Time-Dependent Microwave Heating and Surface Cooling of Simulated Living Tissues

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Abstract—The equation of conduction of heat in a model of living tissues is solved in the case of time-dependent electromagnetic heating and surface cooling. This approach allows thermal transient phenomena in the tissue to be treated as the dynamic behavior of a linear infinite-dimension system. This approach is appropriate when the tissue temperature increase must be controlled. Some results are given in a numerical simulation.

Introduction

RECENT ADVANCES in nonperturbing thermometry allow one to attain temperature control of tissues subjected to electromagnetic heating in hyperthermia for cancer treatment [1]–[3]. Heating is controlled by varying the power dissipation rate in the tissue and by regulating the temperature or the velocity of a cooling fluid [4] forced past the surface of the body. The temperature distribution inside the irradiated body is related to the inputs (e.g., the microwave source power rate and the cooling fluid temperature) by the differential equation of heat conduction and appropriate boundary conditions. Usually a cooling function is added to the standard heat equation in order to take into account the internal cooling effect of the blood circulation *in vivo*. Transient solutions of this equation with microwave induced heat source are available in the literature. Mainster *et al.* [5], Chan *et al.* [6], Priebe and Welch [7] calculated the step response in biological bodies of various geometries by the method of finite differences. In studies on conversion of electromagnetic to acoustic energy by volume heating, Lin [8] estimated the temperature increase with time in a spherical body of biological matter irradiated by plane waves of pulsed microwave energy; conduction and cooling effects were neglected in his analysis. In addition the time-dependent solution for a half-space of biological matter was given by Foster *et al.* [4] and a variational formulation, suitable for numerical computations in complicated geometries, was presented in [9].

To our knowledge, however, solutions of the modified heat-conduction equation, when both the microwave heating and the surface cooling are time varying, seem to be lacking in the open literature. Moreover, in order to control the temperature increase with time in irradiated bodies, a formal solution of the heat-conduction equation, which relates the inputs to suitably chosen outputs (e.g., temperatures at some internal points), is advisable. In this note this relation is worked out by means of a variational formulation of the heat-conduction problem and of simplifying assumptions. A simple application of the theory is also given to show how some practical advantage can be obtained by the use of time-varying microwave heating and surface cooling.

Manuscript received August 7, 1980; revised March 13, 1981. This work was supported in part by the Consiglio Nazionale delle Ricerche.

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Mathematical Model and Formulation

The equation of conduction of heat in a homogeneous volume V of tissue is [4], [9], [10]

$$K \nabla^2 \vartheta - \rho C \dot{\vartheta} - B[\vartheta(\boldsymbol{r}, t) - \vartheta_b(\boldsymbol{r})] = -A_0(\boldsymbol{r}) - A(\boldsymbol{r}, t) \tag{1}$$

where $\vartheta(\boldsymbol{r}, t)$ is the unknown temperature, $\vartheta_b(\boldsymbol{r})$ is the temperature of the arterial blood entering the tissue, $A_0(\boldsymbol{r})$ is the metabolic heat generation per unit volume, $A(\boldsymbol{r}, t)$ is the electromagnetic power dissipated in the unit volume of tissue. Here K (thermal conductivity), ρ (density), C (specific heat), and B are constant coefficients. The term $B(\vartheta_b - \vartheta)$ on the left-hand side accounts for the cooling effect due to blood flow. The relation of B to primary physical and physiological characteristics of living tissues is discussed in [10].

The region outside V is assumed at a constant environmental temperature ϑ_e; moreover a cooling fluid at temperature $\vartheta_c(\boldsymbol{r}, t)$ is supposed to be forced on a portion S' of the surface S of the body. By assuming linear heat transfer at S [11], the boundary conditions are

$$\begin{aligned} K \nabla \vartheta \cdot \boldsymbol{n} + H(\vartheta - \vartheta_c) &= 0, \qquad \text{on } S' \\ K \nabla \vartheta \cdot \boldsymbol{n} + H(\vartheta - \vartheta_e) &= 0, \qquad \text{on } S - S' \end{aligned} \tag{2}$$

where $\boldsymbol{n}$ is the outward normal and H is a constant overall surface heat transfer coefficient. Equation (2) differs from the boundary condition of [10] in that a skin evaporation term is ignored; moreover, the black-body radiation heat loss is accounted for by simple increase of the convective surface heat transfer coefficient. The last approximation is sufficiently adequate only if the temperature differences in (2) are small enough [11].

Since in this model ϑ_e, ϑ_b, and A_0 are assumed to be time independent, it is advantageous to let

$$\vartheta(\boldsymbol{r}, t) = \bar{\vartheta}(\boldsymbol{r}) + v(\boldsymbol{r}, t) \tag{3}$$

where $\bar{\vartheta}$ and v are solutions of the following equations:

$$\nabla^2 \bar{\vartheta} - b^2(\bar{\vartheta} - \vartheta_e) = -a_0(\boldsymbol{r}), \qquad \text{in } V \tag{4a}$$

$$\nabla \bar{\vartheta} \cdot \boldsymbol{n} + h(\bar{\vartheta} - \vartheta_e) = 0, \qquad \text{on } S \tag{4b}$$

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$$\nabla^2 v-(1/\kappa)\dot{v}-b^2 v=-a(\boldsymbol{r},t), \quad \text{in } V \tag{5a}$$
$$\nabla v\cdot \boldsymbol{n}+h(v-v_c)=0, \quad \text{on } S'$$
$$\nabla v\cdot \boldsymbol{n}+hv=0, \quad \text{on } S-S' \tag{5b}$$

and $a_0(\boldsymbol{r})=\{A_0(\boldsymbol{r})+B[\vartheta_b(\boldsymbol{r})-\vartheta_e]\}/K$; $a(\boldsymbol{r},t)=A(\boldsymbol{r},t)/K$; $v_c(\boldsymbol{r},t)=\vartheta_c(\boldsymbol{r},t)-\vartheta_e$; $b^2=B/K$; $h=H/K$; $1/\kappa=\rho C/K$.

The *natural* temperature $\bar{\vartheta}(\boldsymbol{r})$ is that of the tissue in absence of both electromagnetic heating and forced surface cooling which are taken into account by the thermal *increase* $v(,\mathrm{r}\,t)$. Formal solutions for $\bar{\vartheta}(\boldsymbol{r})$ are given in [9]. Here we are primarily interested in solving (5a), (5b) for $t\geqslant 0$ subject to the initial condition

$$v(,\mathrm{r}0)=u(\boldsymbol{r}) \tag{5c}$$

where the *initial* temperature $u(\boldsymbol{r})$ is the result of former ($t<0$) thermal events: $u(\boldsymbol{r})=\vartheta(,\mathrm{r}0)-\bar{\vartheta}(\boldsymbol{r})$. $a(,\mathrm{r}\,t)$ and $v_c(,\mathrm{r}\,t)$ are assumed to be continuous for $t>0$. It is easy to show that v is an extremal of the following functional:

$$F=\int_V\left[\nabla v\cdot\nabla v+(1/\kappa)\frac{\partial(v^2)}{\partial t}+b^2v^2-2av\right]dV+\oint_S hv^2\,dS$$
$$-2\int_{S'}hv_c v\,dS. \tag{6}$$

Now let

$$v(\boldsymbol{r},t)=\sum_{m=1}^{\infty}v_m(t)f_m(\boldsymbol{r}) \tag{7}$$

$$u(\boldsymbol{r})=\sum_{m=1}^{\infty}u_m f_m(\boldsymbol{r}) \tag{8}$$

where f_m is the mth orthonormal eigenfunction of the following self-adjoint positive-definite eigenvalue problem:

$$\nabla^2 f+\lambda^2 f=0 \text{ in } V \qquad \nabla f\cdot\boldsymbol{n}+hf=0 \text{ on } S. \tag{9}$$

As is known, the set of these eigenfunctions is complete. The stationarity of F with respect to $v_m(t)$, $m=1,2,\cdots$, gives

$$\dot{v}_m+\beta_m v_m(t)=s_{m1}(t)+s_{m2}(t) \tag{10}$$

where

$$\beta_m=\kappa(\lambda_m^2+b^2) \tag{11}$$

$$s_{m1}(t)=\kappa\int_V a(\boldsymbol{r},t)f_m(\boldsymbol{r})\,dV \tag{12}$$

$$s_{m2}(t)=\kappa h\int_{S'}v_c(\boldsymbol{r},t)f_m(\boldsymbol{r})\,dS. \tag{13}$$

By taking (5c) and (8) into account, the first-order linear system (10) has the solution

$$v_m(t)=e^{-\beta_m t}u_m+\int_0^t e^{-\beta_m(t-\tau)}[s_{m1}(\tau)+s_{m2}(\tau)]\,d\tau. \tag{14}$$

Substitution of (14) into (7) yields the thermal increase for given electromagnetic heating and forced surface cooling. Note that $A(\boldsymbol{r},t)=Ka(\boldsymbol{r},t)$ must be evaluated before calculating the volume integral (12). $A=\sigma|\boldsymbol{E}(\boldsymbol{r},t)|^2/J$ is the instantaneous power dissipated in the unitary volume of tissue, where σ is the effective electrical conductivity of the tissue, J is the mechanical equivalent of heat, and $\boldsymbol{E}$ is the electric field which is originated inside the body by microwave time-varying irradiation. Therefore, in order to evaluate A, a time-varying electromagnetic field solution is needed. Due to the complexity of the problem, few solutions of this type are available in the literature. However, an approximate expression of A can be used in the particular but relevant case where the electromagnetic irradiating field is sinusoidally varying at $\omega=2\pi f$ angular frequency and the field amplitude is modulated by a slowly varying function $F(t)$ (time-dependence $F(t)\exp(j\omega t)$). Now we write $\boldsymbol{E}(\boldsymbol{r},t)\approx F(t)\boldsymbol{G}(\boldsymbol{r},\omega)\exp(j\omega t)$, where $\boldsymbol{G}(\boldsymbol{r},\omega)$ is the electric field originated in the body by a monochromatic excitation [12]. Moreover, if the induced thermal distributions do not vary appreciably within a period $T=1/f$, it is legitimate to substitute $A(\boldsymbol{r},t)$ with its mean value over one period:

$$A(\boldsymbol{r},t)\approx\frac{\sigma}{2J}F^2(t)|\boldsymbol{G}(\boldsymbol{r},\omega)|^2=P_s(t)R(\boldsymbol{r})/J \tag{15}$$

where $R(\boldsymbol{r})=\sigma|\boldsymbol{G}(\boldsymbol{r},\omega)|^2/(2P_0)$ is the ratio between the power dissipated by the monochromatic excitation in the unitary volume of the body and the power P_0 of the monochromatic source; $P_s(t)=P_0F^2(t)$ ($t>0$) is the actual mean power of the source. If a similar factorization holds for v_c, i.e., $v_c(\boldsymbol{r},t)=Q(\boldsymbol{r})V_c(t)$ (Q is a geometrical form factor and $\vartheta_c(t)=\vartheta_e+V_c(t)$ the temperature of some heat sink external to the body), then (12) and (13) become

$$s_{m1}(t)=\tilde{s}_{m1}P_s(t) \qquad s_{m2}(t)=\tilde{s}_{m2}V_c(t) \tag{16}$$

where

$$\tilde{s}_{m1}=\frac{1}{\rho CJ}\int_V R(\boldsymbol{r})f_m(\boldsymbol{r})\,dV \qquad \tilde{s}_{m2}=\kappa h\int_{S'}Q(\boldsymbol{r})f_m(\boldsymbol{r})\,dS. \tag{17}$$

Finally, substitution of (16) into (14) gives, taking (3) and (7) into account

$$\vartheta(\boldsymbol{r},t)=\bar{\vartheta}(\boldsymbol{r})+\sum_{m=1}^{\infty}f_m(\boldsymbol{r})\Big\{e^{-\beta_m t}u_m$$
$$+\int_0^t e^{-\beta_m(t-\tau)}[\tilde{s}_{m1}P_s(\tau)+\tilde{s}_{m2}V_c(\tau)]\,d\tau\Big\}. \tag{18}$$

Equation (18) is the formal solution which relates the temperature distribution in the tissue to the two control inputs: the microwave source power rate and the surface cooling fluid temperature. Note that the thermal increase as given by this procedure shows explicitly its dependence on the various time constants $\tau_m=1/\beta_m$ of the system, as shown by (18). Note also that τ_m decreases as m increases. By defining the following column vectors $\boldsymbol{v}(t)=[v_m(t)]$, $\boldsymbol{u}(t)=[u_m(t)]$, $\tilde{s}_1=[s_{m1}]$, $\tilde{s}_2=[\tilde{s}_{m2}]$ and the matrix $\Lambda_{mn}=-\beta_m\delta_{mn}$ (δ_{mn} is the Kronecker symbol), (10) can be written in the following form, which is familiar in system theory:

$$\dot{\boldsymbol{v}}=\boldsymbol{\Lambda v}(t)+\tilde{s}_1P_s(t)+\tilde{s}_2V_c(t), \qquad \boldsymbol{v}(0)=\boldsymbol{u}. \tag{19}$$

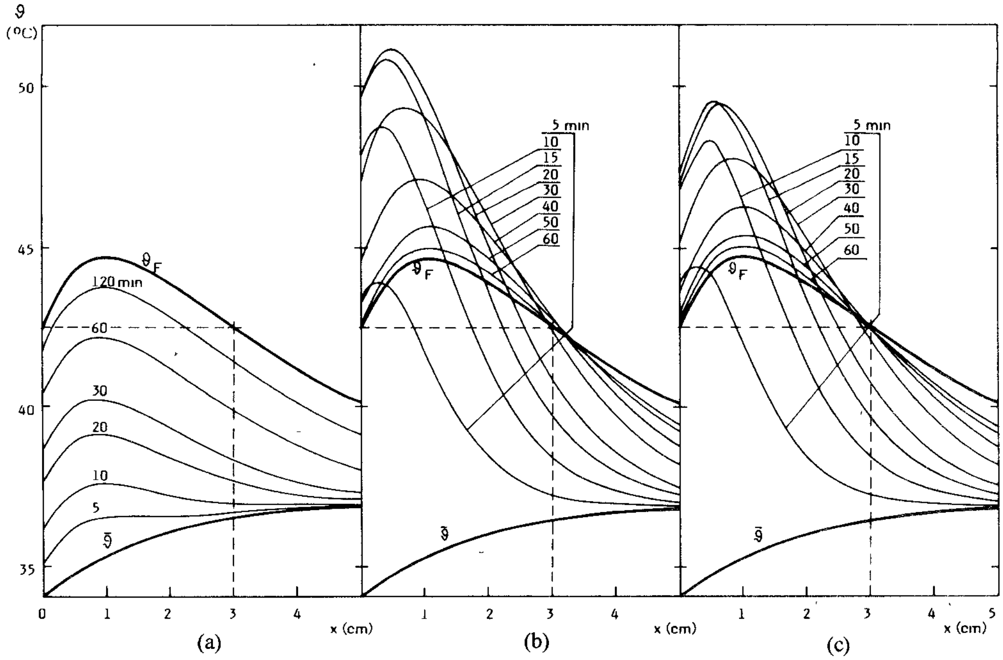

Fig. 1. Temperature $\vartheta(x,t)$ versus x for various values of t (minutes) and for three different variations with time of inputs.

The adopted formalism seems to be appropriate whenever use of pertinent techniques and results of system theory is envisaged, as is in the present case in which the temperature control in microwave hyperthermia is of concern.

In the particular case where P_s and V_c are constant say $\tilde{P}$ and $\tilde{V}$, respectively (this case corresponds to step variations of both inputs at $t=0$), (19) has the solution

$$\boldsymbol{v}(t)=\boldsymbol{\phi}(t)\boldsymbol{u}+[\mathbf{1}-\boldsymbol{\phi}(t)]\boldsymbol{v}_F \tag{20}$$

where

$$\boldsymbol{\phi}(t)=e^{\boldsymbol{\Lambda}t}$$
$$\boldsymbol{v}_F=-\boldsymbol{\Lambda}^{-1}(\tilde{s}_1\tilde{P}+\tilde{s}_2\tilde{V})$$
$$\Lambda^{-1}_{mn}=-\delta_{mn}/\beta_m. \tag{21}$$

$\boldsymbol{v}_F$ has components which are related to the final temperature distribution $\vartheta_F(\boldsymbol{r})$ by

$$\vartheta_F(\boldsymbol{r})=\bar{\vartheta}(\boldsymbol{r})+\boldsymbol{f}^T(\boldsymbol{r})\boldsymbol{v}_F \tag{22}$$

where $\boldsymbol{f}^T(\boldsymbol{r})$ denotes the row vector $[f_m(\boldsymbol{r})]$.

Numerical Example

An example of application of the above formulation follows. Let us consider the case of a homogeneous slab $0\leqslant x\leqslant d$, simulating a living tissue. The region outside the slab is at temperature ϑ_e. For $t>0$ the slab is irradiated by a linearly polarized uniform plane wave at ω angular frequency which impinges normally on the plane $x=0$ and carries the mean power density $P_s(t)$; moreover, a fluid at temperature $\vartheta_c(t)$ is forced uniformly past the same surface. For this structure the expressions of the natural temperature distribution $\bar{\vartheta}(x)$, of the normalized eigenfunctions $f_m(x)$, and of the power density dissipated by a stationary microwave excitation are given in [9] and will not be repeated here. As in [9] we choose the following numerical values for the various geometrical and physical parameters: $f=\omega/(2\pi)=2450$ MHz; $d=0.1$ m; $\vartheta_e=28°$C; $\epsilon/\epsilon_0=47$ (relative dielectric constant); $\sigma=2.21$ S/m; $\rho=1070$ kg/m^3; $C=0.75$ kcal/(kg°C); $K=0.12\times10^{-3}$ kcal/(m·s°C); $H=0.28\times10^{-2}$ kcal/(m^2·s°C); $\vartheta_b=37°$C; $A_0=0.2$ kcal/(m^3·s); $B=0.13$ kcal/(m^3·s°C).

We assume that the temperature of the tissue be raised and maintained above a prescribed level ϑ_K (42.5°C) within the region $0\leqslant x\leqslant x_A<d$. On the other hand, bearing in mind an actual clinical application, it is important that the tissue temperature does not increase exceedingly above ϑ_K. From (21) and (22) by imposing $\vartheta_F(0)=\vartheta_F(x_A)=42.5°$C, we find the levels $\tilde{P}$ and $\tilde{V}$ which produce the lowest thermal increase above ϑ_K. Numerical computations have been carried out for $x_A=0.03$ m and the results are shown on diagrams of Figs. 1–3. In Fig. 1 $\vartheta(x,t)$ is plotted versus x for various values of time according to three different time variations of the inputs which are shown on diagrams of Fig. 2 ($P_s(t)$, mean power density carried by the impinging wave), and Fig. 3 ($\vartheta_c(t)$, temperature of the fluid on the surface $x=0$), respectively. a, b, and c of Fig. 1 refer to the corresponding inputs marked with a, b, c in Figs. 2 and 3.

Fig. 1(a) shows the transient thermal response from the natural distribution ($t<0$) to the final distribution ($t\to\infty$) for step variations of both inputs at $t=0$. The final temperature is reached in more than two hours. When a speeding up of heating is desired, the power density carried by the impinging wave is usually increased at the beginning of treatment. In this case the temperature at convenient locations is continuously monitored and the microwave power is progressively reduced as the desired final temperatures are approached. The diagrams of Fig. 1(b) show the thermal response when the mean power density follows the simple law: $P_s(t)=\tilde{P}+\gamma_p[\vartheta_F(x_A)-\vartheta(x_A,t)]$, $t>0$, where $\gamma_p=0.6$ W/(m^2°C). In this way the prescribed temperature is reached after about 30 min in the region of interest. However, the temperature near the surface $x=0$ reaches

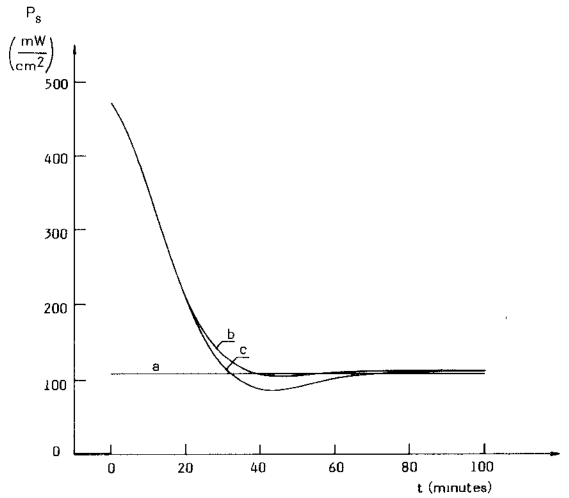

Fig. 2. Variations with time of the mean power density $P_s(t)$ carried by the impinging plane wave which produce the thermal responses of Fig. 1. No microwave radiation for $t<0$. i

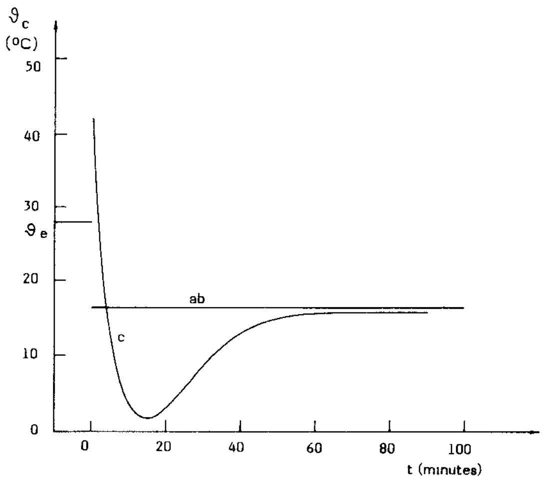

Fig. 3. Variations with time of the temperature of the cooling fluid which produce the thermal responses of Fig. 1. No forced surface cooling for $t<0$.

levels which are clearly excessive. To reduce such a noxious overheating, in turn the temperature of the cooling fluid can be varied to counteract this effect. In our example, the fluid temperature is varied according to $\vartheta_c(t)=\vartheta_e+\tilde{V}+\gamma_c[\vartheta_F(0)-\vartheta(0,t)]$, $t>0$, where $\gamma_c=3$. The diagrams of Fig. 1(c) refer to this case and show how the temperature overshot is reduced.

In the computation the series (18) has been truncated after thirty terms. If forty terms were retained, the change in the calculated temperatures would have been less than 0.05°C.

Conclusion

The problem of the temperature distribution inside simulated living tissues due to time-varying microwave irradiation and surface cooling has been considered. A series expansion solution of this problem has been worked out by means of a variational formulation of the heat-conduction problem. This procedure allows transient phenomena in irradiated bodies to be treated as the dynamic response of linear infinite-dimension systems. A numerical example is given to point out some practical advantages of this approach.

Acknowledgment

The author wishes to thank Prof. G. Gerosa for helpful suggestions.

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