	"



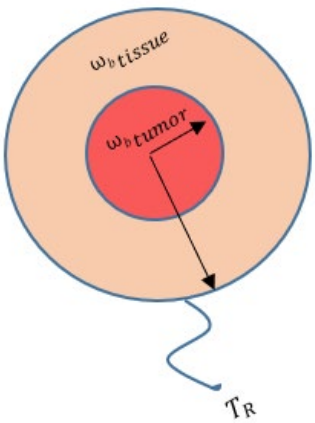
A satisfying finding,

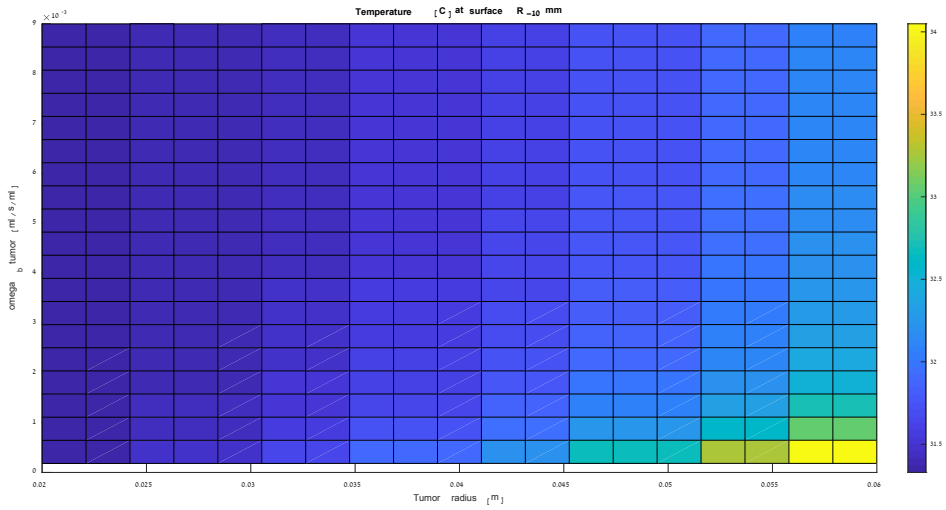
The average surface temperature that was measured in the article was 36.9°C - a value that matches the temperature that we received from the simulation we ran.

The questions that we pointed out, does the temperature inside of the tumor can be extremely high as in our results? This is still a concern and unclear from the literature and we still haven't found an answer for this question.

Does the bio-heat equation can really quantify the complex process in the breast cancer? Or should we take in consideration other parameters as well?

Another interesting graph that we would like to present is the temperature change of the surface in a steady state Vs. the prefusion of the tumor and it's size.





The internal tumor has a perfusion range of $0.00018 \leq \omega_{b\,tumor} \left[\frac{1}{s}\right] \leq 0.009$.

And the surrounding tissue has a constant prefusion of $0.00018 \left[\frac{1}{s}\right]$ (which represent an healthy tissue).

We notice that the surface temperature is higher when the prefusion is lower and the tumor size is highest.

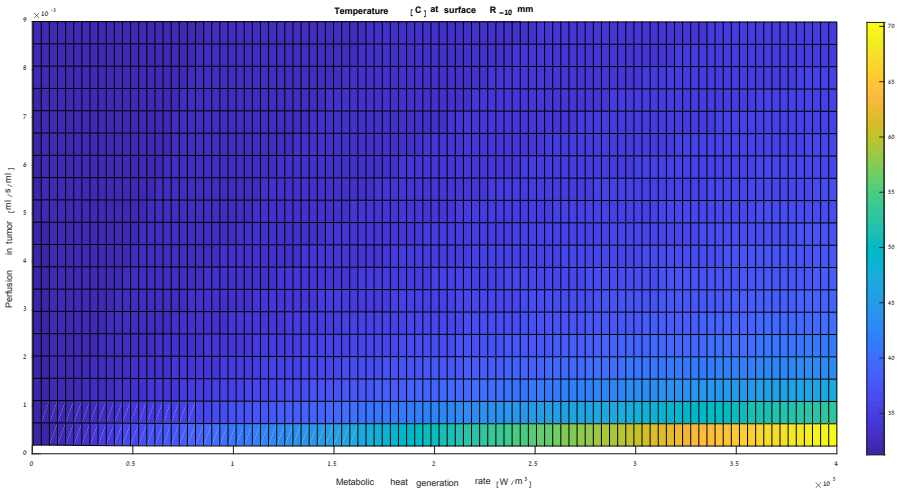
It's a mistake to consider the prefusion in the bio-heat equation, as a source of energy. In our case in fact, it does exactly the opposite.

We decided to quote a section from the "*Heat Transfer and Fluid Flow in Biological Processe*" book (6):

"The term $Wc_b(T - T_a)$*, which accounts for the effects of blood perfusion, can be the dominant form of energy removal when considering heating processes. It assumes that the blood enters the control volume at some arterial temperature* T_a*, and then comes to equilibrium at the tissue temperature. Thus,* ***as the blood leaves the control volume it carries away the energy****, and hence acts as an energy sink in hyperthermia treatment."*

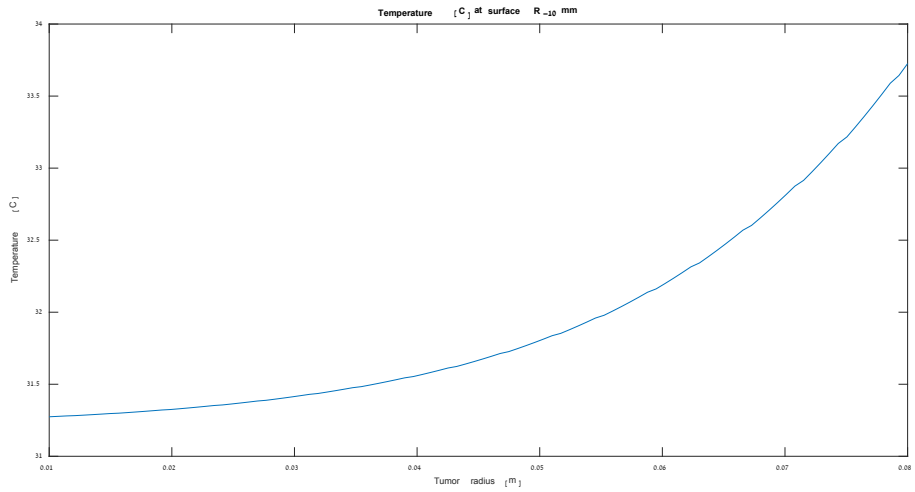
Which means, the high prefusion removes the metabolic heat generated inside the tissue hence decrease the temperature in the surrounding healthy tissue – a process that is beneficial to the healthy surrounding tissue but at same time, unfortunately, supports the tumor growth.

Similar to the graph presented above, we now present a graph of the temperature profile Vs. the tumor prefusion and the internal heat generation:



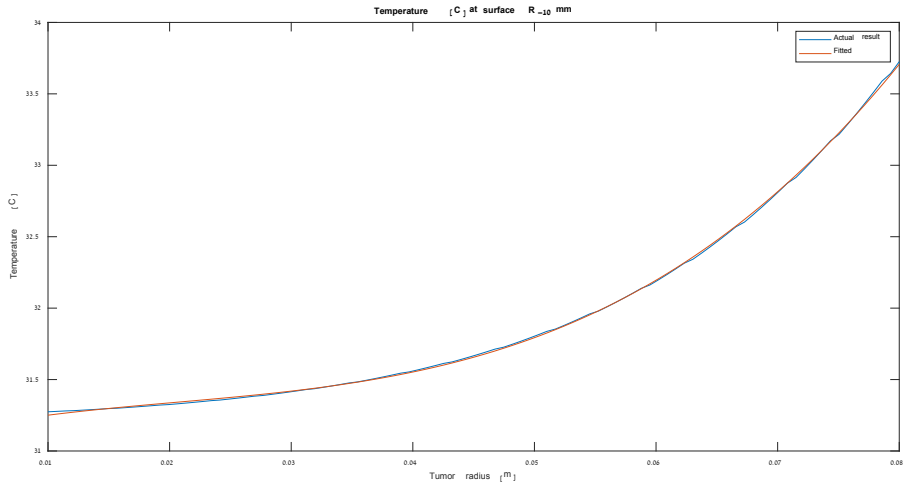
As we explained earlier, we can understand that without the important prefusion, that removes heat from the system, the surface temperature can increase significantly, given an extreme internal heat generation inside the tumor.

The last graph that we will present is the breast surface temperature Vs. the tumor size:



The parameters we used simulating the graph were taken from table number 1 from page 25.

We can easily fit a 3rd order polynomial function using MATLAB:



$$T(r) = 9210.4 \cdot r^3 - 571.9166 \cdot r^2 + 19.323 \cdot r + \quad 31.1054$$

Apart of the information above, we found in Backer's book an explanation that state that there is a significant disadvantage in Penss bio-heat equation because it does not take inconsideration the direction of the blood flow and does not describe a convection prosses.

The Autor describes other heat models such as: Chen and Holmes Model and The Weinbaum and Jiji Model which tries to overcome the bio-heat equation disadvantages.

Indeed, Penss bio-heat equation serves our models but can we find a better mathematic model that will take inconsideration other complicated malignant prosses such as: fast division of the tumor cells, the immune system or medication effects, angiogenesis treatments and many other changes that accrues in the surrounding tumor blood vessels?

References

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All our MATLAB functions can found in the following link:

https://drive.google.com/open?id=1IT4SqWUituYO-FS6phTRRY4mqg0WGKEn