Two Models Simulating Focal Cerebral Cooling as a Therapy for Epilepsy

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I. Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures brought on by excessive and synchronous neuronal activity in the brain. Medical statistics demonstrate that epilepsy is the most common neurological disorder affecting 50 million people worldwide, 40 million of whom live in non-industrialized countries.[1] Studies estimate that over 90% of those who suffer from epilepsy in developing countries do not receive adequate treatment.[1] The permanent threat of seizures places severe restrictions on the day to day living of patients striving to be productive, working members of society.

Over the past 50 years, medical and biological research has made great advancements in understanding the pathogenesis of epilepsy as well as in developing effective treatments for various types of epilepsy. Genetic discoveries have tied familial epilepsies to mutations in ion and voltage-gated channels, while sensitive imaging tests have revealed the focal etiology of more complex, symptomatic epilepsies.[2] Chemical treatments such as anticonvulsant drugs (AEDs) currently provide a small group of patients with an effective means of suppressing seizures. Furthermore, surgical resection of abnormally functioning tissue for lesional and nonlesional epilepsies has been accepted as a mainstream therapeutic option.[3] Patients who suffer from focal neocortical epilepsy, however, pose a therapeutic engineering challenge as seizures for this subset of the population are inadequately managed by conventional treatments. Focal and multifocal seizures arising from the neocortex account for up to half of patients with poorly controlled seizures; advanced surgical treatments have success in only 50-60% of cases.[3] The inefficacy of conventional treatments for focal neocortical epilepsy necessitates the development of alternate treatments.

Attractive alternative therapies include implantable electrical stimulation systems capable of detecting and delivering therapy in an automated closed-loop fashion.[4] One avenue of interest exploits changes in thermal energy to both detect and suppress seizures. Rapid cerebral cooling has been shown to suppress epileptiform activity in various *in vivo* and *in vitro* studies via interference of synaptic transmission and

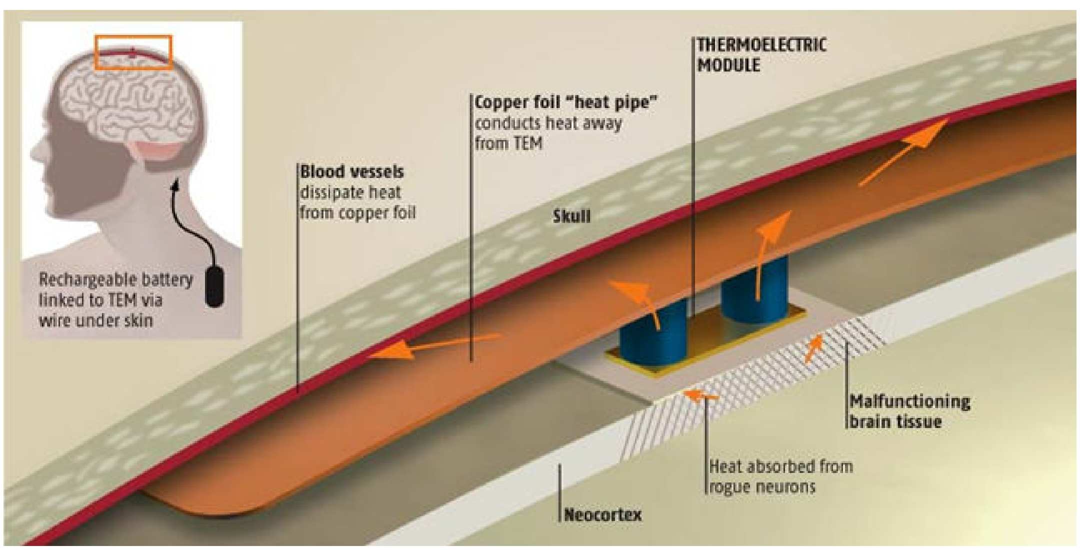

Figure 1: Thermoelectric cerebral cooling device is placed on surface of the brain directly over malfunctioning tissue. Electrical current applied to the device creates the temperature difference between electrodes required for cooling brain tissue. Heat generated by the device is then dissipated by conducting copper foil.[5]

voltage-gated ion channels.[6] Furthermore, brain tissue temperature in close proximity to the epileptogenic zone increases ~1.5 ^{o}C about 30 seconds prior to the onset of a seizure.[4] Proposed implantable devices utilize small thermoelectric (Peltier) modules coupled to seizure detection software to promptly terminate or prevent focal seizures. In the proposed therapy, a thermoelectric module is placed at the cortical surface directly above the epileptogenic focus (Figure 1). The heat released by the device is absorbed and dissipated over a copper plate while the surface of the brain is cooled. Such devices aim to ultimately improve the diagnosis and treatment of focal epilepsies.

II. Physical Constants and Modeling Assumptions

In this study, the feasibility of utilizing cerebral cooling as a treatment for focal epilepsy is explored. Literature describes the technical requirements for small brain cooling devices as being able to rapidly cool one cubic inch of brain tissue from 37 ^{o}C to 20 ^{o}C in approximately 30 seconds.[4] These requirements ensure that focal neocortical seizures are terminated and the spreading of seizures to neighboring tissue is suppressed. This study aims to look at how two different methods of cerebral cooling affect the temperature profile of brain tissue as a function of time and space. The models explored treat the cooling module as a planar device of negligible thickness located at the brain surface and fixed at a constant temperature, T_{dev}. Additionally, heat released by the thermoelectric module is ignored to simplify modeling. In the first method, the device covers a small surface area of tissue. Since the area being cooled is significantly smaller than the volume of the brain, this method can be modeled as a semi-infinite slab. In the second method, the brain is modeled as a sphere with the device encompassing the entire surface of the brain. These two methods are simplified versions of a more complex model discussed below. This study will compare the temperature profiles for each method analytically and numerically if possible.

The physical constants of brain tissue utilized in the calculations are summarized in Table 1. The assumption that brain tissue is homogenous enables the use of a single thermal diffusivity constant in calculations. Furthermore, heat propagation in the brain tissue due to vasculature is neglected when solving differential equations. The selected device temperature for modeling is -50 ^{o}C. Although unrealistic, this low temperature ensures satisfaction of the required cooling to 20 ^{o}C at a depth of 1 inch below the cortical surface within a reasonable length of time.

Table 1: Physical constants and parameters used in calculations

Parameter	Meaning
Heat capacity[4]	$c = 3.6$ J/g/K
Density[4]	$\rho = 1$ g/cm^3
Thermal conductivity[4]	$k = 0.005$ W/cm/K
Thermal diffusivity	$D = 1.389\text{x}10^{-3}$ cm^2/s
Initial temperature of the tissue	37 ^{o}C
Radius of the brain[7]	R = 6.5 cm
Desired depth of cooling	Depth = R – 2.54 cm
Device temperature	$T_{dev} = -50$ ^{o}C

III. Problem Set-up

A. Realistic Spherical Model

The change in temperature of the brain over time resulting from focal surface cooling can be modeled in spherical coordinates as a function dependent on four variables: radial distance from the origin (r), the polar angle (θ), the azimuthal angle (φ), and time (t). The geometry of the brain is thus simplified to that of a sphere. The thermoelectric cooling device can be simplified as a surface boundary condition covering a specified area over r values generalized as $r = r_{device}$ held at constant temperature, T_{dev}. The three dimensional heat equation for this model in spherical coordinates is:

$$\frac{\partial T}{\partial t} = D\left(\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T}{\partial r}\right) + \frac{1}{r^2 \sin\theta}\frac{\partial}{\partial \theta}\left(\sin\theta\frac{\partial T}{\partial \theta}\right) + \frac{1}{r^2 \sin^2\theta}\frac{\partial}{\partial \varphi}\left(\frac{\partial T}{\partial \varphi}\right)\right) \tag{1}$$

The initial condition for this model is simply that the temperature throughout the brain is held uniform at body temperature (37 ^{o}C). The boundary conditions for this model are more complex due to the number of variables and asymmetry introduced by placing the device at a discrete location at the surface of the sphere. The model implies that temperature with respect to r and φ are finite values everywhere at the boundaries. Along the θ coordinate, periodic value and flux boundary conditions apply (Eq. 2-3).

$$T(\theta) = T(\theta + 2\pi) \tag{2}$$

$$\frac{\partial T}{\partial \theta}(\theta) = \frac{\partial T}{\partial \theta}(\theta + 2\pi) \tag{3}$$

Along the radial coordinate $T(r=r_{device}) = T_{dev}$; however, the boundary condition elsewhere along the surface, at $r=r_{elsewhere}$, is a flux condition. At the surface, the flux is equal to the convective heat loss of the brain to its surrounding environment as dictated by Newton's law of cooling (Eq. 4).

$$\frac{\partial T}{\partial r}(r_{elsewhere}) = -D\frac{\partial T}{\partial t} = h(T_{surface} - T_{ambient}) \tag{4}$$

The flux boundary condition is dependent on the heat transfer coefficient, h, and the temperature at the surface as a function of time, $T_{surface}$. Given the asymmetry of this problem and complexity of the inhomogeneous boundary conditions, further simplifications can be made to model the temperature profile and efficiency of focal cooling. Treating this model as a semi-infinite slab and as a sphere with symmetrical boundary conditions simplifies the problem so an analytical solution can be reached.

B. Semi-Infinite Slab

In the first cooling model examined, only a small area of the brain is being cooled which can be approximated as a slab in Cartesian coordinates. The three dimensional heat equation in Cartesian coordinates is:

$$\frac{\partial T}{\partial t} = D\left(\frac{\partial^2 T}{\partial x^2} + \frac{\partial^2 T}{\partial y^2} + \frac{\partial^2 T}{\partial z^2}\right). \tag{5}$$

Since the volume of the brain is significantly larger than the area being cooled, the slab can be approximated as semi-infinite, extending to infinity in the *x*, *y*, and positive *z*-directions. The surface of the slab is defined as the origin in the *z*-direction. The Cartesian heat equation simplifies to:

$$\frac{\partial T}{\partial t} = D\frac{\partial^2 T}{\partial z^2}. \tag{6}$$

Initially, the entire brain will be at body temperature, or 37 °C (Eq. 7). At the top of the slab, or the surface of the brain, the temperature will be T_{dev} (Eq. 8). As *z* approaches infinity, far away enough from the device, temperature is fixed at body temperature (Eq. 9).

Initial condition:	$T(z,0) = 37°C$	(7)
Boundary condition #1:	$T(0,t) = T_{dev}$	(8)
Boundary condition #2:	$T(z \rightarrow \infty, t) = 37°C.$	(9)

C. Spherical

The three-dimensional heat equation in spherical coordinates (Eq. 1) can also be reduced to a one-dimensional problem (Eq. 10).

$$\frac{\partial T}{\partial t} = D\left(\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T}{\partial r}\right)\right). \tag{10}$$

In this model, the brain will be modeled as a sphere with a radius *R*. Since the brain is being cooled evenly across the surface at T_{dev}, the temperature is only dependent on the radius *r* by symmetry. The entire brain will initially be at body temperature, and by symmetry, the flux at the center of the sphere will be 0 (Eq. 11-13).

Initial condition:	$T(r,0) = 37°C$	(11)
Boundary condition #1:	$\frac{\partial T}{\partial r}(0,t) = 0$	(12)
Boundary condition #2:	$T(R,t) = T_{dev.}$	(13)

IV. Analytical Solutions

The one-dimensional heat equations in Cartesian and spherical coordinates are solved analytically (Appendices A and B). The derived analytical solutions for the two cooling methods explored are functions of distance and time (Eq. 14 and Eq. 15).

Semi-Infinite slab case:

$$T(z,t) = \frac{2}{\sqrt{\pi}}(37\text{ °C} - \mathrm{T_{dev}})\frac{\sqrt{\pi}}{2}\mathrm{erf}\left(\frac{z}{\sqrt{4Dt}}\right) + T_{dev}. \tag{14}$$

Spherical case with thermoelectric cooling device encompassing entire surface:

$$T(r,t) = T_{dev} + \sum_{n=0}^{\infty} -\frac{2R}{n\pi}(37 - T_{dev})(-1^n)\frac{1}{r}\sin\left(\sqrt{\frac{n\pi}{R}}r\right)e^{-D\left(\frac{n\pi}{R}\right)^2 t}. \quad (15)$$

V. Results

A. Surface Plots

Three dimensional plots illustrate how the temperature changes as a function of distance and time (Figures 2-4). In the semi-infinite slab model, the surface temperature remains constant at T_{dev} as described by the first boundary condition (Eq. 8). The temperature then starts to slowly increase as the distance from the surface increases until the temperature reaches body temperature (Figure 2). Additionally, the temperature profile plotted looks identical at all lengths of z, which supports and further justifies the use of a similarity solution. In both the analytical and numerical spherical solutions, the temperature varies radially and with time (Figure 3, Figure 4). Over long periods of time, the temperature of the brain tissue will start to decrease to the T_{dev} at the surface. At the surface of the brain, the temperature will start at body temperature, but will then quickly decrease to T_{dev}. However, the analytical and numerical solutions for the spherical models do differ. The analytical solution oscillates at $t = 0$ because of the Fourier series that is used to approximate the solution. The peak seen at $r = 0$, $t = 0$ is an artifact due to the approximate nature of the analytical solution as well as the initial and boundary conditions imposed at that point.

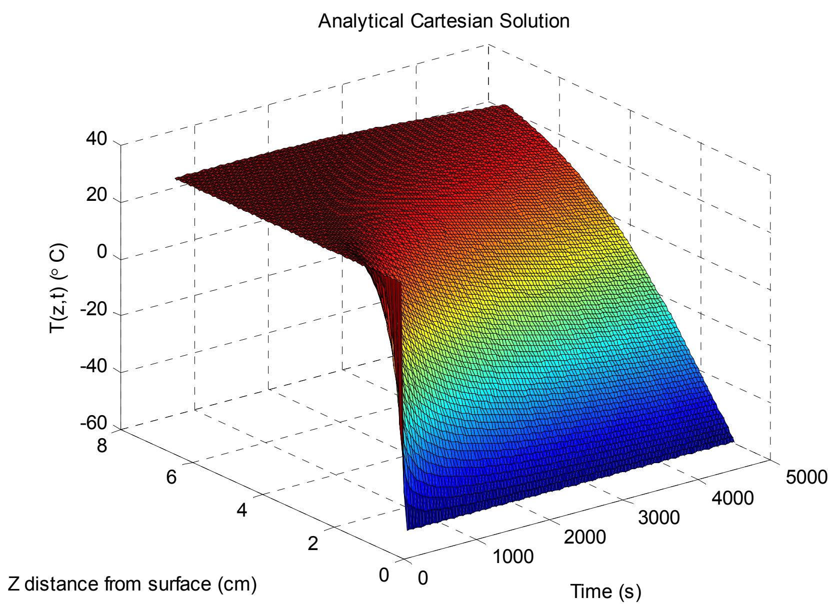

Figure 2. 3D plot of the temperature as a function of distance (cm) and time (s) for the semi-infinite slab model.

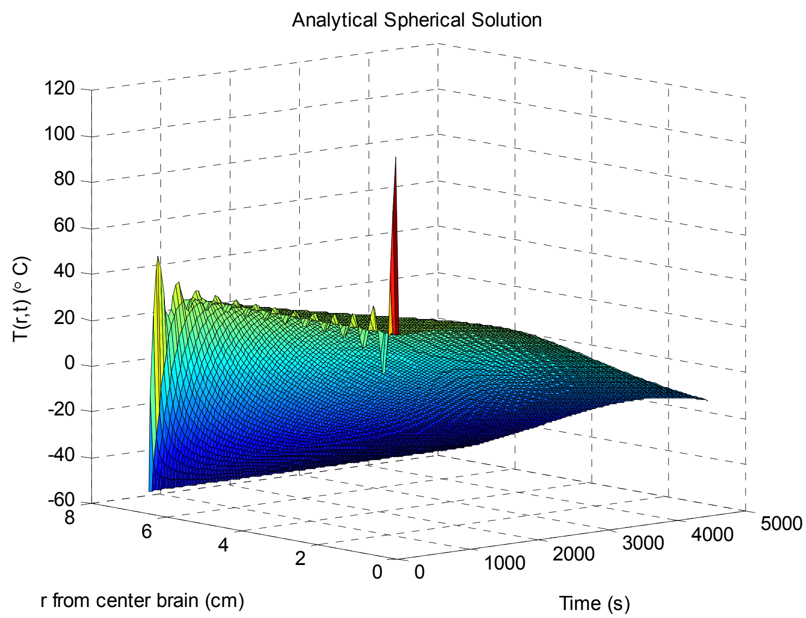

Figure 3. 3D plot of the analytical temperature as a function of distance (cm) and time (s) for the spherical model.

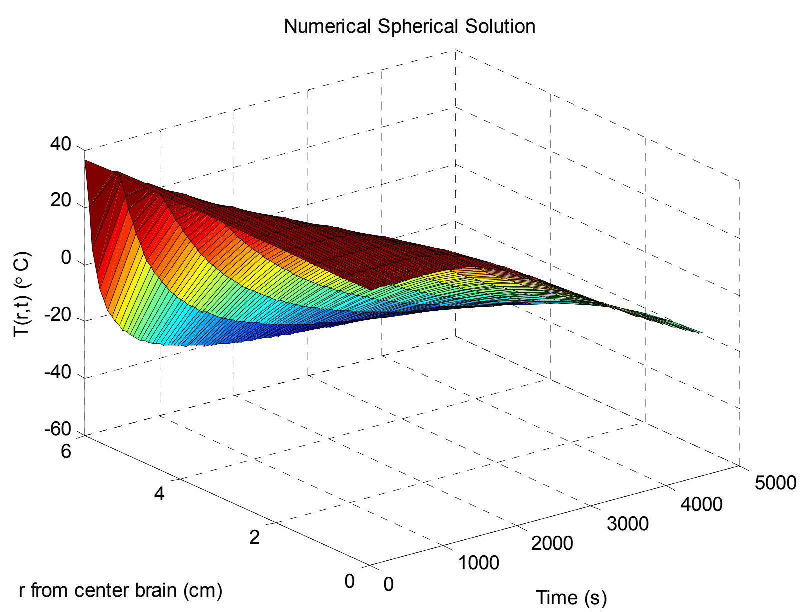

Figure 4. 3D plot of the numerical temperature as a function of distance (cm) and time (s) for the spherical model.

B. Temperature Profiles

The time it takes for the tissue one inch below the surface of the brain to reach 20 °C can be determined from the temperature profiles given in Figures 5-7. The semi-infinite slab model will take approximately 1400 seconds to reach the desired temperature while the spherical model (numerical and analytical) will take about 950 seconds to cool the area. The spherical model requires less time to cool the area beneath the surface to 20 °C because the area being cooled is substantially larger.

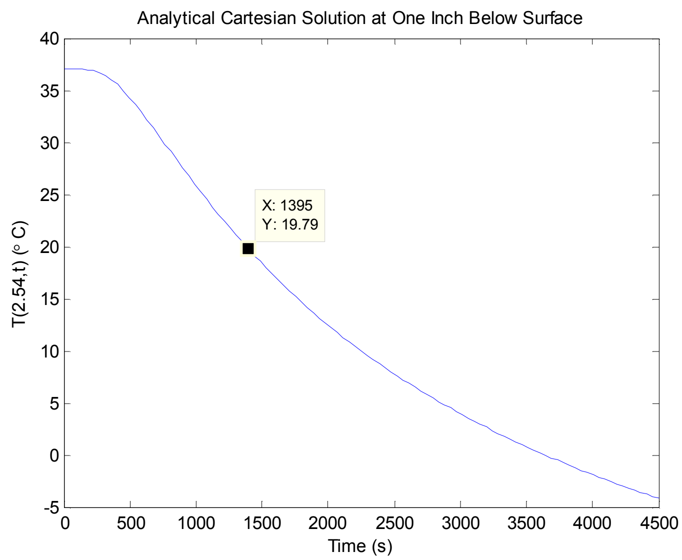

Figure 5. Temperature profile as a function of time (s) at one inch below the surface of the brain for the semi-infinite slab model.

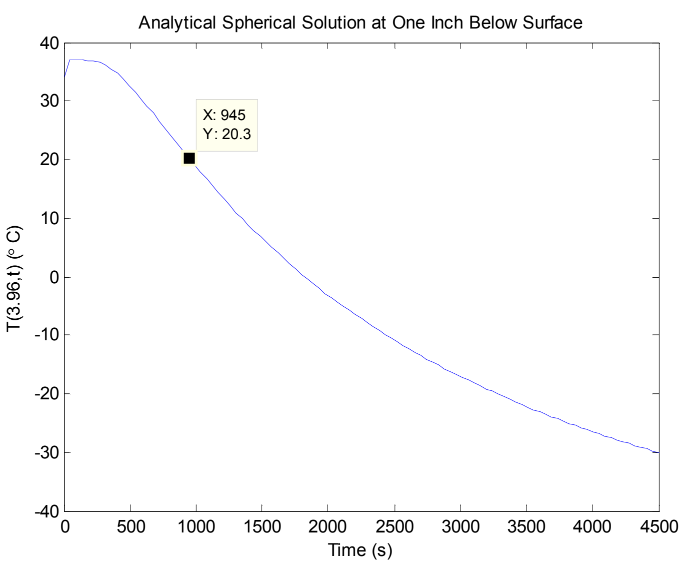

Figure 6. Analytical temperature profile as a function of time (s) at one inch below the surface of the brain for the spherical model.

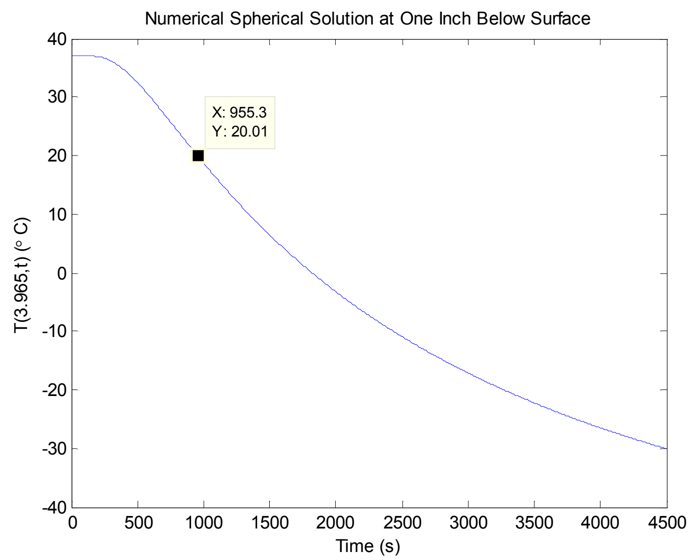

Figure 7. Numerical temperature profile as a function of time (s) at one inch below the surface of the brain for the spherical model.

C. Varying T_{dev}

While both models examined do not satisfy the technical requirements for seizure suppression, T_{dev} can be varied to achieve the desired results (Figures 8-10). For all three solutions at one inch below the surface, the temperature does not reach 20 °C within 30 seconds even if the device starts at -100 °C. While the time to cool decreases as T_{dev} decreases, there is a trade-off between the cooling effects, time, and damage to the surrounding tissues.

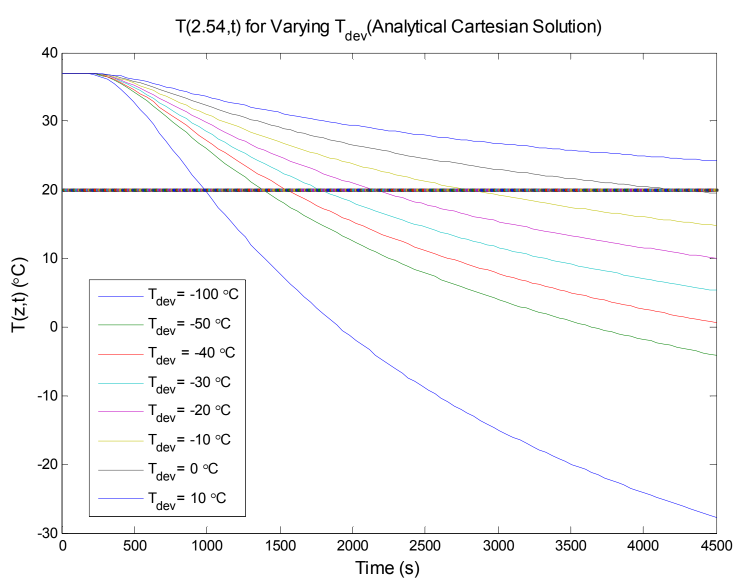

Figure 8. Effect of different device temperatures on the analytical solution one inch below the surface for the semi-infinite slab model.

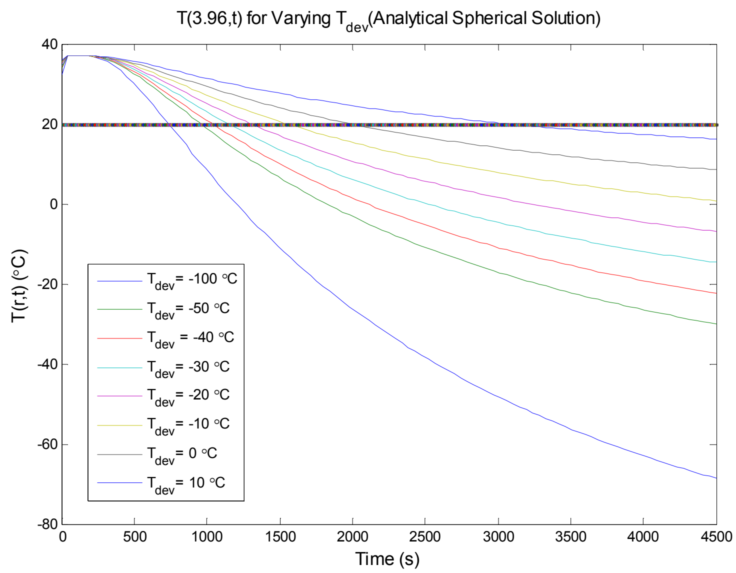

Figure 9. Effect of different device temperatures on the analytical solution one inch below the surface for the spherical model.

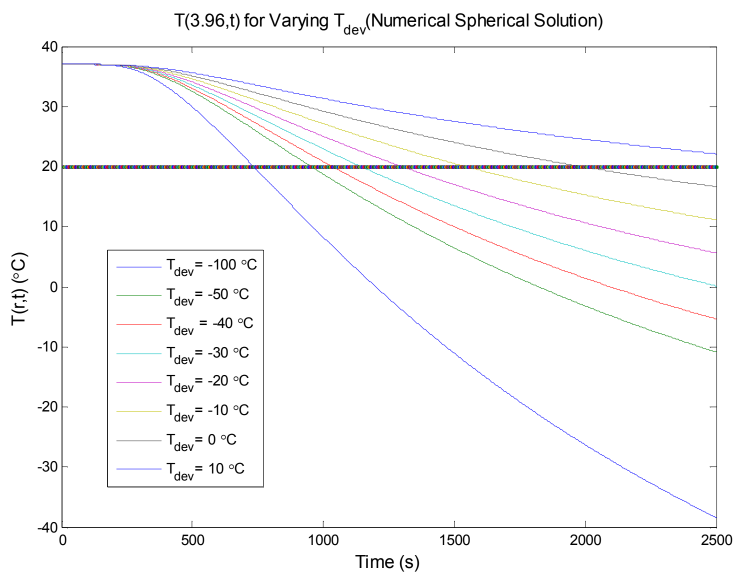

Figure 10. Effect of different device temperatures on the numerical solution one inch below the surface for the spherical model.

VI. Conclusions and Future Work

This study examined two possible methods for cerebral cooling: one that cools a small slab-like portion of the brain and the other that cools the entire spherical surface. Based on the analytical and numerical temperature profiles, neither method is a realistic alternative therapy under the defined constraints of rapidly cooling cortical tissue to a depth of one inch. However, previous studies in rat and mouse models have demonstrated effective seizure control by cooling smaller volumes of affected brain tissue to 20 °C.[8]

Future modeling could examine temperature profiles closer to the surface, at depths on the scale of millimeters rather than inches.

Several assumptions were made that allowed rapid cerebral cooling to be modeled with the two defined methods. The physical constants utilized in calculating the temperature profiles may actually vary because of the layered structure and vasculature of brain tissue. The inhomogeneous nature of the organ could result in non-constant properties that could affect heat transport. Additionally, the complex geometry and cooling mechanism of the device were ignored, but could significantly alter the efficiency of cooling. Future models could examine more dynamic cooling devices that also vary with time. Recent studies have investigated the use of probes and microarrays to facilitate heat transfer into deeper tissues by maximizing the surface area of the brain exposed to the device.[4] Technological advancements in the field of thermoelectric modules for focal epilepsy treatment are being made, allowing for more efficient thermal control. Improvements in these models and devices will enable cerebral cooling to become an increasingly attractive therapy for unmanaged focal neocortical epilepsy.

VII. References

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Appendix A: Analytical Solution for Semi-infinite Slab Model

The slab model extends to infinity in the positive z direction and thus does not have a characteristic length. The three-dimensional heat equation can be reduced to a one-dimensional heat equation (Eq. 1) with an initial condition (Eq. 2) and two boundary conditions (Eq. 3-4). The heat equation (Eq. 1) can then be solved using a similarity solution because the flow, which is invariant for θ and φ, will look identical at all length scales.[9]

$$\frac{\partial T}{\partial t} = D\frac{\partial^2 T}{\partial z^2}. \tag{1}$$

Initial condition: $T(r,0) = 37°C$ (2)

Boundary condition #1: $\frac{\partial T}{\partial r}(0,t) = 0$ (3)

Boundary condition #2: $T(R,t) = T_{dev.}$ (4)

A length scale δ over which the temperature changes minimally from the initial temperature can be defined. The diffusion equation can then be rewritten in terms of the defined length scale (Eq. 5).

$$\frac{1}{\delta^2} = \frac{1}{D}\left(\frac{1}{t}\right). \tag{5}$$

Solving for δ,

$$\delta = \sqrt{Dt}. \tag{6}$$

A dimensionless similarity variable η that combines z and t can be defined (Eq. 7):

$$\eta = \frac{z}{2\delta} = \frac{z}{\sqrt{4Dt}}. \tag{7}$$

Assuming that T is a function of only η, the heat equation (Eq. 1) can be rewritten by substituting in η (Eq. 7).

$$\frac{\partial T}{\partial t} = \frac{\partial T}{\partial t}\cdot\frac{\partial \eta}{\partial \eta} = \frac{\partial T}{\partial \eta}\cdot\frac{\partial \eta}{\partial t} = z\left(-\frac{1}{2}\right)(4Dt)^{-\frac{3}{2}}\frac{\partial T}{\partial \eta} = \frac{-z}{2t\sqrt{4Dt}}\frac{\partial T}{\partial \eta} \tag{8}$$

$$\frac{\partial T}{\partial z} = \frac{\partial T}{\partial z}\cdot\frac{\partial \eta}{\partial \eta} = \frac{\partial T}{\partial \eta}\cdot\frac{\partial \eta}{\partial z} = \frac{1}{\sqrt{4Dt}}\frac{\partial T}{\partial \eta} \tag{9}$$

$$\frac{\partial^2 T}{\partial z^2} = \frac{\partial}{\partial z}\cdot\frac{\partial T}{\partial z}\cdot\frac{\partial \eta}{\partial \eta} = \frac{\partial}{\partial \eta}\cdot\frac{\partial T}{\partial z}\cdot\frac{\partial \eta}{\partial z} = \frac{1}{4Dt}\frac{\partial^2 T}{\partial \eta^2} \tag{10}$$

Substituting the partial derivatives (Eq. 8-10) back into the original differential equation (Eq. 1) results in a differential equation that is only dependent on η (Eq. 11).

$$\frac{\partial^2 T}{\partial \eta^2} = -2\eta\frac{\partial T}{\partial \eta} \tag{11}$$

The initial and boundary conditions can also be written in terms of η:

Initial condition: $T(\eta \to \infty) = 37\ °C$ (12)
Boundary condition #1: $T(\eta = 0) = T_{dev}$ (13)
Boundary condition #2: $T(\eta \to \infty) = 37\ °C.$ (14)

The initial condition and second boundary condition become the same condition in terms of η. A substitution is made to solve the differential equation. Setting $w = \frac{\partial T}{\partial \eta}$, the differential equation becomes:

$$\frac{\partial^2 w}{\partial \eta^2} = -2\eta w. \tag{15}$$

Separating variables,

$$\frac{\partial w}{w} = -2\eta \partial \eta. \tag{16}$$

Integrating,

$$\ln(w) = -\eta^2 + C \tag{17}$$

$$w = e^{-\eta^2 + C} \tag{18}$$

$$w = Ce^{-\eta^2}. \tag{19}$$

Substituting $w = \frac{\partial T}{\partial \eta}$ back into the solution of the differential equation (Eq. 19) and integrating,

$$\frac{\partial T}{\partial \eta} = C_1 e^{-\eta^2} \tag{20}$$

$$\int \partial T = \int C_1 e^{-\eta^2} \partial \eta \tag{21}$$

$$T = C_1 \int e^{-\eta^2} \partial \eta + C_2 \tag{22}$$

$$T = C_1 \frac{\sqrt{\pi}}{2} \operatorname{erf}(\eta) + C_2 \text{ (from integral table).} \tag{23}$$

Applying the boundary conditions,

Boundary Condition #1:
$$T_{dev} = C_1 \frac{\sqrt{\pi}}{2} \operatorname{erf}(0) + C_2$$
$$C_2 = T_{dev} \tag{24}$$

Boundary Condition #2:
$$37\ °C = C_1 \frac{\sqrt{\pi}}{2} \operatorname{erf}(\infty) + T_{dev}$$
$$C_1 = \frac{2}{\sqrt{\pi}} (37\ °C - T_{dev}) \tag{25}$$

The solution for the semi-infinite slab model is:

$$T(\eta) = \frac{2}{\sqrt{\pi}}(37\text{ °C} - \mathrm{T_{dev}})\frac{\sqrt{\pi}}{2}\mathrm{erf}(\eta) + T_{dev} \tag{26}$$

$$\boxed{T(z,t) = \frac{2}{\sqrt{\pi}}(37\text{ °C} - \mathrm{T_{dev}})\frac{\sqrt{\pi}}{2}\mathrm{erf}(\frac{z}{\sqrt{4Dt}}) + T_{dev}} \tag{27}$$

Appendix B: Analytical Solution for Spherical Case

The heat equation in spherical coordinates can be defined by a one-dimensional partial differential equation (Eq.1), an initial condition (Eq. 2), and two boundary conditions (Eq.3-4).

$$\frac{\partial T}{\partial t} = \frac{D}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T}{\partial r}\right) \quad (1)$$

Initial condition: $T(r,0) = 37^oC$ (2)

Boundary condition #1: $\frac{dT}{dr}(0,t) = 0$ (3)

Boundary condition #2: $T(R,t) = T_{dev}$ (4)

The general solution to the PDE may be written as the sum of a particular solution and homogeneous solution, which may be solved for individually utilizing boundary conditions (Eq. 5). The general solution will satisfy:

$$T(r,t) = T_H + T_P \quad (5)$$

<u>Solve for the steady-state (particular) solution to PDE, T_P:</u>

$$\frac{\partial T}{\partial t} = 0 \quad (6)$$

$$\int 0 = \int \frac{\partial}{\partial r}\left(r^2\frac{\partial T}{\partial r}\right) \quad (7)$$

$$C_1 = r^2\frac{\partial T}{\partial r} \quad (8)$$

$$\int \frac{C_1}{r^2}dr = \int dT \quad (9)$$

$$T = \frac{C_1}{r} + C_2 \quad (10)$$

Boundary conditions (Eq. 3-4) are applied to steady state solution (Eq. 10) to solve for the constants (Eq. 12-13).

$$\frac{dT}{dr} = -\frac{C_1}{r^2} = 0 \quad (11)$$

$$C_1 = 0 \quad (12)$$

$$T(R,t) = T_{dev} = C_2 \quad (13)$$

Particular solution for the PDE:

$$T_P = T_{dev} \tag{14}$$

Solve for the homogeneous solution to PDE, T_H:

The homogeneous solution will satisfy homogeneous boundary conditions (Eq. 15-16).

$$\frac{dT_H}{dr}(0,t) = 0 \tag{15}$$

$$T_H(R,t) = 0 \tag{16}$$

The homogeneous solution to the PDE (Eq.1) is determined using the technique of separation of variables.

$$T_H(r,t) = \varphi(r)G(t) \tag{17}$$

Partial differential equation becomes:

$$\frac{dG}{dt}\varphi(r) = \frac{D}{r^2}\frac{d}{dr}\left(r^2\frac{d\varphi}{dr}G(t)\right) \tag{18}$$

$$\frac{1}{DG}\frac{dG}{dt} = \frac{1}{r^2\varphi}\frac{d}{dr}\left(r^2\frac{d\varphi}{dr}\right) = -\lambda \tag{19}$$

The time-dependent solution, G(t) will take the form of:

$$G(t) = e^{-D\lambda t} \tag{20}$$

Solve for the *r*-dependent solution, *φ(r):*

$$-\lambda\varphi = \frac{1}{r^2}\frac{d}{dr}(r^2\frac{d\varphi}{dr}) \tag{21}$$

Solution will take the form of :

$$\varphi(r) = \frac{A\cos(\sqrt{\lambda}r)}{r} + \frac{B\sin(\sqrt{\lambda}r)}{r} \tag{22}$$

At the center of the sphere, the boundary condition of flux = 0 indicates that $\varphi(0)$ = a finite value.

$$\varphi(0) = \frac{A\cos(\sqrt{\lambda}0)}{0} + \frac{B\sin(\sqrt{\lambda}0)}{0} \tag{23}$$

In order to satisfy and apply L'Hopital's rule, constant A must equal 0 since sin(0) will always be 0 and *B* can thus be any constant.

Eigenmode function will become:

$$\varphi(r) = \frac{B\sin(\sqrt{\lambda}r)}{r} \tag{24}$$

Apply second boundary condition at *r*=*R*:

$$\varphi(R) = \frac{B\sin(\sqrt{\lambda}R)}{R} = 0 \tag{25}$$

$$B \neq 0, \sin\left(\sqrt{\lambda}R\right) = 0 \tag{26}$$

$$\lambda = \left(\frac{n\pi}{R}\right)^2, n = 0,1,2,3 \ldots \tag{27}$$

Homogeneous solution:

$$T_H = \sum_{n=0}^{\infty} B_n \frac{1}{r} \sin\left(\sqrt{\lambda}r\right) e^{-D\lambda t} \tag{28}$$

General solution $T(r,t) = T_H + T_P$:

$$T(r,t) = T_{dev} + \sum_{n=0}^{\infty} B_n \frac{1}{r} \sin\left(\sqrt{\lambda}r\right) e^{-D\lambda t} \tag{29}$$

Apply initial condition to solve for B_n:

$$B_n = \frac{2}{R}(37 - T_{dev}) \int_0^R r \sin\left(\frac{n\pi}{R} r\right) dr \tag{30}$$

$$B_n = -\frac{2R}{n\pi}(37 - T_{dev})(-1^n) \tag{31}$$

$$\boxed{T(r,t) = T_{dev} + \sum_{n=0}^{\infty} -\frac{2R}{n\pi}(37 - T_{dev})(-1^n)\frac{1}{r}\sin\left(\sqrt{\lambda}r\right) e^{-D\lambda t}} \tag{32}$$

Appendix C: MATLAB Code

A. Analytical Cartesian Solution: Surface Plot and Temperature Profile at One Inch

```
% Define physical parameters

c = 3.6; %heat capacity J/gK
p = 1; %density 1 g/cm^3
k = 0.005; %thermal conductivity

% Diffusivity constant
D = k/(c*p); %cm^2 / sec
Ti = 37; %Celsius initial temperature of brain tissue
depth = 2.54; %desired cooling depth [cm]

T0 = -50; %(20 - 37*erf(depth/sqrt(4*D*30)))/ (1-erf(depth/sqrt(4*D*30)));

zrange = 6.5; %cm Radius of brain
zinc = zrange/100;
z = 0:zinc:zrange;

trange = 4500; %seconds
tinc = trange/100;
t = 0:tinc:trange;

initial = ones(length(z), length(t));
T = initial;

for n = 1: length(z)
    for e = 1: length(t)
        T(n,e) = (Ti - T0) * erf(z(n) / sqrt(4*D*t(e))) + T0;
    end
end


figure(1)
surf(t, z, T)
title('Analytical Cartesian Solution')
xlabel('Time (s)')
ylabel('Z distance from surface (cm)')
zlabel('T(z,t) (\circ C)')

figure(2)
Distance = find(z==2.535);
plot(t,T(Distance,:));
xlabel('Time (s)')
ylabel('T(2.54,t) (\circ C)')
title('Analytical Cartesian Solution at One Inch Below Surface')
```

B. Analytical Spherical Solution: Surface Plots and Temperature Profile at One Inch

```
% Define physical parameters
c = 3.6; %heat capacity J/gK
p = 1; %density 1 g/cm^3
k = 0.005; %thermal conductivity

% Diffusivity constant
D = k/(c*p); %cm^2 / sec
Ti = 37; %Celsius, brain tissue is initially at body temperature
depth = 2.54; %desired cooling depth [cm]

T0 = -50; %device temperature at the surface;

trange = 4500; %seconds
tinc = trange/100;
t = 0:tinc:trange; %time vector
tskip= 2;

rrange = 6.5; %cm
rinc = rrange/100;
r = 0:0.02:rrange; %radius vector
rskip=2;

R = 6.5; %Radius of brain

initial = ones(length(r), length(t));
T_analytical = initial .* T0; %initialize T_analytical including steady-state

An = 0;
Asin = initial;
Aexp = initial;
nterms = 25;

for n = 1:nterms
    for d = 1:length(r)
        for e = 1:length(t)
            An = (-2*R*(Ti-T0)*(-1)^n)/(pi*n);
            Asin(d,e) = 1/r(d) * sin(pi*n*r(d)/R);
            Aexp(d,e) = exp(-D*(pi*n/R)^2*t(e));
        end
    end
    T_analytical = T_analytical + An .* Asin .* Aexp;

end

figure(1);
surf(t(1:tskip:end), r(1:rskip:end), T_analytical(1:rskip:end,1:tskip:end));
title('Analytical Spherical Solution');
xlabel('Time (s)')
ylabel('r from center brain (cm)')
zlabel('T(r,t) (\circ C)')
```

```
figure(2);
surf(t(2:tskip:end), r(2:rskip:end), T_analytical(2:rskip:end,2:tskip:end));
title('Analytical Spherical Solution without T(0,0)');
xlabel('Time (s)')
ylabel('r from center brain (cm)')
zlabel('T(r,t) (\circ C)')

figure(3);
Distance = find(r==R-2.54);
plot(t, T_analytical(Distance,:))
title('Analytical Spherical Solution at One Inch Below Surface');
xlabel('Time (s)')
ylabel('T(3.96,t) (\circ C)')
```

C. Numerical Spherical Solution: Surface Plot and Temperature Profile at One Inch

```
function spherical
% solution using Matlab's built in "pdepe" in spherical coordinates
% constants
global D Tdev Tnot
D = 1.389*10^(-3); %cm^2/s
time = 4500; %time(seconds)
R = 6.5; %Radius of full brain (cm)
depth = R - 2.54; %depth of interest (cm)
Tnot = 37; % Initial temperature = body temperature (degrees C)
Tdev = -50; %Surface temperature (degrees C), to be solved for


% domain
rmesh = 0:0.02:R; % domain in r
tmesh = 0:0.1:time;  % domain in t
rskip=50;
tskip=500;

sol_pdepe = pdepe(2,@pdefun,@ic,@bc,rmesh,tmesh);  %2 = spherical coordinates

figure(1)
surf(tmesh(1:tskip:end),rmesh(1:rskip:end),sol_pdepe(1:tskip:end,1:rskip:end)
')
title('Numerical Spherical Solution')
xlabel('Time (s)')
ylabel('r from center brain (cm)')
zlabel('T(r,t) (\circ C)')

figure(2)
Distance = find(rmesh==depth);
plot(tmesh, sol_pdepe(:,Distance));
xlabel('Time (s)')
ylabel('T(3.96,t) (\circ C)')
title('Numerical Spherical Solution at One Inch Below Surface')
```

```
% function definitions for pdepe:
% ---------------------------------------------------------------

function [c, f, s] = pdefun(x, t, u, DuDx)
% PDE coefficients functions

global D
c = 1;
f = D * DuDx; % diffusion
s = 0; % homogeneous, no driving term

% ---------------------------------------------------------------

function u0 = ic(x)
global Tnot
% Initial conditions function

u0 = Tnot; % delta impulse at center

% ---------------------------------------------------------------

function [pl, ql, pr, qr] = bc(xl, ul, xr, ur, t)
% Boundary conditions function
global Tdev
pl = 0; % Zero value boundary condition at center (r=0)
ql = 1;  % flux boundary condition at center (r=0)
pr = ur-Tdev; % value bounday condition (r=R)
qr = 0;  % flux boundary condition (r=R)
```

D. Analytical Cartesian Solution: Varying T_{dev}

%SlabPlot is just the function version of pdepe spherical plot. It takes in T_{dev} and outputs the time, distance, and solution vectors.

```
[ tmesh100,z100,sol_pdepe100] = SlabPlot(-100);
[ tmesh50,z50,sol_pdepe50] = SlabPlot(-50);
[ tmesh40,z40,sol_pdepe40 ] = SlabPlot(-40);
[ tmesh30,z30,sol_pdepe30 ] = SlabPlot(-30);
[ tmesh20,z20,sol_pdepe20 ] = SlabPlot(-20);
[ tmesh10,z10,sol_pdepe10 ] = SlabPlot(-10);
[ tmesh0,z0,sol_pdepe0 ] = SlabPlot(0);
[ tmesh10plus,z10plus,sol_pdepe10plus ] = SlabPlot(10);

Distance = find(z100==2.54);
plot(tmesh100, sol_pdepe100(Distance,:),tmesh50,
sol_pdepe50(Distance,:),tmesh40, sol_pdepe40(Distance,:),tmesh30,
sol_pdepe30(Distance,:),tmesh20, sol_pdepe20(Distance,:),tmesh10,
sol_pdepe10(Distance,:),tmesh0, sol_pdepe0(Distance,:),tmesh10plus,
sol_pdepe10plus(Distance,:));
line(0:4500,20)
```

```
xlabel('Time (s)')
ylabel('T(z,t) (\circC)')
title('T(R-2.54,t) for Varying T_d_e_v(Analytical Cartesian Solution)')
legend('T_d_e_v= -100 \circC','T_d_e_v= -50 \circC','T_d_e_v = -40
\circC','T_d_e_v= -30 \circC','T_d_e_v= -20 \circC','T_d_e_v= -10
\circC','T_d_e_v= 0 \circC','T_d_e_v= 10 \circC')
```

E. Analytical Spherical Solution: Varying T_{dev}

%PlotSphericalAnalytical is just the function version of the analytical spherical plot. It takes in T_{dev} and outputs the time, radius, and solution vectors.

```
[ tmesh100,z100,sol_pdepe100] = PlotSphericalAnalytical(-100);
[ tmesh50,z50,sol_pdepe50] = PlotSphericalAnalytical(-50);
[ tmesh40,z40,sol_pdepe40 ] = PlotSphericalAnalytical(-40);
[ tmesh30,z30,sol_pdepe30 ] = PlotSphericalAnalytical(-30);
[ tmesh20,z20,sol_pdepe20 ] = PlotSphericalAnalytical(-20);
[ tmesh10,z10,sol_pdepe10 ] = PlotSphericalAnalytical(-10);
[ tmesh0,z0,sol_pdepe0 ] = PlotSphericalAnalytical(0);
[ tmesh10plus,z10plus,sol_pdepe10plus ] = PlotSphericalAnalytical(10);

Distance = find(z100==3.96);
plot(tmesh100, sol_pdepe100(Distance,:),tmesh50,
sol_pdepe50(Distance,:),tmesh40, sol_pdepe40(Distance,:),tmesh30,
sol_pdepe30(Distance,:),tmesh20, sol_pdepe20(Distance,:),tmesh10,
sol_pdepe10(Distance,:),tmesh0, sol_pdepe0(Distance,:),tmesh10plus,
sol_pdepe10plus(Distance,:));
line(0:4500,20)
xlabel('Time (s)')
ylabel('T(r,t) (\circC)')
title('T(3.96,t) for Varying T_d_e_v(Analytical Spherical Solution)')
legend('T_d_e_v= -100 \circC','T_d_e_v= -50 \circC','T_d_e_v = -40
\circC','T_d_e_v= -30 \circC','T_d_e_v= -20 \circC','T_d_e_v= -10
\circC','T_d_e_v= 0 \circC','T_d_e_v= 10 \circC')
```

F. Numerical Spherical Solution: Varying T_{dev}

%pdePlotspherical is just the function version of pdepe spherical plot. It takes in T_{dev} and outputs the time, radius, and solution vectors.

```
[ rmesh100,tmesh100,sol_pdepe100] = pdePlotspherical(-100);
[ rmesh50,tmesh50,sol_pdepe50] = pdePlotspherical(-50);
[ rmesh40,tmesh40,sol_pdepe40 ] = pdePlotspherical(-40);
[ rmesh30,tmesh30,sol_pdepe30 ] = pdePlotspherical(-30);
[ rmesh20,tmesh20,sol_pdepe20 ] = pdePlotspherical(-20);
[ rmesh10,tmesh10,sol_pdepe10 ] = pdePlotspherical(-10);
[ rmesh0,tmesh0,sol_pdepe0 ] = pdePlotspherical(0);
[ rmesh10plus,tmesh10plus,sol_pdepe10plus ] = pdePlotspherical(10);
```

```
Depth2=6.5-2.54;
Distance = find(rmesh100==Depth2);
plot(tmesh100, sol_pdepe100(:,Distance),tmesh50,
sol_pdepe50(:,Distance),tmesh40, sol_pdepe40(:,Distance),tmesh30,
sol_pdepe30(:,Distance),tmesh20, sol_pdepe20(:,Distance),tmesh10,
sol_pdepe10(:,Distance),tmesh0, sol_pdepe0(:,Distance),tmesh10plus,
sol_pdepe10plus(:,Distance));
line(0:4500,20,'Linestyle','-')
xlabel('Time (s)')
ylabel('T(r,t) (\circC)')
title('T(3.96,t) for Varying T_d_e_v(Numerical Spherical Solution)')
legend('T_d_e_v= -100 \circC','T_d_e_v= -50 \circC','T_d_e_v = -40
\circC','T_d_e_v= -30 \circC','T_d_e_v= -20 \circC','T_d_e_v= -10
\circC','T_d_e_v= 0 \circC','T_d_e_v= 10 \circC')
```