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USING MICROWAVE ENERGY TO TREAT TUMORS

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Abstract—Recently, hyperthermia has been investigated as an alternate therapy for the treatment of tumors. This paper explored the feasibility of preferential hyperthermia as a method of treating deep seated tumors. The overall goal of this research was to determine theoretically if preferential heating could be used to attain the desired thermal dose (DTD) for a two cm diameter tumor. The simulations in this work show that, when using a single rod insert, the model cannot provide enough energy for an entire 2 cm diameter tumor to receive the DTD. However, when using an enhanced design model with multiple (4) rods inserts, the DTD could be attained in a tumor up to 3.5 cm in diameter. This study involved using the model a spherical 2 cm tumor, assuming the tumor is located in deep tissue with a constant perfusion rate and no major blood vessels nearby. This tumor was placed in the center of a cube of healthy tissue. To achieve the preferential heating of the tumor, a rod insert was placed in the center of the tumor and microwave energy was applied to the insert (in the form of volumetric heating). The thermal modeling of this system was based on the Pennes Bioheat equation with a maximum temperature limitation of 80°C. Additional enhanced design models were also examined. These models include 2 cm and 4 cm tumors with four rod inserts symmetrically placed about the tumor and a 4 cm tumor model using a single rod insert with antennae attached to insert to increase energy distribution to the tumor. The simulations show that only the enhanced design cases with four rods inserts can achieve the DTD for an entire 2 cm tumor. The main purpose of this research was to determine if a minimally invasive treatment system using one or more rod inserts could be used to preferentially heat (and attain the DTD) a 2 cm diameter (or larger) tumor. Achieving the DTD for a 2 cm or larger tumor was important because currently the maximum diameter tumor that can be treated via hyperthermia is approximately

2 cm.

In the remainder of this paper. I present the following: First, a background of prior research performed on various subject matters related to basic hyperthermia treatments, combination hyperthermia treatments, and computer modeling. After that, the development and verification of simplified thermal computer models of human tissue is described. Discussed next is the method of calculating the resulting thermal dose, the process of analyzing the results of the simulations of the thermal computer models. Once these introductory topics have been considered, the results of the computer modeling (using the primary thermal model) are presented. First, the effects of varying the perfusion rates in the computer model are explained. Then, a comparison of the overall treatment times, where the optimal treatment time was chosen, is discussed. Presented next is the results of varying the heat input rate. Rates examined include a constant heat generation rate, a constant insert temperature, a pulsed heat generation rate, various ramp heat generation rates, as well as exponential decay heat generation rates.

1. BASIC HYPERTHERMIA TREATMENTS

Hyperthermia has been described as an effective method to treat various types of malignant cells, both *in vitro* and *in vivo* [1] Traditional hyperthermia involves heating the tissue to at least 43°C for one hour, while high intensity thermal therapies involve higher temperature for shorter times. Traditional hyperthermia often involves two distinct phases. During the first phase (typically lasting 10 to 30 minutes), the blood flow to the area often doubles, with no

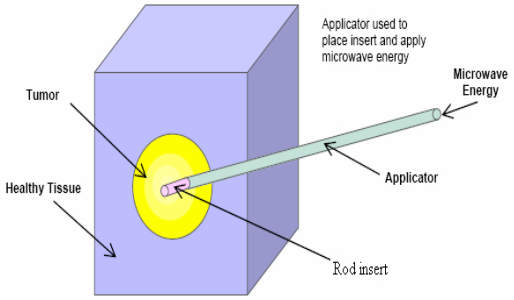

Figure 1. Schematic of the targeted microwave interstitial treatment.

significant cell destruction. However, during the second phase blood flow decreases, which is most likely due to localized microthrombosis in the hottest places in the tissue, and the amount of tissue necrosis increases significantly [2]. Reversible thermal effects have been shown to occur when tumors are briefly heated up to 44°C and then allowed to cool. However, in vivo studies have shown that when tissue is heated above 45°C irreversible tissue changes occur. Again, blood flow is affected when heating the tissue. The blood flow rate in hamsters was found to increase rapidly as the tissue temperature is raised from 32°C to 37°C, and then it was found to continue to increase at a slower rate as the tissue is heated to 44°C [3]. Likewise, hemorrhagic coagulation necrosis was shown to occur when prostate tissue is heated above 45°C, and enhanced results were noted when the intraprostatic temperatures were raised above 50°C [4]. One of the problems with systemic hyperthermia is that areas of normal tissue are heated, as well as the desired tumor area. One approach to circumventing this problem is to cool the blood flow to the normal tissue. A study of this approach used "balanced heat transfer" involving systemic heat absorption and the dissipation rates (due to the extracorporeal blood cooling). The study involved comparing the results of a simplified model using five test dogs, with similar outcomes. These results indicated that systemic blood cooling could be used to limit systemic temperature rise thus allowing an increase in the intratumoral temperature. Another approach is to use drugs to decrease the perfusion within the tumor. This has been shown to improve hyperthermia treatment efficacy. Various drugs have been investigated to reduce perfusion; however, these medications not only decreased the tissue perfusion in the tumor but in the normal tissue as well. New research has shown that an intravenous injection of the substance causes a preferential reduction in the blood flow to the tumor. Using this preferential reduction could allow hyperthermia to be more effective [4].

2. METHODS OF APPLYING HYPERTHERMIA

There are several modalities that can be used to perform hyperthermia treatments (generally these treatments are invasive, but sometimes treatments can be performed noninvasively), with each method having advantages and limitations. Some of these modalities are noninvasive, such as high intensity focused ultrasound, and some are minimally invasive or invasive including microwave ablation, radio frequency (RF) ablation, and laser ablation. there are three crucial parameters in microwave hyperthermia. These parameters, applicable to both invasive and noninvasive treatments, are temperature, time,

and focusing of heat. For these therapies, heat is produced by electromagnetic waves in the frequency range of 300 to 300,000 MHz while frequencies in the range of 300 kHz to 300 MHz are used to generate heat for radio frequency therapies Benefits of microwave and radiofrequency treatments include the ability to apply the hyperthermia treatment directly to the tumor tissue through the invasive usage of probes. In addition, these ablative therapies seem to have very effective results However, these treatment methods do have limitations. One of the significant limitations of these two modalities is the maximum tumor size which can be treated. Generally, the current maximum tumor diameter which can be treated is approximately 2 cm. Another limitation of both modalities includes the lack of accurate and ample methods of monitoring the treatments to ensure that the entire tumor is destroyed. Finally, when probes are used the tips often experience intense heating and focusing the energy in the proper location to ensure tumor destruction is very difficult.

3. COMBINATION TREATMENTS

When used in combination with other therapies such as chemotherapy and radiation therapy, hyperthermia has been proven to have positive synergistic effects e.g., in aiding the treatment of esophageal carcinoma [5]. The effectiveness of combination hyperthermia treatments has also been shown in some clinical trials. A Phase III trial showed that when hyperthermia, monitored via invasive temperature probes, was added to radiation treatments for breast cancer recurrences there were significant improvements, including disease — free survival. However, the depth of the tumor and whether the disease had become systemic also played significant roles. The response of tumors less than 2 cm deep was significantly better than the response of tumors greater than 2 cm deep. In addition, if the disease became systemic, the patients were less likely to have a favorable outcome. For treating deeper tumors, radioactive microspheres have been successfully used apply *in situ* irradiation.

4. TIME-TEMPERATURE RELATIONSHIP FOR THERMAL THERAPIES

A time-temperature relationship for tissue necrosis can be shown for a variety of different tissue and cell types, such as hamster kidney cells. This time-temperature relationship was determined to be that for each 1°C decrease in temperature, the time required to kill the cells increased by a factor of 1.8 [6]. For each degree increase in

Celsius temperature, the time required to cause the same amount of cellular damage is reduced by half. Monitoring temperatures during hyperthermia may be a way to improve hyperthermia treatments. However, manually monitoring temperatures is invasive, time consuming, and inefficient. With the usage of hyperthermia in clinical settings, it is important to find a useful way to determine the relevant thermal dose received by the tissue. Therefore, the concept of equivalent or "degree-minutes" was created. This mathematical model is based on the thermal dose received after 1 hour at 43°C, which is sufficient to be lethal to tissue. When using adequately small time steps, the equivalent time, t_{43}, taken to reach a lethal thermal dose can be described by

$$t_{43} = \sum_{t=0}^{t=final} R^{(43-\overline{T})} \Delta t \tag{1}$$

where t is the current time, T is the average local temperature, and R is 0.5 above 43°C and 0.25 below 43°C [7]. The goals of this paper is Determine if a rod insert could cause an entire 2 cm tumor to receive the desired thermal dose (DTD).

5. BIOHEAT MODEL DEVELOPMENT AND VERIFICATION

The basic thermal model used in this work consisted of a single rod insert embedded in the tumor tissue surrounded by healthy tissue. For the healthy tissue, it was assumed that it was a deep tissue (such as the liver) having no major blood vessels flowing through the tissue (i.e., only perfusion flowing through it). The tumorous tissue was assumed to be spherical in shape, centered in the middle of the healthy tissue being modeled. A simplified thermal computer model of the system, described above, was developed for use in this work. Heat transfer was assumed to follow the Pennes Bioheat Equation [8].

$$\rho_t C_t \frac{\partial T}{\partial t} = k_c \nabla^2 T - \rho_b C_b \omega \left(T - T_b\right) + Q(x, y, z, t) \tag{2}$$

where the properties ρ, C, and k are the density (kg/m^3), specific heat (J/kg/K), and thermal conductivity (W/m/K), respectively, and the subscripts b and t represent the blood and the tissue. The term ω represents the heat removal by blood called the coefficient of perfusion (ml/ml/s), T is the local temperature (K), and heat (W), is added to the system through $Q(x, y, z, t)$. It was assumed that blood enters the tissue at the arterial temperature Ta, and the metabolic heating could

be neglected. Since heat is deposited only in the insert, for the tissue and the tumor portions of the thermal model, Equation (2) is reduced to

$$\rho_t C_t \frac{\partial T}{\partial t} = k_c \nabla^2 T - \rho_b C_b \omega \left(T - T_b\right) \tag{3}$$

Meanwhile, for the insert portion of the thermal model, Equation (2) becomes

$$\rho_t C_t \frac{\partial T}{\partial t} = k_c \nabla^2 T + Q(x, y, z, t) \tag{4}$$

For the purpose of this modeling, the tissue, tumor, and insert were all assumed to have perfect contact at their interfaces. In order to model this bioheat system, the computer simulation used to create a thermal model of a tissue tumor system. 0.1 W of heat was applied to a 1 cm cube of tissue and the heat transfer computed using two different methods. The model result was found to be equivalent to that of the calculated solution to 4 significant figures. This verification was accomplished by examining the steady state temperature at the center of the 1 cm cube of tissue in the computer model and comparing it to the manually calculated temperature to ensure these temperatures matched (they were found to be the same to 4 significant figures). The computer simulation was used to create the thermal model geometries and components as well as to assign the parameter values to the components of the models. The various model that was created include the basic thermal model (with a 2 cm tumor and a single rod insert). The parameter values used for these models are shown in Table 1 and the details of the model components and geometries are described in the rest of this section. These models were also given a constraint on the maximum temperature reached by any point in the system. The maximum temperature value chosen was 80°C and it ensured that neither the tissue in the system nor the blood in the system reach temperatures high enough to cause boiling or cavitations. In addition, for modeling, the heat (microwave energy) added to the system was assumed to be volumetric heating with all heat applied directly to the rod insert. The primary thermal model was developed to represent a tissue system consisting of a 6 cm cube of tissue (each side 6 cm in length), having no major blood vessels flowing through the tissue, with a 2 cm diameter tumor in the center. The tumor was chosen to have a diameter of 2 cm because this represents the general size limitation currently experienced in hyperthermia treatments To this tissue system, a single rod insert was added to the center of the tumor. As a result of symmetry in the tissue system, the necessary thermal model analyzed was only one eighth of the tissue system, as shown in Figure 2.

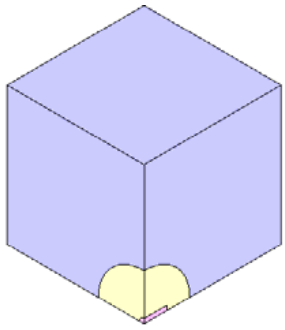

Figure 2. Model of the primary thermal model tissue system.

Table 1. Parameter values used for thermal modeling [8].

Input Parameters	Nominal Value
Tissue	
Density (kg/m^3)	1000
Specific Heat (J/kg/K)	3500
Thermal Conductivity(W/m/K)	0.5
Perfusion Rate (ml/g/min)	2
Tumor	
Density (kg/m^3)	1000
Specific Heat (J/kg/K)	3500
Thermal Conductivity(W/m/K)	0.55
Perfusion Rate (ml/g/min)	2
Rod Insert	
Density (kg/m^3)	3160
Specific Heat (J/kg/K)	675
Thermal Conductivity(W/m/K)	490
Applicator	
Density (kg/m^3)	21500
Specific Heat (J/kg/K)	132
Thermal Conductivity(W/m/K)	71

The rod inserts were made of thin glass tubules filled with rod powder. Rod was chosen as the material for these inserts due to its excellent microwave energy absorption properties. For this feasibility study, the dielectric properties of the materials and the thin glass portion of the insert were neglected. Each thermal model consists of at least one cylindrical rod insert. These inserts have a length, L, of ten millimeters and a diameter, D, of two millimeters, as shown in Figure 3.

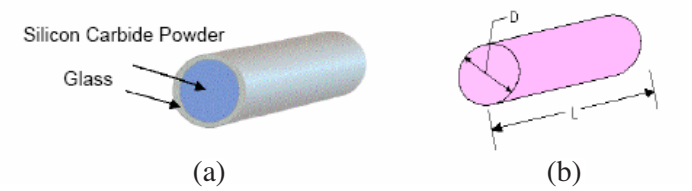

Figure 3. (a) rod insert, (b) model of the rod insert (neglecting glass coating).

6. THERMAL DOSE CALCULATION

There exists a time-temperature relationship for cell death. The amount of energy needed for tissue necrosis is considered the required "thermal dose" for that tissue. In standard hyperthermia, the amount of energy required for tissue necrosis is equivalent to maintaining a temperature of 43°C for one hour. The thermal dose time-temperature relationship, $D(x, y)$, can be defined by the mathematical model presented [9].

$$D(x,y) = \int_0^{t_f} R^{T_r - T(x,y,t)} dt$$

$$R = \begin{array}{ll} .50, & T(x,y,t) \geq T_r; \\ .25, & T(x,y,t) < T_r \end{array} \tag{5}$$

where T_r is the reference temperature of 43°C. Next, the known relationship required for cell death (tissue maintained at 43°C for 1 hour) was applied to Equation (5) to determine the required thermal dose. This resulted in a thermal dose of 3600 s. This thermal dose was standardized by dividing by one hour (3600 s) to yield a unit less value of 1, which defines the threshold for cell death. All thermal doses reported in this work are based on this standardized thermal dose.

7. RESULTS AND DISCUSSION

7.1. Comparison of Overall Treatment Times

To compare the various treatment durations, a constant heat generation rate was applied to the rod insert for a set period of time (five, ten, or fifteen minutes). The rate of heat generation was determined in each case such that the maximum temperature limit of 80°C was not violated. Thus, as the treatment time increases, the heating rate decreases, however the total energy input increases as shown in Table 2. The cumulative thermal dose was calculated for

Table 2. Relations between duration of treatment and amount of tissue achieving the desired thermal dose (DTD).

Duration of Treatment (min)	Energy Input Rate (W)	Total Energy Input (J)	Radial Distance Achieving DTD (cm)	Volume Achieving DTD (cm^3)
5	0.880	264	0.526	0.607
10	0.864	518.4	0.672	1.271
15	0.785	706.5	0.717	1.544

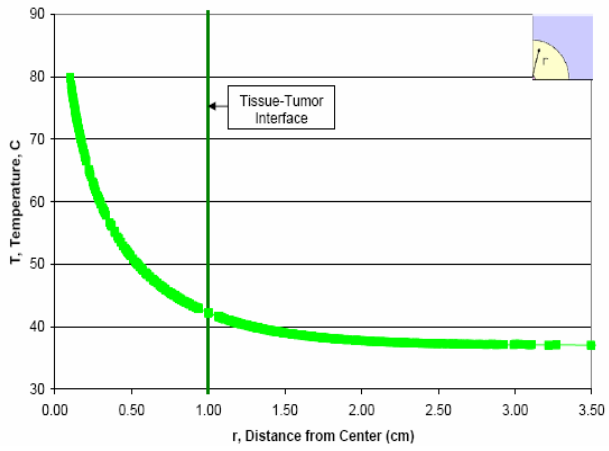

Figure 4. Example of the nodal temperatures for the 10 minute constant heat generation rate treatment.

each case (using the nodal temperatures in finite difference). After each thermal simulation was performed, the thermal dose was calculated for simulation. Figure 4 displays an example of the nodal temperatures for the 10 minute constant heat generation treatment, while Figure 5 shows the thermal dose as a function of the average radius from the insert for the three different treatment times.

Figure 5 shows, as expected, that longer energy treatment times result in a greater volume of tissue receiving the desired thermal dose,

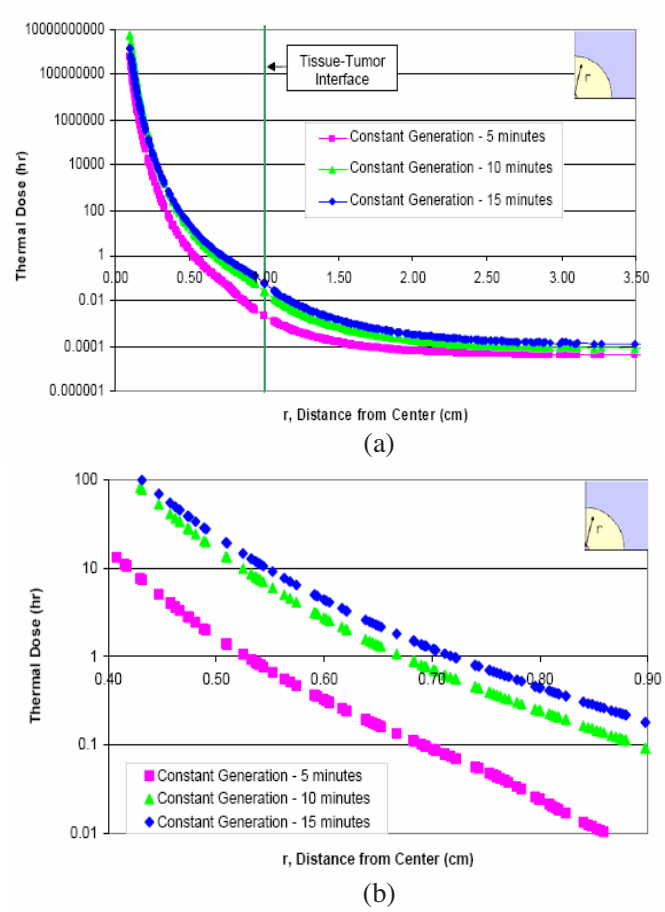

Figure 5. Thermal dose results for the time comparison simulations. (a) shows the thermal dose results of the entire front plane, (b) focuses on the location farthest from the center of the tumor where the desired thermal dose is estimated to occur (at a thermal dose of 1).

DTD. Figure 6 shows the effects of increasing the treatment duration on the volume of tissue achieving the DTD. Examination of this figure also shows that the volume of tissue achieving the DTD does not increase linearly with time. Thus, after considering these results, it was determined that a ten minute treatment time was the most advantageous because it yielded the greatest volume of tissue attaining the DTD for a minimum treatment time Therefore, for the simulations performed in the rest of this study, a 10 minute treatment duration was used.

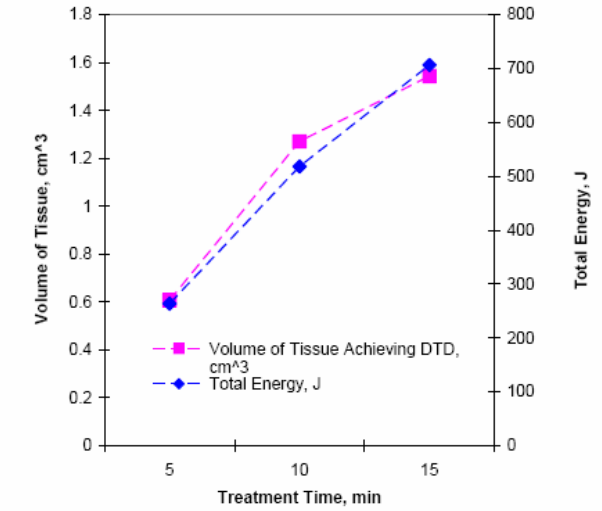

Figure 6. Comparison of treatment time an the resulting volume of tissue achieving the desired thermal dose (DTD).

7.2. Perfusion Comparison

The effects of blood perfusion were determined using several different perfusion rates. This study was important for two reasons. First, tumor blood flow can vary greatly from tumor to tumor and is not completely understood. In addition, currently blood perfusion levels are estimated and exact values are not known. Therefore, a comparison of a range of values was important to understand the effects of variations in blood perfusion on the thermal dose. To accomplish this study, all other properties and loads were maintained while the perfusion rate was varied for each thermal dose simulation. Various rates of perfusion (high, medium, low, and zero) were given to the tumor as shown in Table 3 [11]. The thermal dose for each perfusion

Table 3. Perfusion rates used for perfusion comparison.

Perfusion Rate	
Level	Magnitude ml/g/min
Zero	0
Low	0.5
Medium	2.0
High	6.0

Table 4. Effects of perfusion on the volume of tissue achieving the required thermal dose.

Perfusion Rate	Radial Distance (cm)	Volume (cm^3)	% of Tumor	% Volume Change From No Perfusion
Zero	0.65	1.13	27.0	0
Low	0.64	1.07	25.6	−4.9
Medium	0.63	1.07	25.5	−5.2
High	0.63	1.06	25.3	−6.3

rate was then calculated as Described in last section. The results for the thermal dose are shown in Figure 7 Two important points are evident. First, the effect of perfusion magnitude is relatively small, as there is little difference between the low, medium, and high values. Secondly, the effect of the presence of perfusion is relatively small. Therefore, perfusion has a small effect on the calculation of thermal dose as discussed below.

As Figure 7 shows, when there is no perfusion, the desired thermal dose (DTD) is achieved by all cells that are about 0.65 cm from the center of the tumor. Meanwhile, at the highest rate of perfusion, the DTD expected to occur for cells that are less than 0.63 cm away from the center of the tumor. The effects of perfusion on the volume of tissue achieving the DTD are summarized in Table 4.

As mentioned earlier, accounting for perfusion in the thermal

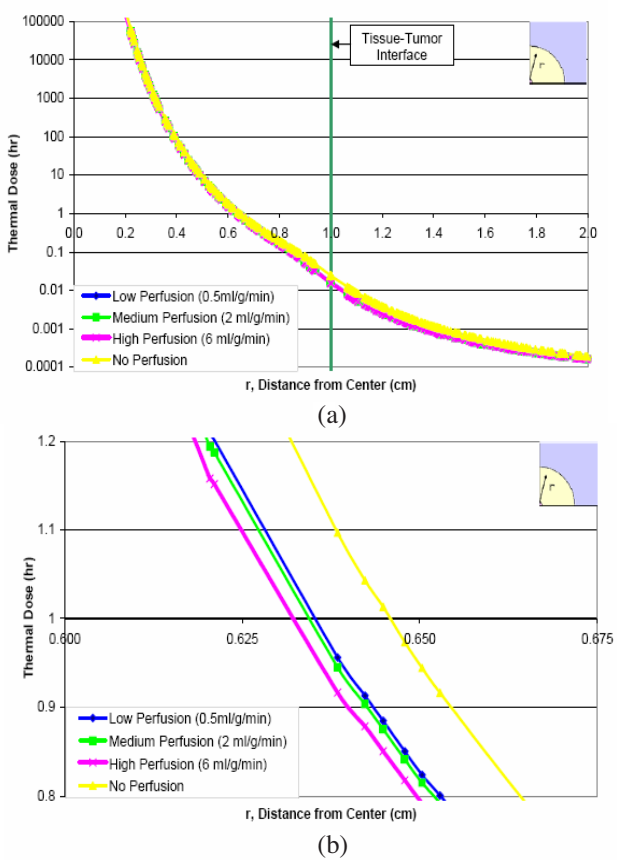

Figure 7. Thermal dose results of perfusion study simulations. (a) shows the thermal dose results of the entire front plane, (b) focuses on the location farthest from the center of the tumor where the desired thermal dose (DTD) occurs (at a thermal dose of 1).

model has some effect on the solution; however, the exact rate of perfusion is not as significant (i.e., $\sim$ 5% of the affected volume as shown in Table 4). Therefore, for the simulations performed in the rest of this study, the medium rate of perfusion (2 ml/g/min) was used.

7.3. Effects of Heat Input Rate

The effects of the functional form of the heat rate applied to the rod insert were examined to determine the effects on the cumulative thermal dose. both extreme cases of a constant heating rate and a

constant temperature in the insert were examined along with other variable heating rates. These heating rates included pulse function generations, ramped heating generations (with both single and multiple slopes), and exponential decay heat generations as outlined in the following sections. These various heating scenarios were examined to determine the optimum heating protocol.

7.3.1. Constant Generation Rate

To determine the maximum thermal dose possible with a constant heat generation rate, various thermal simulations were performed with different constant heat generation rates applied to a single rod insert in the primary thermal model (with a perfusion rate of 2 ml/g/min). For each simulation, the constant heat generation rate was applied for ten minutes. Based on the result in last section a constant heat generation rate of 0.86 W was used. At this point, the simulation was performed again, this time letting the system cool for ten minutes (until it the maximum temperature was less than 40°C) after applying the constant heat generation rate for ten minutes. After the thermal simulation completed, the thermal dose was calculated for front and side planes, These results are shown in Figure 8.

Figure 8 shows that the maximum distance from the center that is expected to reach the desired thermal dose (DTD) is almost the same

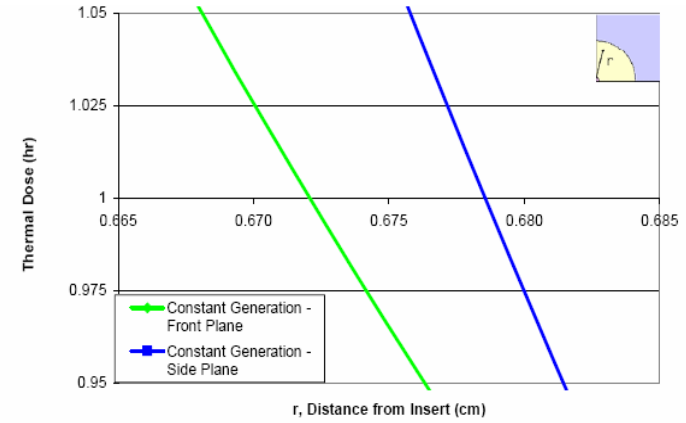

Figure 8. Front and side plane thermal dose results for the constant heat generation simulations focusing on the location farthest from the center of the tumor where the desired thermal dose (DTD) occurs (at a thermal dose of 1).

for the front and side planes. The radial distance from the center that achieves the DTD is 0.672 cm for the front plane and 0.676 cm for the side plane, a difference of less than 0.05 mm. Next, the estimated volume of tissue attaining the DTD was calculated. This volume was calculated using two different formulas: the spherical volume formula and the ellipsoid volume formula. The spherical volume formula indicated that 1.27 cm^3 of tissue reached the DTD while the ellipsoid volume formula indicated that 1.28 cm^3 of tissue reached the DTD. The difference in these two methods is less than one percent. Therefore, the rest of the primary thermal model simulations will only consider the spherical volume method (using the results from the front plane). Although this model indicates that the tissue within a radial distance of over .67 cm from the center attains the DTD this is not far enough for the entire tumor to achieve the DTD, for a 2 cm diameter tumor. Therefore, additional heat generation rates and patterns were examined.

7.3.2. Constant Insert Temperature

Next, the case where the rod insert was held at a constant temperature of 80°C was examined. This thermal simulation represents the ideal case where the amount of energy applied to the insert constantly maintains the insert at the maximum temperature. Although maintaining a constant temperature of 80°C cannot be achieved practically, this case demonstrates the maximum attainable thermal dose for the primary thermal model with the current restraints of the system. The constant temperature simulation was performed by maintaining the insert temperature at 80°C for ten minutes then allowing the system to cool another ten minutes (until the maximum temperature was less than 40°C). Once the constant temperature simulation was completed, the thermal dose results were evaluated and compared to the constant heat generation rate case. This comparison is shown in Figure 9. As expected (shown in the figure), the constant temperature simulation achieved the desired thermal dose (DTD) over a greater distance from the center than did the constant generation simulation. In the constant temperature simulation, cells are expected to achieve the DTD up to about 0.70 cm from the center, as shown in Figure 9. This yields a volume of tumor attaining the DTD of approximately 1.46 cm^3. So, as expected, changing the heat input to the rod insert affects the cumulative thermal dose. Therefore, additional heat generation rates were examined to determine if they could improve upon the thermal dose achieved with a constant heat generation rate and approach the thermal dose with the insert set at a constant temperature of 80°C. However, examination of the

constant insert temperature thermal dose results reveals that even in this optimal case, where the insert is maintained at a constant temperature of 80°C, an entire 2 cm diameter tumor does not receive the DTD. Nevertheless, additional heat generation rates (including pulse function heat generation rates, ramp heat generation rates and exponential decay heat generation rates) were studied determine an optimum form of heat generation (one that approaches the constant insert temperature results).

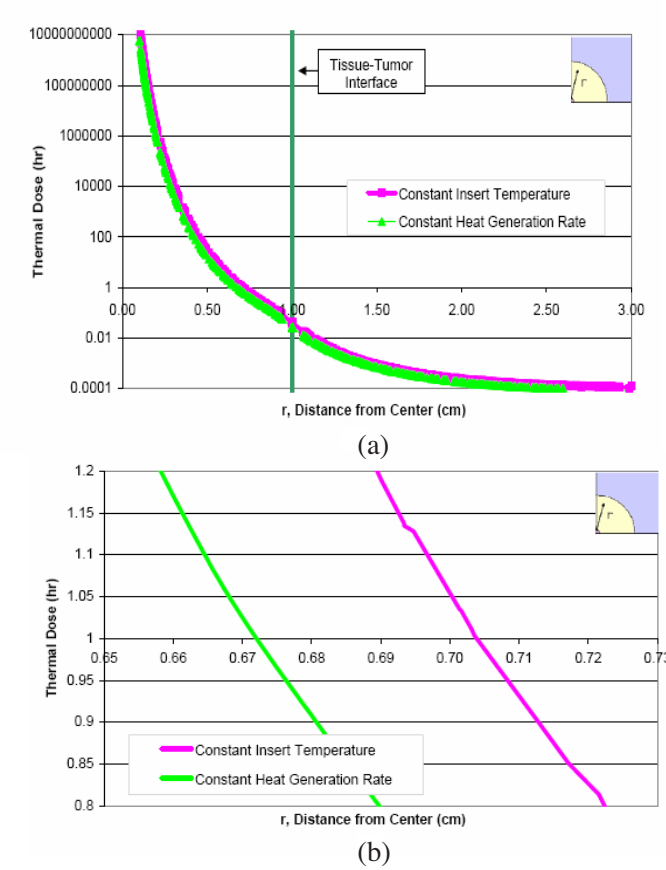

Figure 9. Thermal dose results for the constant heat generation and constant insert temperature simulations. (a) shows the thermal dose results of the entire front and side planes, (b) focuses on the location farthest from the center of the tumor where the DTD occurs (at a thermal dose of 1).

7.3.3. Pulse Function Generation Rate

The next form of heat generation applied to the rod insert was a pulse heat generation input. Many different pulses were evaluated to determine if they could be used to increase the cumulative thermal dose the primary thermal model experienced when undergoing a ten minute treatment. All of the pulse generation inputs had the same restraints on the simulation as the constant heat generation rate (the only change was the energy applied to the insert) including the maximum model temperature of 80°C. The most promising pulse input is shown in Figure 10. This pulse input had 0.92 W applied to the insert for 28 seconds and then no energy (a cooling period) applied for two seconds, which was repeated during the new treatment time. The primary thermal model was run using this pulse heat generation rate with all other parameters the same as those defined for the constant heat generation simulation. Once the pulse heat generation rate simulation was completed, the thermal dose results were evaluated and compared to the constant heat generation rate and the constant temperature cases. These comparisons are shown in Figure 11. As the figure shows, the cumulative thermal dose for pulsed heat generation input is almost as large as the cumulative thermal dose for the constant heat generation rate.

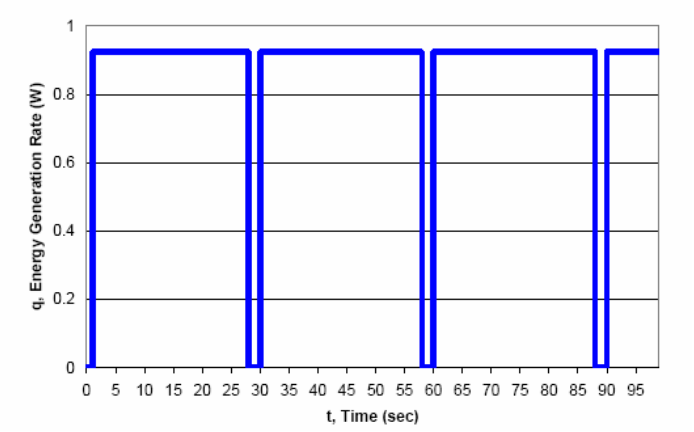

Figure 10. The pulse heat generation rate used for the primary thermal model pulse input simulation.

This was expected because considering the total energy applied to the model, the total amount of energy applied when using the pulse heat generation was almost identical to the total energy applied in the

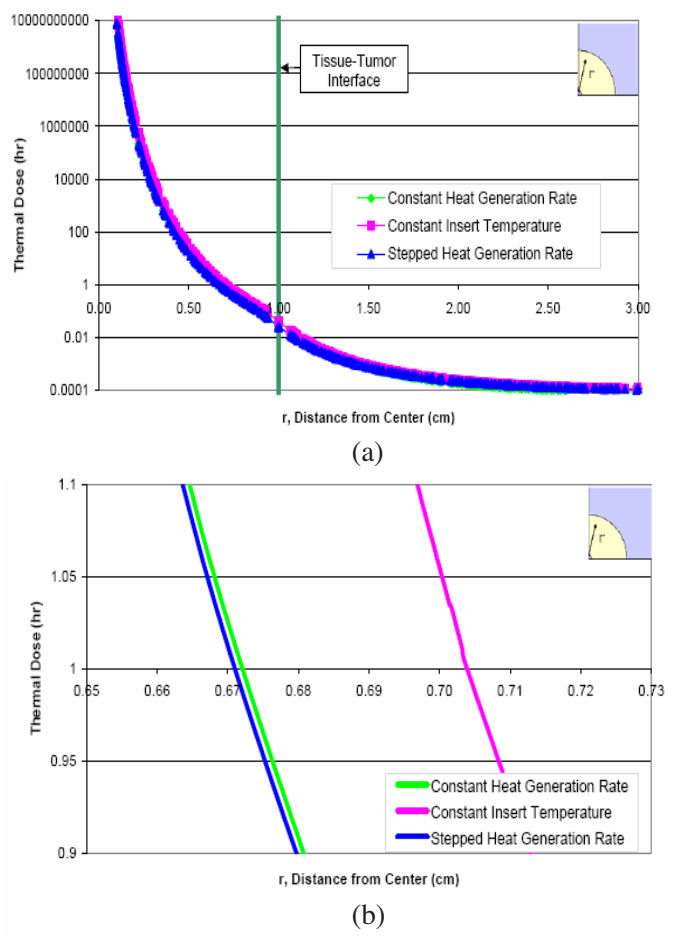

Figure 11. Comparison of the thermal dose results for the constant heat generation, pulse heat generation rate, and constant insert temperature simulations. (a) shows the thermal dose results of the entire front and side planes, (b) focuses on the location farthest from the center of the tumor where the DTD occurs (at a thermal dose of 1).

constant generation simulation The resulting difference between the radial distances expected to achieve the DTD for the two cases is less than 0.45 percent. Thus, the pulse heat generation rate is not better than the constant heat generation rate because no additional energy could be added to the simulation (due to the system constraint of a

maximum temperature of 80°C) by using the pulse heat generation rate.

7.3.4. Ramped Generation Rate

The next heat generation rate forms investigated were ramped heat generation rate functions. These generation rates included single slope ramps and ramp generations with multiple slopes. As expected, the multiple slope ramp generations had better cumulative thermal dose results than the single slope ramp generations. In addition, these results led to the examination of exponential heat generation rates discussed later in this section.

1-Single Slope Inputs

As explained earlier, the single slope ramp heat generation rate was examined next. This heat generation form was chosen because it allows the tumor to experience a larger rate of energy input in the beginning and a decreasing amount throughout the rest of the simulation. The goal was to quickly heat the insert and maintain that high temperature without exceeding the maximum temperature limit of 80°C. After examining several different single slope ramps, the most effective single slope ramp heat generation rate for the primary thermal simulation was determined. This single slope ramp started with an energy generation rate applied to the rod insert of 1.04 W and steadily decreased to 0.72 W over the ten minute treatment period, as shown in Figure 12. This heat generation heat was used to run the simulation

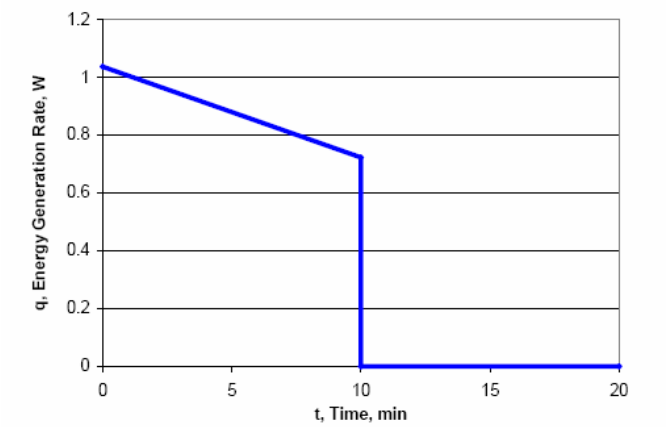

Figure 12. The single slope heat generation rate used for the primary thermal model single slope input simulation.

along with all other parameters of the constant heat generation rate simulation. The resulting cumulative thermal dose was determined and is shown in Figure 13, where it is compared with the cumulative thermal doses of the constant heat generation rate and the constant insert temperature cases. As expected, the single-slope ramp heat generation input produces a greater cumulative thermal dose than the constant heat generation but a smaller cumulative thermal does than

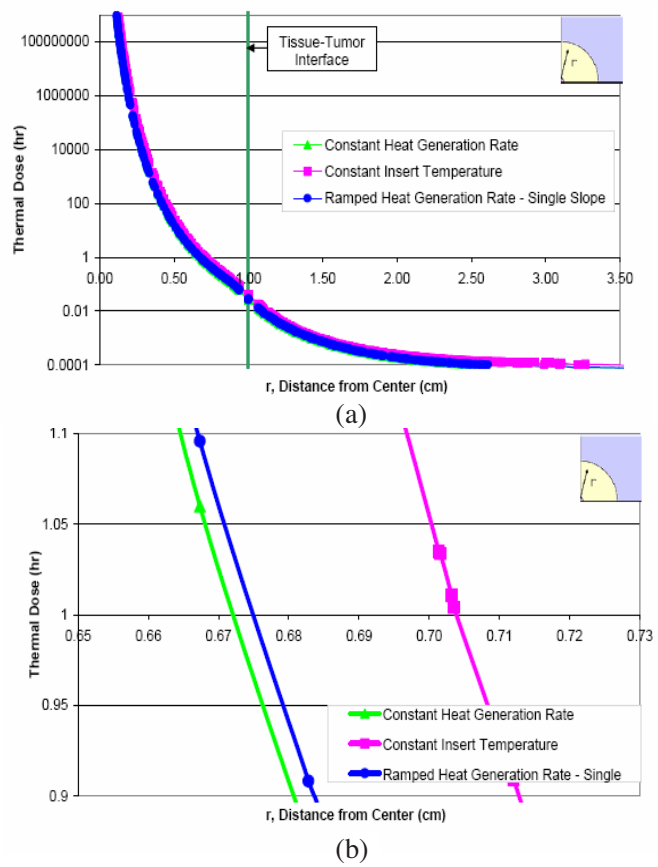

Figure 13. Comparison of the thermal dose results for the constant heat generation, ramped single slope) generation rate, and constant insert temperature simulations. (a) shows the thermal dose results of the entire front and side planes, (b) focuses on the location farthest from the center of the tumor where the desired thermal dose (DTD) occurs (at a thermal dose of 1).

the constant insert temperature simulation. The single-slope ramp simulation did achieve the DTD slightly farther out than the constant generation simulation (about 0.05 mm). Thus, a 1.35 percent greater volume of tissue (1.29 cm^3) is expected to reach the DTD in the single-slope ramp generation case than in the constant heat generation rate case (1.27 cm^3).

Thus, using a single-slope ramp heat generation rate allows for a slightly greater thermal dose to be delivered to the tumor while remaining within the system constraints However, it was believed that more energy could be delivered to the system, and thereby a greater thermal dose, by applying a multi-sloped heat generation rate.

2-Multiple Slope Inputs

The multiple slope ramp heat generation rate allows the insert to obtain additional energy at the beginning of the simulation (when the need for a temperature increase hence additional energy is the greatest). Then, the amount of energy added decreases as the simulation continues. The best multiple-slope ramp heat generation rate, for the primary thermal simulation, was determined after examining the results of numerous different multi-slope ramp heat generation rates. This multi-slope heat generation rate(used with all other parameters of the constant heat generation rate simulation) began with an initial energy generation rate applied to the rod insert of 1.07 W which was constantly decreased to an energy generation rate of 0.88 W over five minutes. Then, at five minutes, the slope of the energy generation was changed.

This time, the energy generation began at 0.88 W the ending energy generation rate of the first slope and was constantly decreased to 0.86 W over the final five minute period. Then, the simulation was allowed to cool without adding any further energy (as with the constant heat generation rate simulation), as shown in Figure 14. At this point, the resulting cumulative thermal dose was determined. Figure 15 shows the comparison of the multiple-slope ramp generation cumulative thermal dose with the cumulative thermal doses of the constant heat generation rate and the constant insert temperature cases.

The figure shows, as expected, the multiple-slope ramp heat generation input produces a greater cumulative thermal dose than the constant heat generation but a smaller cumulative thermal dose than the constant insert temperature simulation. Closer examination of the simulation results reveals that the expected lethal cumulative thermal dose is achieved up to 0.69 cm from the center of the tumor for the multiple-slope ramp heat generation rate while the constant heat generation rate is only able to attain this cumulative desired

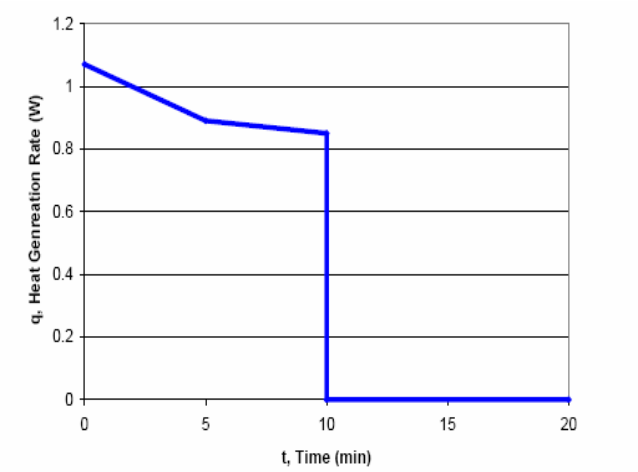

Figure 14. The multiple slope heat generation rate used for the primary thermal model multiple slope input simulation.

thermal dose (DTD) up to 0.67 cm from the center. The increase in the distance from the center where the cumulative thermal does is achieved means that a greater volume of 1.39 cm^3, compared to 1.27 cm^3 in the constant heat generation rate case is. Thus, applying this multiple-slope ramp heat generation rate to the rod insert (instead of a constant heat generation rate) increases the volume of tissue that receives the DTD by 9.39 percent while remaining within the constraints of the system.

7.3.5. Exponential Decay Heat Generation Input

The exponential heat generation curve can almost be thought of as an infinite number of slopes for a ramp generation. As the number of slopes in the ramp heat generation rate increased so too did the cumulative thermal doses. The exponential heat generation rate allows for the maximum amount of energy (significantly more than in the constant heat generation rate case) to be added to the rod insert at the beginning of the simulation, to increase the temperature as close to 80°C as possible. Then, there is a rapid decrease in the amount of energy added which allows for the temperature to be maintained near 80°C without exceeding this limitation. Many different exponential heat generation rates were examined to determine the optimum rate. The heat generation rate was determined by multiplying the value inserted into the model (in W/m^3) by the volume of the rod insert.

This heat generation rate, E (in watts), is described by

$$\mathrm{E} = 0.8639 + 0.3927\mathrm{e}^{-(t-1)/100} \tag{6}$$

where t is the current time. The first term of the heat generation rate is the minimum energy added to the simulation and was added

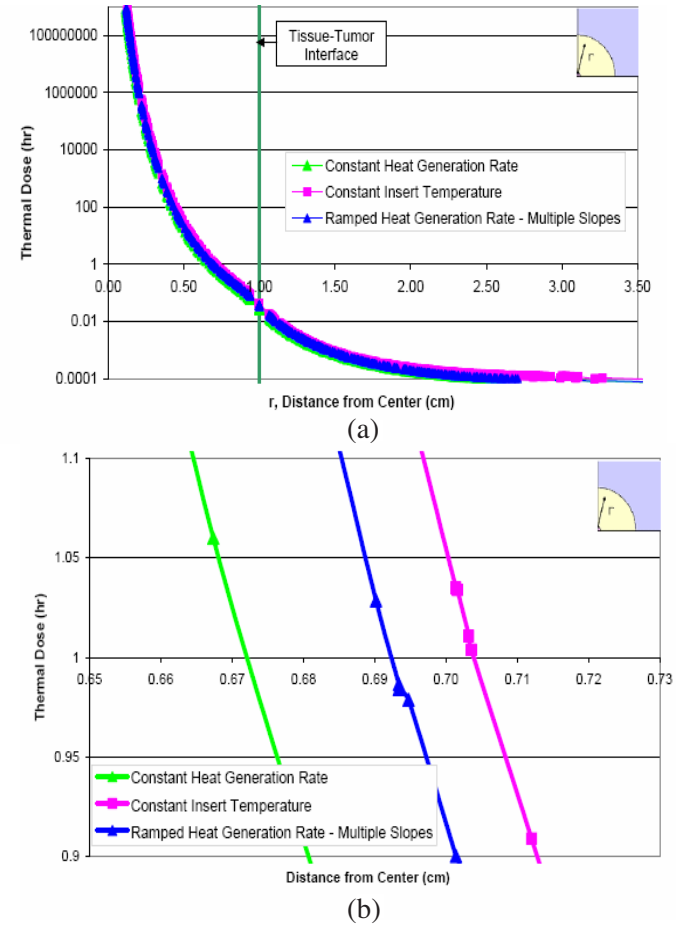

Figure 15. Comparison of the thermal dose results for the constant heat generation, ramped (multiple slope) generation rate, and constant insert temperature simulations. (a) shows the thermal dose results of the entire front and side planes, (b) focuses on the location farthest from the center of the tumor where the desired thermal dose occurs (at a thermal dose of 1).

at all heating times. Meanwhile, the second term of the equation represents the initial surge of energy and the decay of this energy. This equation was used to apply the exponential heat generation rate to the primary thermal model simulation and a graphical representation of Equation (6) is shown in Figure 16. As with the other simulations, energy was applied to the rod insert for ten minutes (at a rate described by Equation (6)) with all other simulation parameters the same as with the constant heat generation simulation. At this point, the resulting cumulative thermal dose was determined. Figure 17 shows the comparison of the exponential heat generation cumulative thermal dose with the cumulative thermal doses of the constant heat generation rate and the constant insert temperature cases.

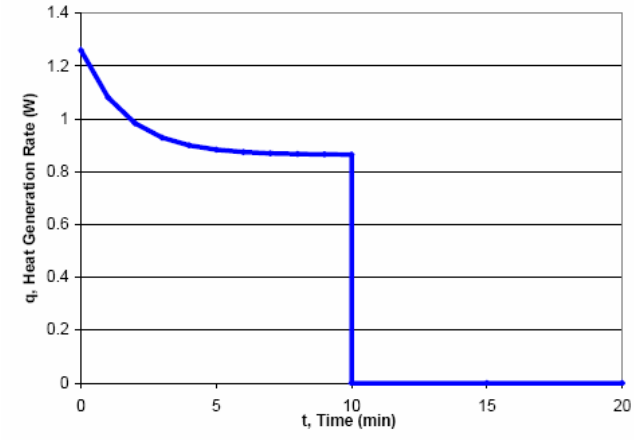

Figure 16. The exponential decay heat generation rate used for the primary thermal model exponential decay input simulation.

As expected the exponential heat generation input produces a significantly greater cumulative thermal dose than the constant heat generation and a slightly smaller cumulative thermal dose than the constant insert temperature simulation.

Closer examination of the cumulative thermal dose results indicates that when using an exponential heat generation rate, cells are expected to receive the desired thermal dose (DTD) at a radial distance of up to 0.70 cm from the center. This represents a slight increase (+0.03 cm) in the radial distance from the center where cells are expected to attain the DTD when compared with the constant heat generation rate. This increase in the distance from the center where the DTD is received means that a greater volume of the tumor

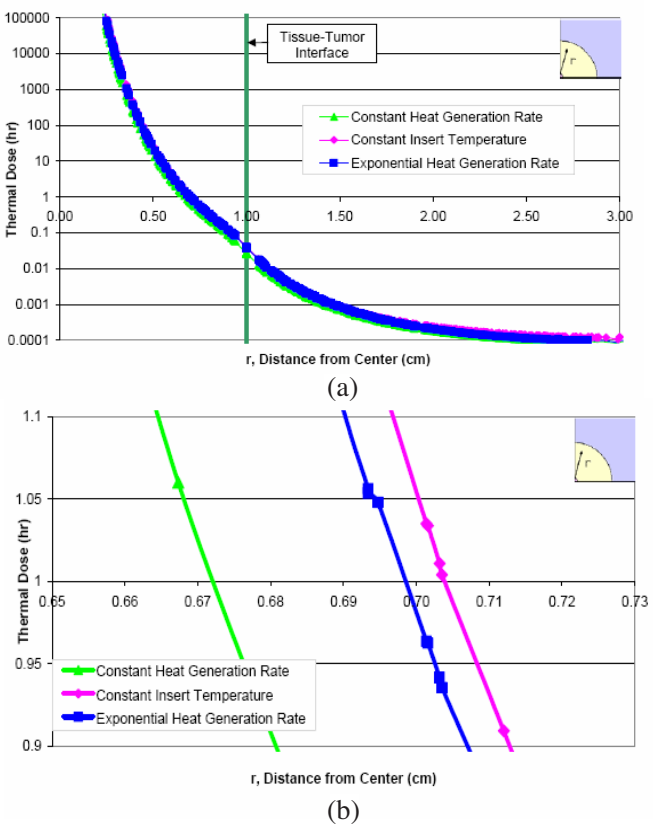

Figure 17. Comparison of the thermal dose results for the constant heat generation, exponential generation rate, and constant insert temperature simulations. (a) shows the thermal dose results of the entire front and side planes, (b) focuses on the location farthest from the center of the tumor where the desired thermal dose occurs (at a thermal dose of 1).

will attain the DTD. The volume expected to achieve the DTD in the exponential heat generation case is 1.43 cm^3 compared to 1.27 cm^3 in the constant heat generation case and 1.46 cm^3 in the constant insert temperature case. As a result the volume of tissue achieving The DTD when using the exponential heat generation n rate represents a 12.3 percent increase in volume when compared to the constant heat generation case and a decrease of only 2.31 percent when comp the constant insert temperature case.

8. CONCLUSION

The results of the primary thermal model simulations are shown in Table 4. As the table shows, the best simulation is the constant insert temperature case. However, this is the theoretical best that can be achieved. The best that can be achieved in practice is the exponential heat generation simulation, which produces results closest to the constant insert simulation. As expected, even using the optimal heat generation rate there still was not enough energy applied to the insert to allow an entire two centimeter tumor to receive the DTD (can achieve the DTD in a tumor up to approximately 1.4 centimeters). Therefore, more than one insert will be needed to be able to destroy the tumor.

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