MATHEMATICAL MODEL AND EXPERIMENTAL STUDY ON TRANSIENT TEMPERATURE PROFILES AROUND A CYLINDRICAL HEAT SOURCE INSIDE AN *IN VITRO* TISSUE

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ABSTRACT

In treatment of tumor by hyperthermia, the temperature profile around the heat source is the major factor influencing the effect of hyperthermia. In this study, a mathematical model of the transient temperature profiles around a cylindrical heat source inside an *in vitro* tissue has been developed. Experiments with an *in vitro* pork liver have been conducted to study the change of liver temperature around a nickel-chromium alloy wire heated by direct current at fixed power. Computer simulation of the mathematical model can be used to help doctors to predict the change of temperature profiles in the tissue during thermal therapy

The results show that liver temperature near the heating source can be controlled in a desired range for hyperthermia, say, 45~70 ℃, by a simple on-off control of the power of heat source. For example, heating power is switched on for 300 seconds firstly, then off and on each for 50 seconds repeatedly. The results also show that as the distance from the heat source increases, the tissue temperature decreases, and the magnitude of temperature oscillation due to power off and on decreases too.

There are two parameters, thermal conductivity (k) and heat transfer coefficient (h), in the mathematical model. It has been found that there exists a zone, in the range of $0.66 \leq k \leq 0.74$ W/m-K and $130 \leq h \leq 155$ W/m²-K, where the average error between mathematical model and experimental model is less than 2.40℃. When temperature dependency of thermal conductivity, $k=0.4981+0.0008T$, is considered, there exists a minimum of average error of 2.59 ℃ at h=210 W/m²-K. However, for a wide range of heat transfer coefficient between 150 and 280 W/m-K, the average error is less than 3℃.

INTRODUCTION

Thermal therapy is currently implemented as a minimally invasive alternative to traditional surgery in the treatment of benign disease and cancer, as well as repair of sport injuries and tissue reshaping or modification [1]. Thermal therapy is widely known and electromagnetic (EM) energy, ultrasonic waves, and other thermal-conduction-based devices have been used as heating sources [2]. Habash et al. made an excellent review on several topics of thermal therapy, including introduction to thermal therapy [2], hyperthermia techniques [3], ablation techniques [4] and electromagnetic and thermal dosimetry [5].

In general, thermal therapy is categorized into the following three different modalities according to the temperature level and time duration [2]:
1. Diathermia. Heating up to 41°C, with applications in physiotherapy for the treatment of rheumatic diseases;
2. Hyperthermia. The temperature of a part of the body or of the whole body can be raised to a higher-than-normal level (41–45°C), which may allow other types of cancer treatments (radiation therapy or chemotherapy) to work better; and
3. Thermal ablation. Very high temperatures (above 45°C) can be used to destroy cells within a localized section of a tumor.

Classical hyperthermia relies on a temperature of 42°C to 45°C for periods of 30 to 60 min to cause irreversible cellular damage [6]. As the tissue temperature rises to 50°C, the time required to achieve irreversible cellular damage decreases exponentially. Protein denaturation occurs and leads to immediate cell death. Vaporization of tissue water is superimposed on this process between 100°C and 300°C. In addition, carbonization, charring, and smoke generation occurs at 300°C to 1000°C [7-9].

Thermal therapy techniques are becoming more acceptable as a minimally invasive alternative for the treatment of some cancers and other forms of benign diseases [1]. However, evaluation of human exposure risk to EM sources or the corresponding heat, especially patients and personnel working in this field, is a difficult task because it involves many physical, biological, and chemical variables. In clinical settings, the major objective of thermal therapy is to achieve an efficacious treatment outcome without damaging normal tissues. Dewhirst et al. [10] summarized the basic principles that

govern the relationships between thermal exposure (temperature and time of exposure) and thermal damage, with an emphasis on normal tissue effects. Habash et al. [2] claimed that much more work needs to be done to clarify what the thresholds for thermal damage are in humans. They also stated that the challenges to the development of thermal therapy includes defining a biologically effective thermal dose, equipment to deliver accurate thermal dose, accurate measurement of thermal dose, and clinical trials to test the efficiency of thermal dose.

One of the important factors influencing the success of thermal therapy is the prediction and control of temperature distribution in the tissue. Pennes [11] established a mathematical model to solve the heat transfer problem in the tissue. His model suggests the net heat transfer from blood to tissue was proportional to the temperature difference between the arterial blood entering the tissue and the venous blood leaving the tissue. Many investigators [12-18] have followed or modified Pennes model to study the temperature profiles inside the tissue. It is the purpose of this research to establish a mathematical model, which is another modification of Pennes model, in order to simulate the transient temperature profiles around a cylindrical heat source inside an *in vitro* tissue. The heating power will be time-dependent and temperature dependency of thermal conductivity will be considered in the model. Finally, *in vitro* experiments with pork liver will be conducted to prove the feasibility of the mathematical model.

NOMENCLATURE

a	[W/m-K]	constant in temperature dependency of thermal conductivity.
b	[W/m-K^2]	constant in temperature dependency of thermal conductivity.
C_p	[J/kg-K]	heat capacity of tissue.
h	[W/m^2-K]	heat transfer coefficient.
k	[W/m-K]	thermal conductivity.
L	[m]	length of the cylindrical heat source
n	[-]	number of temperature data obtained from each thermocouple.
P	[W]	power of the heat source.
r	[m]	radial coordinate.
r_0	[m]	radius of the cylindrical heat source.
r_n	[m]	radius of the tissue.
t	[s]	time.
T	[℃]	temperature of the tissue.
T_∞	[℃]	ambient temperature.

Special characters

α	[m^2/s]	thermal diffusivity defined in Eq. (5)
β	[1/s]	defined in Eq. (6)
γ	[m/s]	defined in Eq. (7)
ρ	[kg/m^3]	density of tissue

Subscripts

i		temperature data at various time.
j		temperature data at various position.

Superscripts

M		model calculation.

MATHEMATICAL MODEL

Consider a cylindrical heat source inside an *in vitro* tissue as shown in Figure 1. The unsteady-state energy balance in the control volume can be written as

$$\rho C_p 2\pi r \Delta r L \frac{\partial T}{\partial t} = k\frac{\partial T}{\partial r}2\pi r L\bigg|_{r+\Delta r} - k\frac{\partial T}{\partial r}2\pi r L\bigg|_{r} - 4\pi r \Delta r h(T - T_\infty) \quad (1)$$

where T is the temperature of the tissue, t is time, r is radial coordinate, ρ and C_p are the density and heat capacity of tissue, respectively, k is the thermal conductivity, h is the heat transfer coefficient, L is the length of the cylindrical heat source, as well as the thickness of the tissue, and T_∞ is the ambient temperature. The last term on the right-hand-side of Eq. (1) stands for the heat loss from the top and bottom of the tissue to the surroundings. Since *in vitro* tissue is considered in this study, the heat loss by blood perfusion and heat generated by the normal process in the body are neglected.
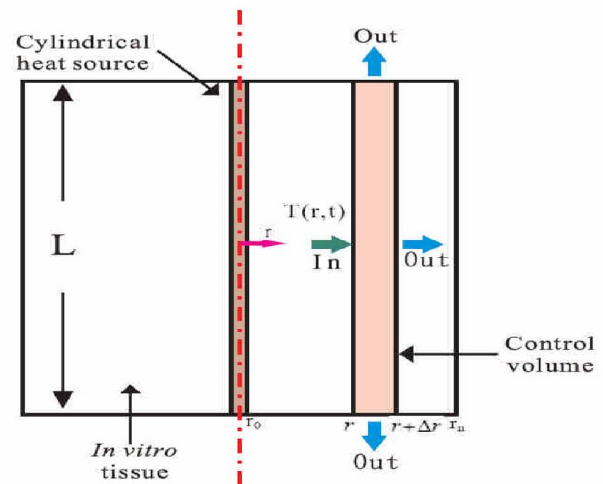

Figure 1 Control volume in an *in vitro* tissue with cylindrical heat source.

Dividing Eq. (1) with $2\pi r L \Delta r$ and limiting Δr to zero gives

$$\rho C_p \frac{\partial T}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}\left(rk\frac{\partial T}{\partial r}\right) - \frac{2}{L}h(T - T_\infty) \quad (2)$$

It has been reported by several researches that thermal conductivity is a linear function of temperature [19,20], i.e.,

$$k = a + bT \quad (3)$$

where a and b are constants. Substituting Eq. (3) into (2) and rearranging gives

$$\frac{\partial T}{\partial t} = \alpha\left[\frac{\partial^2 T}{\partial r^2} + \frac{1}{r}\frac{\partial T}{\partial r}\right] + \gamma\left(\frac{\partial T}{\partial r}\right)^2 - \beta(T - T_\infty) \quad (4)$$

where

$$\alpha = \frac{k}{\rho C_p} \quad (5)$$

$$\beta = \frac{2h}{\rho C_p L} \tag{6}$$

$$\gamma = \frac{b}{\rho C_p} \tag{7}$$

The initial condition for Eq. (4) is

$$T = T_\infty \qquad \text{at } t = 0, \ r_0 \leq r \leq r_n \tag{8}$$

where r_0 is the radius of the cylindrical heat source, and r_n is the radius of the tissue. The boundary conditions for Eq. (4) can be written as

$$-k\frac{\partial T}{\partial t} = \frac{P}{2\pi r_0 L} \qquad \text{at } t > 0, \ r = r_0 \tag{9}$$

where P is the power of the heat source, and

$$-k\frac{\partial T}{\partial t} = h(T - T_\infty) \qquad \text{at } t > 0, \ r = r_n \tag{10}$$

NUMERICAL METHOD

The partial differential equation, Eq. (4), had been transformed to a system of ordinary differential equations by fourth-order finite difference method before the ODE's were solved by fourth-order Predictor-Corrector method. The details of the transformation and the Fortran program are listed elsewhere [21].

EXPERIMENTAL

The experiments were conducted by heating an *in vitro* pork liver with a Ni-Cr alloy wire and direct current, as shown in Figure 2. The power supply provided direct current at a fixed voltage or fixed current. The temperatures of the pork liver at 3, 5 and 7 mm from the central line of heating source were measured by K-type thermocouples. A device made of 80 mm by 80 mm plexiglass with holes of 1.2 mm diameter that were drilled precisely by laser beam, as shown in Figure 2, was used to ensure the thermocouples to be in the desired positions. The thermocouples were connected to a data acquisition module and then to a personal computer. LabVIEW 8.6 software by National Instrument, U.S.A., was used to integrate the hardware of the entire system and to design user-friendly interfaces for the experiment. The experiments were conducted at a fixed voltage of 0.90V, corresponding to a current of 1.70A and a power of 1.53W. The length of Ni-Cr alloy wire, which is the thickness of the pork liver, is 24 mm. It was programmed to switch the heating power on for 300 seconds firstly, then off and on each for 50 seconds for a total of three iterations. Temperature data at the positions of 3, 5 and 7 mm from the heating source were recorded in the computer every second.
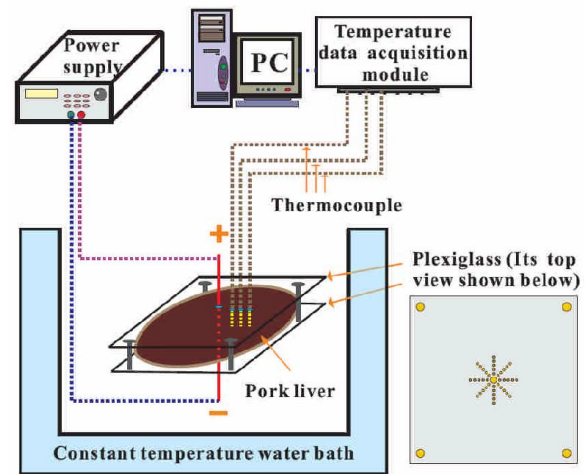

Figure 2 Experimental set-up

RESULTS AND DISCUSSION

The parameters used in computer simulation are adopted from Button et al. [21] as follows:

k = 0.508 W/m-K,

$$\rho C_p = 3.81 \times 10^6 \text{ J/m}^3\text{-K}$$

Figure 3 shows a comparison of temperature of *in vitro* pork liver between experimental data and model calculations. The value of heat transfer coefficient, h=204 W/m²-K is obtained by single-variable data regression. The average error, the average difference between model calculations and experimental data as defined below, is 2.54°C.

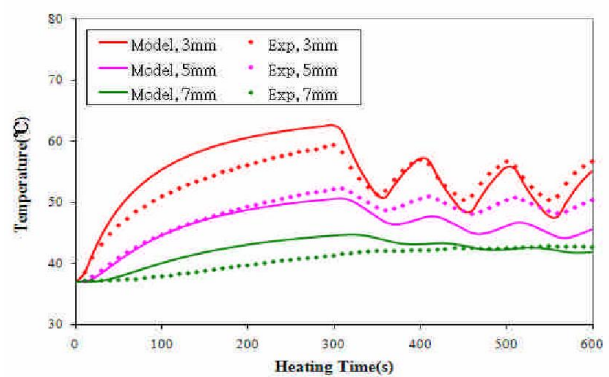$$\text{Average error} = \sqrt{\frac{1}{3n}\sum_{j=1}^{n}\sum_{i=3,5,7}\left(T_{i,j} - T_{i,j}^{M}\right)^2}$$

Figure 3 Comparison of tissue temperatures between experimental data and model calculations by single-variable search (k=0.508 W/m-K, h*=204 W/m²-K, Err=2.54°C)

where T_{ij} is experimental data, T^M_{ij} is model calculations, and n is number of temperature data from each thermocouple.

It can be seen from the figure that, at r=3mm, the tissue temperature increases from 37℃ to 59℃, due to power-on for 300s, then drops down to 51℃, due to power-off for 50s. The temperature increases again up to 57℃, due to power-on again for 50s, then drops again down to 50℃, due to power-off again for 50s.The figure also shows that as the distance (r) increases, the tissue temperature decreases, and the magnitude of temperature oscillation due to power off and on decreases too.

If both thermal conductivity and heat transfer coefficient are used for data regression, the results will be k*=0.722 W/m-K and h*=133 W/m²-K, with the average error reducing slightly to 2.39 ℃ . Figure 4 shows a comparison between model calculations and experimental data for this case. The results of two-parameter data regression show that many sets of (k,h) provide relatively good fit between mathematical model and experimental data. Figure 5 shows the distribution of thermal conductivity and heat transfer coefficient for an average error less than 2.4℃. It can be seen from the figure that there exists a zone in the range of 0.66≦k≦0.74 W/m-K and 130≦h≦155 W/m²-K, where the average error is less than 2.4℃. In other words, the average error is not very sensitive to the variation of thermal conductivity and heat transfer coefficient.
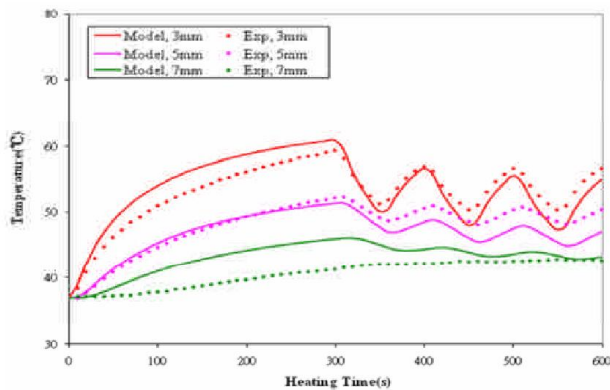

Figure 5 Distribution of thermal conductivity and heat transfer coefficient for average error less than 2.4 ℃ .

Figure 4 Comparison of tissue temperatures between model calculations and experimental data by two-variable search (k*=0.722 W/m-K, h*=133 W/m²-K, Err=2.39℃)

Figure 6 Effect of heat transfer coefficient (h) on average error when k=0.4981+0.0008T W/m-K.

If the temperature dependency of thermal conductivity reported by Valvano et al. [20] is considered, the average error can be calculated as function of heat transfer coefficient only. Figure 6 shows the effect of heat transfer coefficient (h) on average error when k=0.4981+0.0008T. It can be seen that there exists a minimum at h=210 W/m²-K, however, for a wide range of h between 150 and 280 W/m-K, the average error is less than 3 ℃ . It is concluded that when the temperature dependency of thermal conductivity is considered, the average error is not very sensitive to the variation of heat transfer coefficient.
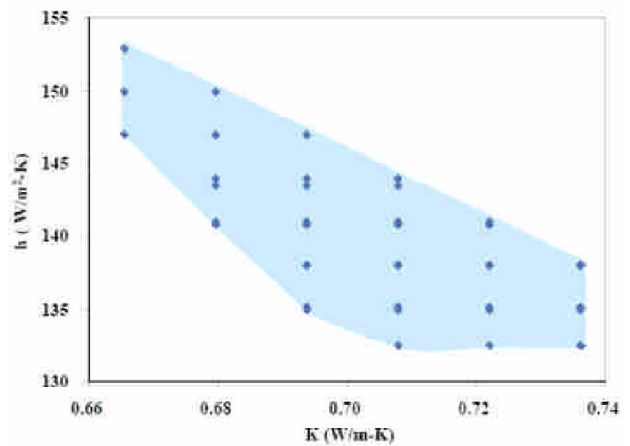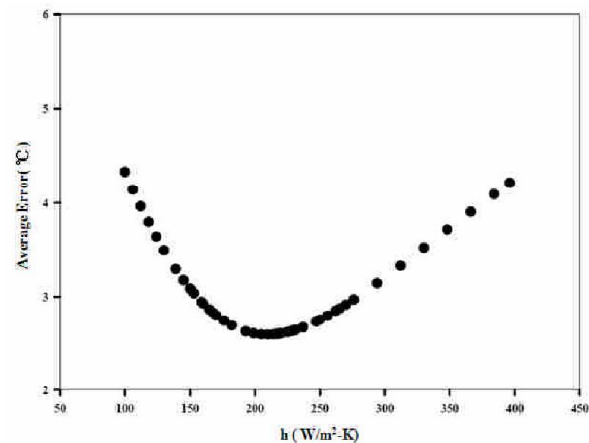
Table 1 summarizes the results of this research where Case 1 and 3 are single-variable search and Case 2 is two-variable search. It can be found from the table that Case 2 has slightly lower value of average error. Since the experimental error in temperature measurement for *in vitro* pork liver is about 3~5 ℃, due that the pork liver is not homogeneous, it is concluded that single-variable searches, Case 1 and 3, are good enough for the mathematical model. Furthermore, the temperature dependency of thermal conductivity adopted from Valvano et al. [20] is valid between 3℃ and 45℃. It is extended to use at 80 ℃ in Case 3 of this study due that the temperature coefficient is small. If temperature dependency of thermal conductivity at higher temperature is available, the average error for Case 3 might decrease.

Table 1 Average error and the optimal values of thermal conductivity (k) and heat transfer coefficient (h)

Parameters	Case 1	Case 2	Case 3
k (W/m-K)	0.508	0.722*	0.4981+0.0008T
h (W/m²-K)	204*	133*	210*
Average error (°C)	2.54+	2.39++	2.59+

* optimal value by data regression.
\+ result of single-variable search.
\++ result of two-variable search.

CONCLUSION

A mathematical model of the transient temperature profiles around a cylindrical heat source inside an *in vitro* tissue has been developed with time-dependent heating power and temperature-dependent thermal conductivity. Experiments with pork liver have been conducted to study the transient behavior of liver temperature and to prove the feasibility of the mathematical model that can help doctors to estimate the variation of temperature profiles in the tissue during thermal therapy

The results show that liver temperature near the heating source can be controlled in a desired range for hyperthermia, say, 45~70 °C, by a simple on-off control of the power of heat source. For example, heating power is switched on for 300 seconds firstly, then off and on each for 50 seconds repeatedly for additional 300 seconds. The results also show that as the distance from the heating source increases, the tissue temperature decreases, and the magnitude of temperature oscillation due to power off and on decreases too.

There are two parameters, thermal conductivity (k) and heat transfer coefficient (h), in the mathematical model. It has been found that there exists a zone where the average error between mathematical model and experimental model is less than 2.40 °C. When temperature dependency of thermal conductivity is considered, there exists a minimum of average error of 2.59 °C at h=210 W/m²-K, however, for a wide range of h between 150 and 280 W/m-K, the average error is less than 3 °C. It is concluded that when the temperature-dependent thermal conductivity is used, the simulation result is not very sensitive to the heat transfer coefficient and single-variable search is good enough for the mathematical model.

REFERENCES

[1] Diederich C.J., Thermal ablation and high-temperature thermal therapy: overview of technology and clinical implementation, *Int. J. Hyperthermia*, Vol. 21, 2005, pp. 745–53.

[2] Habash R.W.Y., Bansal R., Krewski D., and Alhafid H.T., Thermal therapy, part 1: an introduction to thermal therapy, *Critical Reviews in Biomedical Engineering,* Vol. 34, 2006, pp. 459–489.

[3] Habash R.W.Y., Bansal R., Krewski D., and Alhafid H.T., Thermal therapy, part 2: hyperthermia techniques, *Critical Reviews in Biomedical Engineering,* Vol. 34, 2006, pp. 491–542.

[4] Habash R.W.Y., Bansal R., Krewski D., and Alhafid H.T., Thermal therapy, part 3: ablation techniques, *Critical Reviews in Biomedical Engineering,* Vol. 35, 2007, pp. 37-121.

[5] Habash R.W.Y., Bansal R., Krewski D., and Alhafid H.T., Thermal therapy, part 4: electromagnetic and thermal dosimetry, *Critical Reviews in Biomedical Engineering,* Vol. 35, 2007, pp. 123-182.

[6] Welch A.J., Motamedi M., Rastegar S., Le Carpentier G.L., and Jansen D., Laser thermal ablation, *Photochem Photobiol,* Vol. 53, 1991, pp. 815–23.

[7] Lepock J.R., How do cells respond to their thermal environment?, *Int J Hyperthermia,* Vol. 21, 2005, pp. 681–687.

[8] Germer C.T., Roggan A., Ritz J.P., Isbert C., Albrecht D., Muller G., and Buhr H. J., Optical properties of native and coagulated human liver tissue and liver metastases in the near infrared range, *Lasers Surg. Med.,* Vol. 23, 1998, pp. 194–203.

[9] Haemmerich D., and Laeseke P.F., Thermal tumour ablation: devices, clinical applications and future directions, *Int. J. Hyperthermia,* Vol. 21, 2005, pp.755–760.

[10] Dewhirst M.W., Viglianti B.L., Lora-Michiels M., Hanson M., and Hoopes P.J., Basic principles of thermal dosimetry and thermal thresholds for tissue damage from hyperthermia, *Int. J. Hyperthermia*, Vol. 19, 2003, pp. 267–94.

[11] Pennes H.H., Analysis of tissue and arterial blood temperatures in the resting human arm, *J. Appl. Physio,* Vol. 1, 1948, pp. 93–122.

[12] Weinbaum S., and Jiji M., A new simplified bioheat equation for the effect of blood flow on local average tissue temperature, *J. Biomech. Eng.,* Vol.107, 1985, pp.131–139.

[13] Dewey W.C., Li X.L., and Wong R.S., Cell killing, chromosomal aberrations, and division delay as thermal sensitivity is modified during the cell cycle, *Radiat. Res.,* Vol.122, 1990, pp. 268–274.

[14] Waters E.R., and Schaal B.A., Heat shock induces a loss of rRNA-encoding DNA repeats in Brassica nigra, *Proc Natl. Acad. Sci., USA,* Vol. 93, 1996, pp.1449–1452.

[15] Leonhardt E.A., Trinh M., Forrester H.B., Johnson R.T., and Dewey W.C., Comparisons of the frequencies and molecular spectra of HPRT mutants when human cancer cells were X-irradiated during G1 or S phase, *Radiat. Res.,* Vol. 148, 1997, pp.548–60.

[16] Mason P. A., Walters T. H., DiGiovanni J., Beason C. W., Jauchem J.R., Dick, Jr. E.J., Mahajan K., Dusch S.J., Shields B.A., Merritt J.H., Murphy M.R., and Ryan K.L., Lack of effect of 94 GHz radio frequency radiation exposure in an animal model of skin carcinogenesis, *Carcinogenesis,* Vol. 22, 2001, pp.1701–1708.

[17] Imaida K., Taki M., Watanabe S., Kamimura Y., Ito T., Yamaguchi T., Ito N., and Shirai T., The 1.5 GHz electromagnetic near-field used for cellular phones does not promote rat liver carcinogenesis in a medium-term liver bioassay, *Jpn. J. Cancer Res.,* Vol. 89, 1998, pp.995–1002.

[18] Tell R. A., and Harlen F., A preview of selected biological effects and dosimetric data useful for development of radiofrequency safety standards for human exposure, *J. Microw. Power,* Vol. 14, 1979, pp. 405–24.

[19] Bhattacharya A., and Mahajan R.L., Temperature dependence of thermal conductivity of biological tissues, P*hysiological Measurement,* Vol. 24, 2003, pp. 769-783

[20] Valvano J.W., Cochran J.R., and Diller K.R., Thermal conductivity and diffusivity of biomaterials measured with self-heating thermistors., *International Journal of Thermophysics,* Vol. 6, No. 3, 1985, pp. 301-311

[21] Lee P.S., Unsteady-state temperature profiles around a cylindrical heat source in a dead tissue, *Master Thesis,* Tatung University, Taipei, Taiwan, 2009.

[22] Button T., Barbour S., Cermignani J.D., Crugnale E., McGill R. E., and Spacht G., Magnetic resonance guided hyperthermia, *U. S. Patent,* No. 5,492,122, Feb. 20, 1996.