BEHAVIOUR OF LIVING TISSUES SUBJECTED TO HIGH-TEMPERATURE HEATING BY MEANS OF ELECTROMAGNETIC IMPLANTS

P. Badini*, P. De Cupis*, G. Gerosa*, M. Giona**

Dipartimento di Ingegneria Elettronica*, Dipartimento di Ingegneria Chimica**,
Università *La Sapienza*, via Eudossiana 18, 00184, Roma

Abstract

The clinical necrosis of living tissues by means of high-temperature implants to be heated through electromagnetic induction is theoretically studied. Non-linear and non-stationary phenomena relevant to the action of the temperature-regulation system and to the cellular death process, as like as the alteration of the local electromagnetic properties due to the high temperature elevation are taken into account, by means of an interlaced solution procedure for the electromagnetic problem and for the thermal one. The model is validated through comparison with experimental clinical data.

I-INTRODUCTION

High-Temperature Hyperthermia (HTH) has its roots in the ancient medical practice of cauterization; nevertheless, from a scientific and rational view-point it represents a recent technique, that is nowadays widely used in cerebral surgery, in oncologic therapy (for deep-seated neoplastic nuclei), in orthopaedics. The most efficient way to realize HTH is the introduction into the target tissue of thermal metallic probes to be heated by means of electromagnetic (EM) induction; in fact, since no "mechanical" connection with the external sources is necessary, the sessions can be repeated without multiple insertion-removal operation and so minimizing infection risks. Moreover, the EM induction permits to obtain a more efficient temperature control of the probes avoiding the generation of spurious cysts [1].

It is important to accurately determine the amplitude of the necrosis core in the target region around the implants and its growing trend at each time of the therapeutic session, in order to optimise the duration of the treatment with respect to the temperature or the power level of the implants. From a theoretical point of view, it is necessary to study the thermal propagation problem inside the living tissue, on the ground of a Thermal Transfer Equation (TTE) whose conductivity coefficient and convective exchange parameter have the following properties: first, as a consequence of the local thermo-control processes, they must be (non-linearly) dependent on the temperature [2]; second, they must be dependent also on the physiologic status of the tissue, which is represented by a point-wise "necrosis level" field and by the corresponding space-time evolution equation (that shall correctly represent the irreversibility of the thermal death phenomenon) to be solved in conjunction with the TTE. Moreover, during the treatment simulation, for a correct evaluation of the EM excitation of the implants it is necessary to continuously adjust the EM parameters (e.g. the complex electric permittivity) in the tissue region close to the implants according to the variation of the local temperature and of the physiological status (e.g. the occurrence of the necrosis phenomenon alters the water and saline contents of the tissue).

II-FORMULATION

In order to furnish a quantitative description of the necrosis phenomenon in a portion of living tissue subjected to HTH we introduce the space-time dependent field n representing the necrosis level in the range between 0 (non-necrotic wealthy status) and

1 (fully-necrotized status), whose evolution is described by means of the following equation (Bio-Necrotic Equation, BNE):

$$\left.\frac{\partial n}{\partial t}\right|_{\vec{r},t} = \frac{h^{\infty}\left(T\left(\vec{r},t\right)-T_d\left(\vec{r}\right)\right)-n\left(\vec{r},t\right)}{t\left(\vec{r}\right)}\cdot h^{\infty}\left(\left.\frac{\partial T}{\partial t}\right|_{\vec{r},t}\right) \qquad (1)$$

equipped with the initial condition $n\left(\vec{r},0\right)=0$ relevant to time t=0; $h^{\infty}\in C^{\infty}_{\mathbb{R}}$ is a compact function approximating the Heaviside unit-step function. As one can see from Eq. (1), for a given point $\vec{r}$ of the biologic body volume V_B, that is initially non-necrotic, when the temperature $T\left(\vec{r},t\right)$ raises during the applicative session, ($\partial T/\partial t>0 \rightarrow h^{\infty}\left(\partial T/\partial t\right)\approx 1$), as the necrosis threshold $T_d\left(\vec{r}\right)$ is exceeded, the necrosis level $n\left(\vec{r},t\right)$ begins to evolve toward the level 1, with a characteristic transition time $t\left(\vec{r}\right)$; the irreversibility of such necrosis phenomenon is correctly taken into account: in fact, as the temperature lowers at the end of the session, the presence of the term $h^{\infty}\left(\partial T/\partial t\right)\approx 0$ for $\partial T/\partial t<0$ forbids any decrease of the necrosis level. Since the necrosis field n is interdependent with the temperature field T, one has to solve Eq. (1) together with the Fourier-Laplace TTE:

$$c\left(\vec{r},T\left(\vec{r},t\right),n\left(\vec{r},t\right)\right)\left.\frac{\partial T}{\partial t}\right|_{\vec{r},t} - \nabla\bullet\left[K\left(\vec{r},T\left(\vec{r},t\right),n\left(\vec{r},t\right)\right)\nabla T\big|_{\vec{r},t}\right]-Q\left(\vec{r},T\left(\vec{r},t\right),n\left(\vec{r},t\right)\right)=0 \qquad (2)$$

where c is the product of the mass density times the specific heat, K is the thermal conductivity and Q represents the heat sources. The living tissue is represented as the superposition of two isotropic coexisting continua, the solid molecular continuum and the liquid haematic continuum, i.e. the micro capillary system [2]; therefore, the thermal conductivity can be expressed as the sum of two contributes:

$$K\left(\vec{r},T,n\right)=K_m\left(\vec{r}\right)+K_p\left(\vec{r},T,n\right)=K_m\left(\vec{r}\right)+k_p\left(\vec{r}\right)W_p\left(\vec{r},T,n\right) \qquad (3)$$

where K_m is the conductivity of the molecular part, whilst K_p is the conductivity of the haematic part, that is assumed to be proportional to the specific blood flow density W_p:

$$W_p\left(\vec{r},T,n\right)=\left(1-n\right)\cdot\Omega_{p0}\left(\vec{r}\right)\cdot\exp\left[b\left(\vec{r}\right)\left(T-T_{p0}\right)\left\{1-l\left[T_d/\left(T_d-T\right)\right]^{y}\right\}\right] \qquad (4)$$

where $\Omega_{p0}(\vec{r})$ is the micro-capillary flow density for $T=T_{p0}$ (temperature of the arterial blood), $b\ (\vec{r})$, l and y are experimental best-fitting coefficients.

The additional convective thermal exchange flow between the molecular medium and the haematic medium, due to blood motion, [2] is represented as follows:

$$Q_c\left(\vec{r},T,n\right)=-u_p\left(\vec{r}\right)\cdot\left[T-T_{p0}\right]\cdot W_p\left(\vec{r},T,n\right) \qquad (5)$$

The physiological metabolism has to be considered as a positive source term:

$$Q_M\left(\vec{r},T,n\right)=\Phi_M\left(\vec{r},T\right)\cdot\left(1-n\right) \qquad (6)$$

where Φ_M gives the non-pathological temperature-dependent metabolic heat for n=0.

Moreover, it has to be considered the direct loss effect inside the living tissue due to the EM implant excitation, i.e. the source term $Q_{EM}\left(\vec{r},t\right)$ for $\vec{r}\in V_B$, see section II.1

In conclusion, in Eq. (8) we have $Q = Q_c + Q_M + Q_{EM}$.

Finally, proper boundary conditions [1] have to be imposed on the boundary of the implant volume V_I:

$$-\oint_{\partial V_I} \vec{n} \bullet K \nabla T dS = \Pi_I(t),\ t \in \Delta t_P;\quad T(\vec{r},t) = T_I(t),\ \vec{r} \in \partial V_I,\ t \in \Delta t_T \tag{7}$$

where $\Pi_I(t)$ and $T_I(t)$ are the implant regulation functions relevant to the power-control phase Δt_P (switch-on, switch off intervals) and to the temperature-control phase Δt_T (stabilized regime at the Curie-point), respectively; $\vec{n}$ is the outward normal unit vector. Additional boundary conditions must be imposed in order to consider border effects; e.g. in the presence of a surrounding medium at temperature T_e we let [2]:

$$\vec{n} \bullet \nabla T\big|_{\vec{r},t} + [T(\vec{r},t) - T_e] h_e = 0,\quad \vec{r} \in \Sigma \tag{8}$$

where Σ is the external boundary of the body and h_e is a proper thermal exchange coefficient. Finally, the following continuity condition on temperature and heat flow must be assumed on inner discontinuity surfaces S_g [2]:

$$T(\vec{r}^{+},t) = T(\vec{r}^{-},t)\ ;\quad [K\vec{n} \bullet \nabla T]_{\vec{r}^{+},t} = [K\vec{n} \bullet \nabla T]_{\vec{r}^{-},t},\ \vec{r} \in S_g \tag{9}$$

where apex `+' and `-' represent left and right limits along the normal direction $\vec{n}$.

II.1 The electromagnetic problem

From a dynamic point of view, it is an experimental evidence that thermal and necrotic transients (10^{-1}–10^{1} s) are much slower than EM ones; therefore, once fixed a suitable time discretization grid $\{t_n\}_{n \in N}$ for the TTE and the BNE, at a given time t_n the EM induced power can be evaluated on the basis of the Poynting theorem by means of the following expression:

$$Q_{EM}(\vec{r},t_n) = \frac{1}{2}\,\mathrm{Re}\left\{ iw \left[\begin{array}{l} m(\vec{r}, T(\vec{r},t_{n-1}); w) \left|\vec{H}(\vec{r},w;t_n)\right|^2 + \\ +e(\vec{r}, T(\vec{r},t_{n-1}), n(\vec{r},t_{n-1}); w) \left|\vec{E}(\vec{r},w;t_n)\right|^2 + \end{array} \right] \right\} p(t_n) \tag{10}$$

where $\vec{E}(\vec{r},w;t_n)$, $\vec{H}(\vec{r},w;t_n)$, represent the electric field and the magnetic field in the frequency domain, respectively; w is the (angular) frequency of the excitation current sources; the 'additional' presence of time t_n in the w-domain EM field argument takes into account the slow-varying alteration of the EM properties of the medium due to the simultaneous evolution of the temperature and of the necrosis level[1]: in fact, in V_B the complex electric permittivity e is significantly dependent both on T and n, whereas in V_I the complex magnetic permeability m can meaningfully depend on T, as a consequence of the transition phenomena between paramagnetic and ferromagnetic status; $i = +\sqrt{-1}$, $p(t)$ is the slow-varying power level modulation controlled by the operator during the clinical session (switch-on/regime/switch-off).

Starting by the w-domain Maxwell equations ($\vec{J}_e(\vec{r},w)$, $\vec{J}_m(\vec{r},w)$ are the electric and magnetic sources which model the external EM power generator),

$$\nabla \times \begin{bmatrix} \vec{E}(\vec{r},w;t_n) \\ \vec{H}(\vec{r},w;t_n) \end{bmatrix} = iw \begin{bmatrix} -m(\vec{r}, T(\vec{r},t_{n-1}); w)\, \vec{H}(\vec{r},w;t_n) \\ e(\vec{r}, T(\vec{r},t_{n-1}), n(\vec{r},t_{n-1}); w), \vec{E}(\vec{r},w;t_n) \end{bmatrix} + \begin{bmatrix} -\vec{J}_m(\vec{r};w) \\ \vec{J}_e(\vec{r};w) \end{bmatrix} \tag{11}$$

we decompose the EM field in the superposition of an incident part plus a scattered part, i.e. $[\vec{E}, \vec{H}] = [\vec{E}_i, \vec{H}_i] + [\vec{E}_s, \vec{H}_s]$; the first one is equivalent to the radiation that the same source system should induce in free-space,

---

[1] By virtue of the previous dynamic considerations we can consider the T and n distributions relevant to the anticipated time t_{n-1} instead of the current time t_n; in such way an iterative interlaced procedure for the solution of the EM problem in conjunction with the TTE-BNE system is obtained.

$$\nabla\times\begin{bmatrix}\vec{E}_{\rm i}(\vec{r};w)\\ \vec{H}_{\rm i}(\vec{r};w)\end{bmatrix}=iw\begin{bmatrix}-m_0\vec{H}_{\rm i}(\vec{r};w)\\ e_0\vec{E}_{\rm i}(\vec{r};w)\end{bmatrix}+\begin{bmatrix}-\vec{J}_m(\vec{r};w)\\ \vec{J}_e(\vec{r};w)\end{bmatrix},\qquad(12)$$

and then obtainable *una tantum* on the ground of the dyadic Green functions, i.e.:

$$\begin{bmatrix}\vec{E}_{\rm i}(\vec{r};w)\\ \vec{H}(\vec{r};w)_{\rm i}\end{bmatrix}=\iiint\begin{bmatrix}\underline{\underline{G}}_E^e & \underline{\underline{G}}_E^m\\ \underline{\underline{G}}_H^e & \underline{\underline{G}}_H^m\end{bmatrix}_{\vec{r},\vec{r}';w}\bullet\begin{bmatrix}\vec{J}_e(\vec{r}';w)\\ \vec{J}_m(\vec{r}';w)\end{bmatrix}d\vec{r}'\ ;\qquad(13)$$

the second one is due to the presence of the body ($e\neq e_0\ \forall\vec{r}\in V_B\cup V_I$; $m\neq m_0\ \forall\vec{r}\in V_I$):

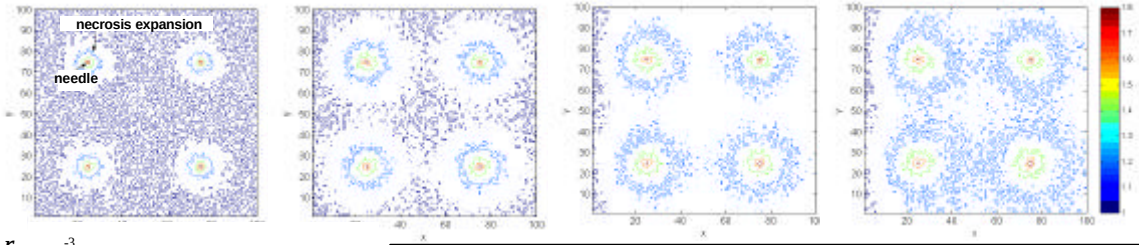
$$\nabla\times\begin{bmatrix}\vec{E}_{\rm s}(\vec{r},w;t_n)\\ \vec{H}_{\rm s}(\vec{r},w;t_n)\end{bmatrix}=iw\begin{bmatrix}-m_0\vec{H}_{\rm s}(\vec{r},w;t_n)\\ e_0\vec{E}_{\rm s}(\vec{r},w;t_n)\end{bmatrix}+\begin{bmatrix}-iw\{m(\vec{r},T(\vec{r},t_{n-1});w)-m_0\}\vec{H}(\vec{r},w;t_n)\\ iw\{e(\vec{r},T(\vec{r},t_{n-1}),n(\vec{r},t_{n-1});w)-e_0\}\vec{E}(\vec{r},w;t_n)\end{bmatrix}\qquad(14)$$

Analogously to the solution relevant to free-space given by Eq. (13) we can obtain the following integral equation (whose numerical solution can be efficiently performed by means of the Moment Method through an associated algebraic system [3,4]), where the inhomogeneities of e and m play the role of field sources:

$$\begin{bmatrix}\vec{E}_{\rm s}(\vec{r},w;t_n)\\ \vec{H}_{\rm s}(\vec{r},w;t_n)\end{bmatrix}=\begin{bmatrix}\vec{E}(\vec{r},w;t_n)\\ \vec{H}(\vec{r},w;t_n)\end{bmatrix}-\begin{bmatrix}\vec{E}_{\rm i}(\vec{r};w)\\ \vec{H}_{\rm i}(\vec{r};w)\end{bmatrix}_{\vec{r},w}=$$
$$=\iiint\begin{bmatrix}\underline{\underline{G}}_E^e & \underline{\underline{G}}_E^m\\ \underline{\underline{G}}_H^e & \underline{\underline{G}}_H^m\end{bmatrix}_{\vec{r},\vec{r}';w}\bullet\begin{bmatrix}iw\{e(\vec{r}',T(\vec{r}',t_{n-1}),n(\vec{r}',t_{n-1});w)-e_0\}\vec{E}(\vec{r}',w;t_n)\\ iw\{m(\vec{r}',T(\vec{r}',t_{n-1});w)-m_0\}\vec{H}(\vec{r}',w;t_n)\end{bmatrix}d\vec{r}'\qquad(15)$$

III-RESULTS

The model is validated through the comparison of numerical simulations, relevant to a 2D liver tissue geometry whereinto 4 thermal needles are inserted, with experimental data relevant to oncologic clinical sessions.



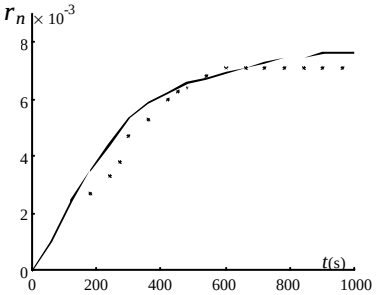


Fig. 1 (UP) Temperature and necrosis expansion in a muscle region with 4 implanted needles; plots from left to right are relevant to crescent times t=100s, 400s, 700s, 1100s; regime temperature $T_I(t)\equiv$105°C after the switch-on transient Δt_P=[0s,100s]

Fig. 2 (LEFT): Comparison between experimental measured* and simulated necrosis expansions r_n (around a single implant) vs. time t.

* Experimental data from clinical session were furnished by Prof. Riccardo Maceratini and Dr. Marcello Caratozzolo of the "IV Clinica Chirurgica-Facoltà di Medicina e Chirurgia" , *La Sapienza* University of Rome.

BIBLIOGRAPHY

[1] Atkinson, W. J., Brezovich, I. A., and Chakraborty, D. P., 1984, "Usable Frequencies in Hyperthermia with Thermal Seeds," IEEE Transactions on Biomedical Engineering, **31**(1) , pp. 70-75

[2] Bardati, F., and Gerosa, G., 1990, "On the solution of the non-linear bio-heat equation," Journal of Biomechanics, **23** (8), pp. 791-798.

[3] J.J.H. Wang, "*Generalized Moment Methods in Electromagnetics*", J.Wiley & Sons, New York, 1991

[4] D.E. Livesay, K.M. Chen, "Electromagnetic fields induced inside arbitrarily shaped biological bodies",' *IEEE Trans. Microwave Theory Tech.*, MTT-22, Dec. 1974, pp.1273-1280.