Theoretical Mathematical Model on Temperature Regulation during Wound Healing After Plastic Surgery of Two Dimensional Human Peripheral Regions

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Abstract: Human is the most significant creature on the earth having various complex biological structures. Skin the foremost and important organ of the body with many different functions is always a center of attraction for medical scientist. Protecting the skin is important. If the skin is unable to function properly, it will affect the entire parts of the body. Pathogens will enter the body cause harm to the internal environment and hence the different systems in our body may not be able to function properly. Thermoregulation due to skin plays an important role to maintain body core temperature. Any disorder in skin causes various disorderly idiosyncrasies. Present study deals with the thermal regulation in human tissues in wounding to healing process. All physiological essential factors responsible for healing are taken into consideration for real case studies. All estimations are based on bio-heat equation associated with bio physical and biochemical reactions. The present study deals with the theoretical model for the estimation of temperature variation in the human peripheral region. The study involves the essential factors responsible for the temperature distribution, the central blood flow, the heat transfer coefficient due to exchange of the temperature between the atmospheric temperatures and human periphery. The effect of the atmospheric temperature has been analyzed theoretically.

I. Introduction

The human body requires a stable core temperature 37°C (±0.5°C), to maintain cell metabolic activity. Core temperature is the balance between heat gain produced by cell metabolism and heat loss from various mechanisms, including respiration via the lungs and evaporation via the skin. Core temperature is controlled by the hypothalamus in the brain. Extreme temperature deviations, for example hypothermia (decrease in core temperature) or hyperthermia (increase in core temperature), can lead to cold or heat injuries or in extreme cases, death[1].

The normal range of human body temperature varies due to an individual’s metabolism rate. The higher the metabolic rate, higher is the normal body temperature or the lower the metabolic rate; the lower is the normal body temperature. Heat is transported from body core to the body surface through skin. Skin is the most important and the largest organ of integumentary system made up of multiple layers. It is the first line of defense, which covers and guards the underlying muscles, bones, ligaments and internal organs. Skin is the interface with the environment, plays an important role in protecting against infectious agents called pathogens and excessive water loss[2]. The SST region (skin and subcutaneous region) is structurally divided into three sub layers viz. epidermis, dermis and hypodermis or subcutaneous layer.

Therefore protection of skin is very important as it helps to control the entire body temperature. Any disorder in skin causes lots of irregularities in proper functioning. Wound is always a centre of attraction not only for surgeons but researchers too. The natural processes that occur during normal wound healing are very complicated and complex [3]. Wound healing depends on various internal and external factors. Internal factors i.e. physiological factors like metabolism, blood flow, tissue density, tissue temperature and cell density etc., all these play very vital role in timely healing[4]. None of the internal and external factors are ignorable. Tissue temperature is not only important for proper functioning of biological organs but is it equally important for wound healing process. Hyper and hypothermia both the cases are not good for wound healing resulting chronic wound and keloid scar.

Thus, it is imperative to study the temperature changes during the wound healing process. A mathematical model is presented to estimate the effect of ambient temperature to the SST tissues during the healing. The main objective of the study is to investigate the temperature profiles in human tissues of surface peripherals at different ambient temperature using Finite element method due to the irregular geometry of human peripheral.

II. Materials And Methods

Present study deals with the bioheat equation given by Penne’s[5] included the terms diffusion, perfusion and rate of metabolic heat. Perl[6] developed a model with Fick’s perfusion principle along with heat...
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diffusion. Later many researchers used Perl’s model to estimate temperature profiles of human tissues in various conditions[7-12]. Main objective of this study is to develop a model for temperature distribution in the layers of SST region at different ambient temperature during healing process.

Various investigations have been made in this regard like wound healing time in bones[13], effect of surface curvature on wound healing in bone[14] and required growth factors in wound healing[15] etc., but the heat transfer mechanisms were neglected in all the above research. The temperature distribution within the skin due to externally applied heat depends on various factors such as the rate of energy removal by blood flow, conductive heat transport and metabolic heat generation. This prediction of the temperature distribution within the skin can be used as an effective tool for the application of the appropriate amount of heat to the wounded area of the skin.

It is evident from the experimental facts that from wounding to healing various temperatures play significant role. Body core temperature, skin temperature, ambient temperature and wound-bed temperature are very important for healing the wound timely [16-17]. Experiments [16] showed that the wound bed temperature and temperature of cleansing solution during wound healing are very important for timely healing. Robert Gannon [17], concluded in his studies that the proper healing of wound occurs only at appropriate body temperature, ambient temperature and temperature of cleansing solution. Physiological parameters like blood mass flow rate, metabolism, tissue conductivity and oxygen circulation in wounds etc. depend on body temperature [18]. Several reasons for healing of wounds due to the application of heat have been reported in the literature. Excessive temperature rise may damage the tissues in the wound region while lower temperatures may not improve the healing process. People with diabetes have poor blood circulation, poor resistance to infection, and poor local nutrition causes abnormal or delayed wound healing [19]. Several clinical studies have reported that application of heat to wounds for some extent may improve condition of wound which may help to heal the diabetic wound faster. One such study was conducted using noncontact normothermic wound therapy (NNWT) for the healing chronic full thickness pressure ulcers [20]. An article published in newsletter stated the importance of skin temperature and can be used as a powerful capability to heal. Horwitz and Abramson reported in 1960 that wound healing will be fast if the tissue temperature of patients maintain from out source [21].

III. Formation Of Mathematical Model

The estimation of thermoregulation throughout the perfused tissues in human body can be obtained by the solution of Perl’s Bio-heat Equation

\[
\left( \frac{\partial}{\partial x} \right) \left( K \frac{\partial T}{\partial x} \right) + \left( \frac{\partial}{\partial y} \right) \left( K \frac{\partial T}{\partial y} \right) + \frac{m_b c_b}{\rho} (T_b - T) + S = \rho c \frac{\partial T}{\partial t}
\]

(1)

Here S is the heat regulation due to metabolism and \( m_b c_b (T_b - T) \) as blood flow through the various capillaries in the tissues. \( T_b, K, \rho, c, m_b \) and \( c_b \) are body core temperature, thermal conductivity, density and specific heat of tissue; blood mass flow rate and specific heat of blood respectively. Right hand side of eq.(1) shows the storage of heat in tissues. The first two terms of the left hand side represents conduction of heat in the tissues, caused by the temperature gradient and third term is for heat transport between the tissues and microcirculatory blood perfusion. The last term represent heat generation due to metabolism. Finite element Method is used to get numerical estimation of the equation (1) for realistic solution to obtain temperature profile of perfused biological tissues. In this regard the domain of interest where the solution is sought is divided into finite number of parts called element. Here one dimensional linear element is taken into consideration.

The outer surface of the body is exposed to the environment and heat loss at this surface takes place due to conduction, convection, radiation and evaporation. Thus the boundary conditions at the outer surface is

\[-K \frac{\partial T}{\partial n} = h(T - T_a) + LE \text{ for } t > 0\]

(2)

Where \( h \) heat transfer coefficient, \( T_a \) is atmospheric temperature and \( \partial T / \partial n \) is the partial derivatives of T along outward normal to the boundary surface. First term of the L. H. S. of equation is the heat loss due to convection and radiation and second term is L and E are the latent heat and rate of evaporation respectively.

At the inner boundary surface, the core temperature \( (T_b) \) being constant for all time i.e.

\[T = T_b \text{ for } t \geq 0\]

(3)

Also at the interface between adjoining layers viz. subcutaneous and dermis, subdermis and epidermis \( T_1 = T_2 \)
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\[
\left( K \frac{\partial T}{\partial n} \right)_i = \left( K \frac{\partial T}{\partial n} \right)_j
\]

(4)

Equation (4) represents continuity of temperature and heat flux between different subdomain of the region under study. Thermal graph of tissues during healing process is obtained by reducing partial differential Equation (1) under the boundary and surface conditions given by equation (2) and (3)

IV. Solution Of The Model By Using Finite Element Method

The weak form of bio-heat equation (1) combined with boundary conditions can be obtained using the finite element method (FEM) [22] and written for the \( e \)th element as

\[
I^e = \frac{1}{2} \int_{x_i}^{x_j} \left[ K^e \left( \frac{\partial T^e}{\partial x} \right)^2 + M^e (T_b - T^e)^2 - 2S^e T^e + \rho C \frac{\partial (T^e)^2}{\partial t} \right] dx
\]

(5)

\[
+ \frac{1}{2} \left[ h(T^e - T_a)^2 + 2LET^e \right] \text{ for epidermis only}
\]

Here second term of the equation (5) is valid for the elements \( e \) adjoining the outermost surface of the skin and taken equal to zero for remaining elements.

Variation across the element can be expressed as

\[
T(x, y) = N_i T_i + N_j T_j + N_k T_k = \left[ N(x, y) \right] \overline{T}
\]

(6)

Where I, j and k are local nodes, N is the is the shape function associated with node i and j. Using Galerkin’s method the weight function \( v \) and the interpolation function for \( T \) are chosen to be the same.

The local stiffness matrix, capacitance matrix and vector matrix are evaluated as

\[
I^e = I^e_K + I^e_M - I^e_S + I^e_p + I^e_{11} + I^e_{12}
\]

(7)

where

\[
I^e_K = \frac{1}{2} \int_{x_i}^{x_j} K^e \left( \frac{\partial T^e}{\partial x} \right)^2 dx, \quad I^e_M = \frac{1}{2} \int_{x_i}^{x_j} \left[ M^e (T_b - T^e)^2 \right] dx
\]

(8)

\[
I^e_S = \int_{x_i}^{x_j} \left[ S^e T^e \right] dx, \quad I^e_p = \frac{1}{2} \int_{x_i}^{x_j} \rho C \frac{\partial (T^e)^2}{\partial t} dx
\]

\[
I^e_{11} = \frac{1}{2} \left[ h(T^e - T_a)^2 \right], \quad I^e_{12} = LET^e
\]

for each element in the domain and then assembled into the global system of linear ordinary differential equations

\[
\frac{dI^e}{dT^e} = \sum_r \frac{dI^e_r}{dT^e}; \quad r = K,M,S,\rho,\delta_1,\delta_2
\]

(9)

The matrix form of eq. (9) is as follows

\[
\frac{dI^e}{dT^e} = \left[ A^e \right] [T^e] + \left[ A^e_1 \right] \left[ T^e \right] + \left[ A^e_2 \right] \left[ T^e \right] - \frac{\partial T^e}{\partial t} \left[ A^e_3 \right] + \left[ A^e_4 \right] \left[ T^e \right] + \left[ A^e_5 \right] \left[ T^e \right] + \left[ A^e_6 \right]
\]

(10)
The theoretical mathematical model on temperature regulation during wound healing after plastic surgery involves the division of the region under study into \( n_e \) elements using \( n_n \) nodes. All the elements are assembled to get integral \( I \) as follows

\[
I = \sum_{e=1}^{n_e} I^e
\]

Extremising \( I \), we get

\[
\frac{dl}{dT}_{n_e} = \sum_{e=1}^{n_e} [D^e]_{n_x \times p} \frac{dl^e}{dT^e}_{p=1} = 0
\]

Here

\[
\frac{dl}{dT} = \begin{bmatrix}
\frac{\partial l}{\partial T_1} \\
\frac{\partial l}{\partial T_2} \\
\vdots \\
\frac{\partial l}{\partial T_{n_n}}
\end{bmatrix}
\]

\[
[D^e] = \begin{bmatrix}
0 & 0 & 0 & \ldots & 1 & 0 & \ldots & 0 & 0 \\
0 & 0 & 0 & \ldots & 0 & 1 & \ldots & 0 & 0
\end{bmatrix}_{2 \times n_n}
\]

\[
[B^e] = \begin{bmatrix}
\frac{\partial N^e_i}{\partial x} & \frac{\partial N^e_j}{\partial x} & \frac{\partial N^e_k}{\partial x} \\
\frac{\partial N^e_i}{\partial y} & \frac{\partial N^e_j}{\partial y} & \frac{\partial N^e_k}{\partial y}
\end{bmatrix}_{2 \times p}
\]

The expression on the right-hand side of the equation (8) for \( r=\delta_1 \) and \( \delta_2 \), will be summed up for the elements on the boundary of the outer surface of the SST region. Equation (8) was computed separately and then substituted into equation (12). \( I_k, I_m, I_s \) and \( I_p \) will be the functions of nodal temperatures \( T_1 \) and \( T_j \) for linear elements.

In this study the region of interest (SST region discretized into 11 sub-layers. The subcutaneous, dermis and epidermis layers consist of 5, 4 and 2 sub-layers respectively. Each sub layer is assumed to have equal thickness of 0.1 cm and length 10 cm. The region consists of total number of 88 triangular elements \( (n_e) \) and 60 nodes \( (n_n) \) (Fig. 1).

![Finite element model of SST region having triangular element, numerals with red colour indicate nodes and with blue colours indicate element numbers](Fig. 1)
The global equation system is then formed from these finite element equations. The Crank Nicolson Method is used in order to compute the time dependent simultaneous differential equations of temperature. Final system of algebraic equation can be written as

\[
\left( \frac{1}{2}[K_{c}] + \frac{1}{\Delta t}[C] \right)\{T_{n+1}\} = \left( \frac{1}{2}[K_{c}] + \frac{1}{\Delta t}[C] \right)\{T_{n}\} + \frac{1}{2}\{(R)_{n+1} + \{R\}_{n}\}
\]

(13)

\[
[K_{c}][T] = \{R\}
\]

where \[K_{c} = \left( \frac{1}{2}[K_{c}] + \frac{1}{\Delta t}[C] \right)\{T_{n+1}\},\{R\} = \left( \frac{1}{2}[K_{c}] + \frac{1}{\Delta t}[C] \right)\{T_{n}\} + \frac{1}{2}\{(R)_{n+1} + \{R\}_{n}\}\]

Where the sub script \((n+1)\) denotes the current time step and \(n\) denotes the previous time step. Finite Element (FE) formulation of the Bio heat equation is equivalent to the FE formulation of conduction heat transfer in the human body. \([K_{c}]\) stiffness matrix is for volumetric blood flow in tissues and \(\{R\}\), the residual, forcing vector denotes arterial blood temperature and metabolic heat generation. The main advantage of FE method is that the approximate value can be converted in to the exact value by increasing the number of elements and time step size. However increasing the number of elements and time step size causes the increase in computational cost.

V. Assumption And Numerical Computations

The SST region has three natural layers namely subcutaneous, dermis and epidermis. The physiological properties are almost uniform in subcutaneous tissues. So the values of K, M and S are assumed for this region is constant. In the dermis layer, these values are most variable, so K, M and S are calculated using Lagrange’s Interpolation Polynomial between epidermis and subcutaneous tissue. In epidermis layer, due to no blood vessels, the values of M and S are taken zero and K as constant.

Therefore mathematically it can be written as:

\[
K(x,t) = \zeta(t) \sum_{d=0}^{1} \alpha_{d}x^{d}, \quad M(x,t) = \psi(t) \sum_{d=0}^{1} \beta_{d}x^{d}, \quad S(x,t) = \zeta(t) \sum_{d=0}^{1} \gamma_{d}x^{d}
\]

(14)

Here the thickness of SST region is along x axis, therefore, changes in these parameters are the functions of x only. The values for \(\alpha_{d}, \beta_{d}\) and \(\gamma_{d}\) are calculated layer wise. For normal region the values of K, M and S depend on position and for abnormal region (wounded region) K, M and S depend on position and time both, therefore \(\zeta(t), \psi(t)\) and \(\zeta(t)\) are taken increasing functions of time for abnormal region and after a period of time K, M, S are assumed to attain the values like normal region. Mathematically it can be written as

\[
\zeta(t) = V_{0} + V_{1}e^{-\gamma t}, \quad \psi(t) = (\mu_{0} + \mu_{1}e^{-\gamma t}), \quad \zeta(t) = \left( \theta_{0} + \theta_{1}e^{-\gamma t} \right)
\]

(15)

In wounded tissues metabolic activity and energy due to blood flow are very less or almost negligible as compared to the healthy tissues. As wounded tissues will become healthy their functioning becomes normal. Initially the value of per eq. (16) \(\zeta(0) = \frac{1}{2}, \quad \zeta(\infty) = 1; \quad \psi(0) = 0, \quad \psi(\infty) = 1; \quad \zeta(0) = \frac{1}{20}, \quad \zeta(\infty) = 1\)

MODEL-1: Numerical solution of problem (1), (2)–(4) for a constant thermal conductivity (K) in tissues, blood mass flow(M) rate and rate of metabolism (S) are time dependent for abnormal region

In this section results are calculated on the following assumption: for normal region of human body heat transfer in tissues, blood mass flow rate and rate of metabolism are taken as a constant and only position dependent whereas for abnormal region, K depends only on position, M and S are dependent on both position and time.

\[
K(y,t) = \sum_{d=0}^{1} \alpha_{d}y^{d}, \quad M(y,t) = \psi(t) \sum_{d=0}^{1} \beta_{d}y^{d}, \quad S(y,t) = \zeta(t) \sum_{d=0}^{1} \gamma_{d}y^{d}
\]

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\[ \psi(t) = \left( \mu_0 + \mu e^{-\mu t} \right), \quad \zeta(t) = \left( \theta_0 + \theta e^{-\theta t} \right) \]

Where

VI. MODEL-2: Numerical solution of problem (1), (2)–(4) for time dependent heat transfer (K) in tissues, blood mass flow rate (M) and rate of metabolism (S) for abnormal region

In this section K, M and S for normal region are assumed constant and for abnormal region K, M and S are all assumed as an increasing function of time and position.

\[ K(y,t) = \sum_{d=0}^{1} \alpha_d y^d, \quad M(y,t) = \psi(t) \sum_{d=0}^{1} \beta_d y^d, \quad S(y,t) = \zeta(t) \sum_{d=0}^{1} \gamma_d y^d \]

\[ \zeta(t) = \left( \nu_0 + \nu e^{-\nu t} \right), \quad \psi(t) = \left( \mu_0 + \mu e^{-\mu t} \right), \quad \zeta(t) = \left( \theta_0 + \theta e^{-\theta t} \right) \]

Where

VII. Results and Discussions

Table 1: Material properties of tissues[10]

<table>
<thead>
<tr>
<th>Tissues</th>
<th>Thermal conductivity (k[W/m/°C])</th>
<th>Blood Density of Tissues ρ (gm/cm3)</th>
<th>Latent Heat L (cal/gm)</th>
<th>Specific Heat of Tissues c (cal/gm °C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermis</td>
<td>0.060</td>
<td>1.090</td>
<td>579.0</td>
<td>0.830</td>
</tr>
<tr>
<td>Dermis</td>
<td>0.045</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>0.030</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: M, S and E for different atmospheric temperature

<table>
<thead>
<tr>
<th>Atmospheric Temperature T_a (°C)</th>
<th>Rate of Evaporation E (gm/cm²/min)</th>
<th>Blood Mass Flow Rate M (cal/cm²min. °C)</th>
<th>Rate of metabolism S (cal/cm²min¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>0</td>
<td>0.0030</td>
<td>0.0357</td>
</tr>
<tr>
<td>23</td>
<td>0, 0.24x10⁻³, 0.48x10⁻⁷</td>
<td>0.0180</td>
<td>0.0180</td>
</tr>
<tr>
<td>33</td>
<td>0.24x10⁻³, 0.48x10⁻⁷</td>
<td>0.0315</td>
<td>0.0180</td>
</tr>
</tbody>
</table>

Model 1&2, deals with the two dimensional Mathematical Models using finite Element Method to study temperature variations of human peripheral region during wound healing process after plastic surgery. In both the models, the SST region is assumed to be of the width 1.1 cm and length 5 cm, discretized into very small triangular elements into 11 sub-layers. The subcutaneous, dermis and epidermis layers consist of 5, 4 and 2 sub-layers respectively. Each sub layer is assumed to have equal thickness of 0.1 cm and length 10 cm. The region consists of total number of 88 triangular elements (n_K) and 60 nodes (n_n).

Linear variation in temperature is considered within the elements. In Model–1, the physiological parameters M and S are assumed as increasing functions of time whereas K is kept same as that of the tissues of donor site ignoring the effect of rate of thermal conductivity i.e. \( \mu=0.01, \xi(t)=1 \). Then moving towards more realistic situation, Model-2 incorporates time dependency of K also for transplanted tissues along with M and S (\( \nu=0.01 \)). This is due to the transplanted tissues have minimum thermal conductivity at first just after the surgery, which increase slowly with time to become at par with that of the normal ones.

For abnormal region, the significant fall in temperature is noted in Model- 2, whereas no such difference is observed in Model–1. This shows that thermal conductivity plays an important role in the body. The graphs of Model–2 are nearly justify the experimental facts given by the Gannon[17], that wound temperature drops significantly at first due to ambient temperature and takes 100 minutes to return to the normal temperature and 3 hours to restart cell mitotic division.

Numerical solutions are obtained for sub-dermis region, dermis region and epidermis region. Solid lines represent temperature of healthy tissue whereas dotted lines represent temperature of wounded tissues. It is assumed that initially the SST region is insulated i.e. \( T_b=37° \) at \( t=0 \), with the release of insulation (during the dressing of wound), the temperature profile is prepared for different ambient temperatures and different rates of evaporation.
In all the graphs the fall in temperature is more in wounded tissue than that of the tissues of normal region due to different rate of metabolism, thermal conductivity and blood mass flow. The fall in tissue temperature is noted more at the skin surface (epidermis) in comparison to the interior tissues (dermal and subcutaneous) because more heat loss occurs at the surface due to conduction, convection, radiation and evaporation.

It is also noticed that at same rates of evaporation the decline in tissue temperature is more at lower atmospheric temperature. Since the temperature of skin is affected dramatically when the environmental condition changes. For higher rates of evaporation at the same atmospheric temperature, the fall in tissue temperature of epidermis, dermis and subcutaneous is noted more i.e. at $T_a=23^\circ C$, the fall in tissue temperature is more for $E=0.48x10^{-3}$ than that of $E=0$. It shows that the rate of evaporation significantly affects on temperature profile in the region. The results obtained in the model are agreement to the physiological facts.

In the present study, it is observed that with the release of insulation more heat loss takes place from the abnormal region. Hence more and fast temperature fall is noted about 20 minutes for abnormal region (open wound) and slow temperature fall for about 20 minutes for normal region. At the time of wounding the values of physiological parameters in injured tissues are negligible and with the increase in time the value of these physiological parameters also increases. In this period of wound healing process, biological and chemical processes take place gradually. These processes are responsible to increase tissues temperature. Very small and gradual increment for about 100 minutes is noted for gradually healed tissues and tends to become steady. Due to normal process in the tissues of normal region temperature becomes almost steady after 20 minutes. The steady state occurs when the physiological parameters of abnormal region starts attaining the values equal to that of the normal tissues. For different atmospheric temperature and different rate of evaporation, temperature profile varies layer wise for both the cases. For the same atmospheric temperature the fall in tissue temperature is more for higher rates of evaporation.

**For The Same Atmospheric Temperature The Fall In Tissue Temperature Is More For Higher Rates Of Evaporation (Model-2)**

**Abnormal Region ($T_b=37^\circ C$)**

1*: Maximum fall in temperature till 20 min.
2*: Maximum rise in Temperature after 250 min

![Graph showing temperature profile](image-url)
**VIII. Conclusions:**

Experiment reveals that wound temperature drops significantly on dressing change for few minutes and takes about 40 minutes for a freshly cleansed wound to return to normal temperature. It takes about 3 hours for cell mitotic division to restart\(^{[17]}\). In present study all the graph show that fall in tissue temperature, rapidly about 10 minutes for normal region and about 20 minutes for abnormal region (wound area). Fall in tissue temperature is found more in abnormal region because more heat loss takes place from the surface of this region due to open wound. During mitotic division of cell in wound, wound temperature increases very slightly. The same results are noticed theoretically that after about 40 minutes tissue temperature of wound increases very slightly and slowly till about 3 hours and 20 minutes and after it become steady. Tissue temperature of normal region becomes almost stable after 20 minutes. Experimentally wound temperature is recorded to be 32.6°C, when wound is cleansed with cleansing solution and warmed at ambient-temperature 29 °C\(^{[16]}\). Experimental studies on human wounds found that wounds cleansed with ambient-temperature solution led to a 2º drop in wound temperature. In all the graphs, the fall in tissue temperature is more at the skin surface (epidermis) in comparison to the interior tissues (dermal and subdermal) because more heat loss occurs at the surface due to conduction, convection, radiation and evaporation.

**Model-1:** Only M and S are time dependent for abnormal region
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Model-2: K, M and S are time dependent for abnormal region.
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