

**EXISTENCE AND UNIQUENESS SOLUTION OF THE DUAL-PHASE-LAG
BIO-HEAT TRANSFER DURING MAGNETIC HYPERTHERMIA
TREATMENT**

Ayeni R.O¹, Erinle-Ibrahim L.M.² and Gbadamosi Babatunde¹

- 1. Pure and Applied Mathematics department Ladok Akintola University of
Technology, Ogbomoso*
- 2. Mathematics department Tai Solarin University of Education,
Ijagun, Ijebu-ode*

Abstract

Magnetic fluid hyperthermia is one of hyperthermia modalities for tumor treatment. The control of temperatures is necessary and important for the treatment quality. Living tissue is highly non-homogenous and the velocity of heat transfer in it should be limited. This work examines the existence of the steady case of Liu and Chen (2009) and proof the uniqueness of the theorem. The proof shows that only when gradient is specified that the solution is guaranteed.

Introduction

In magnetic tumor hyperthermia, the magnetic particles are localized at the tumor tissue, then an alternating magnetic field is applied to the target region, which heats the magnetic particles by magnetic hysteresis losses. These particles might act as localized heat sources (Liu and chi, 2009), worked on analysis of the temperature rise behaviors in biological tissues during hyperthermia treatment within the dual-phase-lag mode, which accounts for the effect of local non-equilibrium on the thermal behavior. The control of the

blood perfusion rate is helpful to have an ideal hyperthermia treatment. The lag times affect the bio-heat transfer at the early times of heating. This work develops a hybrid numeric based on the Laplace transform, change of variables and the modified discretization technique in conjunction with the hyperbolic shape functions for solving the present problem. This similar method was used to solve various non-Fourier heat transfer problems and obtained the accurate result (Liu, 2007, 2008). The dual phase lag (DPL) model is used to predict the temperature rise behavior in a two layer concentric spherical region during magnetic tumor hypothermia treatment. The DPL model describes a macroscopic temperature with a micro-structural effect by introducing the phase lag times of heat flux and temperature gradient (Tzou, 1996). From the measurement temperature in Ref (Mitra et al 1995), Antaki (2005) predicted the phase lag time of heat flux to be 14-16s and the phase lag time temperature gradient to be 0.043-0.056s for processed meat.

Hyperthermia technique also improves the efficiency of other cancer therapies such as, chemotherapy and radiotherapy. Isolated cells, which would not respond to chemotherapy or radiation alone, would be subjected to heat treatment. Hyperthermia in conjunction with chemotherapy causes the drug to penetrate deeper into the tumor while augmenting the efficacy of the drug delivered to the tumor. The increased efficacy of simultaneous utilization of the hyperthermia and radiotherapy or chemotherapy has been demonstrated in heat treatment of certain types of diseases (Wust, et al.,2002), such as breast cancer (Vernon et al,1996), cervical and bladder cancer (Zee,et al 2000), rectal cancer (Rau 1998), prostate cancer (Van Vulpen, 2004), head and neck cancer

(Brize1999), superficial tumors, lung and stomach cancer and pancreas and liver metastases.

A comprehensive analytical investigation of bioheat transport through the tissue/organ is carried out including thermal conduction in tissue and vascular system, blood- tissue convective heat exchange, metabolic heat generation and imposed heat flux. Utilizing local thermal non-equilibrium model in porous media theory, exact solution for blood and tissue phase temperature profiles as well as overall heat exchange correlations are established, two primary tissue/ organ model representing isolated and uniform conditions, while incorporating the pertinent effective parameters, such as volume fraction of the vascular space, ratio of the blood and the tissue matrix thermal conductivities, interfacial blood-tissue heat exchange, tissue/organ depth, arterial flow rate and temperature, body core temperature, imposed hyperthermia heat flux, metabolic heat generation, and blood physical properties.(Mahjood and Vafai 2009).

Mathematical Formulation

We consider Liu and Chen (2009)

$$\left. \begin{aligned} k_1 \frac{1}{r^2} \frac{\partial}{\partial r} \left[r^2 \left(\frac{\partial T_1}{\partial r} + \tau_{T1} \frac{\partial^2 T}{\partial t \partial r} \right) \right] &= \left(1 + \tau_{q1} \frac{\partial}{\partial r} \right) \left[\rho_1 c_1 \frac{\partial T_1}{\partial t} - \omega_{b1} \rho_b c_b (T_b - T_1) - q_{m1} - q_{r1} \right] \\ &\quad \text{for } 0 \leq r \leq R \\ k_2 \frac{1}{r^2} \frac{\partial}{\partial r} \left[r^2 \left(\frac{\partial T_1}{\partial r} + \tau_{T2} \frac{\partial^2 T}{\partial t \partial r} \right) \right] &= \left(1 + \tau_{q1} \frac{\partial}{\partial r} \right) \left[\rho_2 c_2 \frac{\partial T_2}{\partial t} - \omega_{b2} \rho_b c_b (T_b - T_1) - q_{m2} \right] \\ &\quad \text{for } R \leq r \leq \infty \end{aligned} \right\} \quad (1)$$

the temperature and heat flux at the interface of two regions is continuous. The boundary conditions are described as

$$\begin{aligned}
\frac{\partial T_1(0,t)}{\partial r} &= 0 \quad \text{and} \quad T_1(0,t) \quad \text{is finite} \\
T_1(R,t) &= T_2(R,t) \\
T_1(R,t) &= T_2(R,t) \\
T_2(\infty,t) &= T_i
\end{aligned} \tag{2}$$

and the initial conditions are

$$T_k(r,0) = T_i, \quad \frac{\partial T_k(0,t)}{\partial t} = 0, \quad \text{and} \quad q_r(r,0) = 0 \quad k = 1, 2 \tag{3}$$

where the subscript k is the number of layer, $k = 1$ and $k = 2$ means the tumor and the normal tissue, respectively. The initial temperature T_i is regarded as the arterial temperature.

T is the temperature, k the heat conductivity, q the heat flux, t the time, and r the space variable, τ_q means the phase lag of the heat flux and τ_T means the phase lag of temperature gradient. The heat flux precedes the temperature gradient for $\tau_q < \tau_T$. The temperature gradient precedes the heat flux for $\tau_q > \tau_T$.

where ρ, c, k , and T denote density, specific heat, thermal conductivity, and temperature respectively in two regions. ρ_b, c_b and ω_b respectively are density, specific heat and perfusion rate of blood. q_m is the metabolic heat generation and only is a function of r in the problem.

Method of Solution

Steady state

We consider the steady case

$$\text{Let } H_i = r(T_i - T_b), \quad i = 1, 2$$

We assume that, following Liu and Chen (2009)

$$T_i(0,t) = \lim_{r \rightarrow 0} \frac{H_i}{r} + T_i = \frac{dH_i}{dr} + T_i$$

The steady case gives

$$\left. \begin{aligned} k_1 \frac{d^2 H_1}{dr^2} &= \omega_{b1} \rho_b c_b H_1 + (q_{m1} + q_{r1})r & \text{for } 0 \leq r \leq R_0 \\ k_2 \frac{d^2 H_2}{dr^2} &= \omega_{b2} \rho_b c_b H_2 + q_{m2}r & \text{for } R_0 \leq r \leq R \end{aligned} \right\} \quad (4)$$

The boundary conditions are

$$\left. \begin{aligned} H_1(0) &= 0 \\ H_1(R_0) &= H_2(R_0) \\ H_2(R) &= 0 \end{aligned} \right\} \quad (5)$$

Existence and Uniqueness of Solution

Theorem 1: Problem (4) which satisfies boundary (5) has a unique solution

Proof: We shall use shooting method technique

$$\text{Let } \begin{aligned} x_1 &= r \\ x_2 &= H_i \\ x_3 &= \frac{dH_i}{dr} \end{aligned} \quad i = 1, 2$$

Then , we obtain

$$\begin{aligned} x_1' &= 1 \\ x_2' &= x_3 \\ x_3' &= \frac{\omega_{b1} \rho_b c_b}{k_1} x_2 + \frac{q_{m1} + q_{r1}}{k_1} x_1 & \text{for } 0 \leq r \leq R_0 \\ &= \frac{\omega_{b2} \rho_b c_b}{k_2} x_2 + \frac{q_{m2}}{k_2} x_1 & \text{for } R_0 \leq r \leq R \end{aligned}$$

together with the boundary conditions

$$x_1(0) = 0$$

$$x_2(0) = 0$$

$$x_3(0) = \alpha \quad (\text{guessed})$$

Now

$$x_1' = 1 = f_1(x_1, x_2, x_3)$$

$$x_2' = x_3 = f_2(x_1, x_2, x_3)$$

$$x_3' = \frac{\omega_{b1}\rho_b c_b}{k_1} x_2 + \frac{q_{m1} + q_{r1}}{k_1} x_1 \quad \text{for} \quad 0 \leq r \leq R_0$$

$$\frac{\omega_{b2}\rho_b c_b}{k_2} x_2 + \frac{q_{m2}}{k_2} x_1 \quad \text{for} \quad R_0 \leq r \leq R$$

that

$$x_3' = f_3(x_1, x_2, x_3) \quad \text{for} \quad 0 \leq r \leq R_0$$

$$f_4(x_1, x_2, x_3) \quad \text{for} \quad R_0 \leq r \leq R$$

Then,

$$\frac{\partial f_1}{\partial x_i} = 0 \quad i = 1, 2, 3$$

$$\frac{\partial f_2}{\partial x_1} = 0,$$

$$\frac{\partial f_2}{\partial x_2} = 0,$$

$$\frac{\partial f_2}{\partial x_3} = 1$$

Also

$$\frac{\partial f_3}{\partial x_1} = \frac{q_{m1} + q_{r1}}{k_1},$$

$$\frac{\partial f_3}{\partial x_2} = \frac{\omega_{b1}\rho_b c_b}{k_1},$$

$$\frac{\partial f_3}{\partial x_3} = 0,$$

$$\frac{\partial f_4}{\partial x_1} = \frac{q_{m2}}{k_2}$$

$$\frac{\partial f_4}{\partial x_2} = \frac{\omega_{b2}\rho_b c_b}{k_2}$$

$$\frac{\partial f_4}{\partial x_3} = 0$$

Since all $\frac{\partial f_i}{\partial x_i}$ are continuous and bounded. Hence, the problem has a unique solution.

This completes the proof.

Non-dimensionalization of equation

Let

$$H = r(T - T_b)$$

Then

$$\left. \begin{aligned} k_1 \left(1 + \tau_{r1} \frac{\partial}{\partial t} \right) \frac{\partial^2 H_1}{\partial r^2} &= \left(1 + \tau_{q1} \frac{\partial}{\partial t} \right) \left[\rho_1 c_1 \frac{\partial H_1}{\partial t} - \omega_{b1} \rho_b c_b H_1 \right] + (q_{m1} + q_{r1}) r & \text{for } 0 \leq r \leq R_0 \\ k_2 \left(1 + \tau_{r2} \frac{\partial}{\partial t} \right) \frac{\partial^2 H_2}{\partial r^2} &= \left(1 + \tau_{q1} \frac{\partial}{\partial t} \right) \left[\rho_2 c_2 \frac{\partial H_2}{\partial t} - \omega_{b2} \rho_b c_b H_1 \right] + q_{m2} r & \text{for } R_0 \leq r \leq R \end{aligned} \right\} \quad (6)$$

The boundary and initial conditions are

$$\left. \begin{aligned} H_1(0) &= 0 \\ H_1(R_0, t) &= H_2(R_0, t) \\ q_1(R_0, t) &= q_2(R_0, t) \\ H_2(\infty, t) &= 0 \end{aligned} \right\} \quad (7)$$

and

$$H_k(r, 0) = 0, \quad \frac{\partial H_k(r, 0)}{\partial t} = 0, \quad q_k(r, 0) = 0 \quad k = 1, 2$$

Let

$$r' = \frac{r}{R_0}, \quad H' = \frac{H}{H_0}, \quad H_0 = R_0 T_b, \quad t' = \frac{t}{\tau_q}$$

Then

$$\frac{\partial}{\partial r} = \frac{\partial}{\partial r'} \frac{\partial r'}{\partial r} = \frac{1}{R_0} \frac{\partial}{\partial r'}$$

$$\frac{\partial}{\partial t} = \frac{1}{\tau_q} \frac{\partial}{\partial t'}$$

So,

$$\left. \begin{aligned} k_1 \left(1 + \frac{\tau_{T1}}{\tau_q} \frac{\partial}{\partial t'} \right) \frac{H_0}{R_0^2} \frac{\partial^2 H_1'}{\partial r'^2} &= \left(1 + \frac{\tau_{q1}}{\tau_q} \frac{\partial}{\partial t'} \right) \left[\frac{\rho_1 c_1}{\tau_q} H_0 \frac{\partial H_1'}{\partial t'} - \omega_{b1} \rho_b c_b H_0 H_1' + (q_{m1} + q_{r1}) R_0 r' \right] \\ &\quad \text{for } 0 \leq r' \leq 1 \\ k_1 \left(1 + \frac{\tau_{T2}}{\tau_q} \frac{\partial}{\partial t'} \right) \frac{H_0}{R_0^2} \frac{\partial^2 H_2'}{\partial r'^2} &= \left(1 + \frac{\tau_{q2}}{\tau_q} \frac{\partial}{\partial t'} \right) \left[\frac{\rho_2 c_2}{\tau_q} H_0 \frac{\partial H_2'}{\partial t'} - \omega_{b2} \rho_b c_b H_0 H_2' + q_{m2} R_0 r' \right] \\ &\quad \text{for } R_0 \leq r' \leq \infty \end{aligned} \right\} \quad (8)$$

where

$$\left. \begin{aligned} \left(1 + \tau_{11} \frac{\partial}{\partial t'}\right) \frac{\partial^2 H_1'}{\partial r'^2} &= \left(1 + \tau_{12} \frac{\partial}{\partial t'}\right) \left[\frac{\rho_1 c_1}{\tau_q^2 k_1} R_0^2 \frac{\partial H_1'}{\partial t'} + \frac{\omega_{b1} \rho_b c_b R_0^2}{k_1} H_1 + \frac{(q_{m1} + q_{r1})}{k_1 H_0} R_0 r' \right] \\ &\quad \text{for } 0 \leq r' \leq 1 \\ \left(1 + \tau_{21} \frac{\partial}{\partial t'}\right) \frac{\partial^2 H_1'}{\partial r'^2} &= \left(1 + \tau_{22} \frac{\partial}{\partial t'}\right) \left[\frac{\rho_2 c_2}{\tau_q^2 k_2} R_0^2 \frac{\partial H_2'}{\partial t'} + \frac{\omega_{b2} \rho_b c_b R_0^2}{k_2} H_2' + \frac{q_{m2}}{k_2 H_0} R_0^3 r' \right] \\ &\quad \text{for } 1 \leq r' \leq \infty \end{aligned} \right\}, \quad (9)$$

$$\tau_{11} = \frac{\tau_{T1}}{\tau_q}, \quad \tau_{12} = \frac{\tau_{q1}}{\tau_q}, \quad \tau_{21} = \frac{\tau_{T2}}{\tau_2}, \quad \tau_{22} = \frac{\tau_{22}}{\tau_q}$$

$$\frac{\partial^3 H_2}{\partial t \partial r^2} = c \frac{\partial^2 H_2}{\partial t^2} + d \frac{\partial H_2}{\partial t}, \quad 1 \leq r < \infty$$

where

$$\begin{aligned} a &= \frac{\tau_{12} \rho_1 c_1 R_0^2}{\tau_{11} \tau_q^2 k_1}, & b &= \frac{R_0 \omega_{b1} \rho_b c_b}{k_1 \tau_{11}} \\ c &= \frac{\tau_{22} \rho_2 c_2 R_0^2}{\tau_{21} \tau_q^2 k_2}, & d &= \frac{R_0 \omega_{b2} \rho_b c_b}{k_2 \tau_{21}} \end{aligned}$$

Theorem 2: Problem (6) and (7) has unique solution

Proof: By method of separation of variables

$$\frac{\partial H_1}{\partial t}(r, t) = \sum_{n=1}^{\infty} b_n e^{-\frac{1}{a}(n^2 \pi + b)t} \sin n \pi r,$$

where

$$b_n = \frac{2}{\pi} \int_0^1 f_1(r) \sin n \pi r dr$$

and

$$\frac{\partial H_2}{\partial t}(r,t) = \frac{e^{-\frac{d}{c}t}}{2\sqrt{\frac{\pi t}{c}}} \int_0^\infty \left[e^{-\frac{(r-\varepsilon)^2}{4t}} + e^{-\frac{(k+\varepsilon)^2}{4t}} \right] f(\varepsilon) d\varepsilon$$

We shall now assume that

$$1 + \tau_{11} \frac{\partial}{\partial t'}, \quad 1 + \tau_{21} \frac{\partial}{\partial t'} \text{ are}$$

$$\tau_{11} \frac{\partial}{\partial t'}, \quad \text{and} \quad \tau_{21} \frac{\partial}{\partial t'} \text{ respectively}$$

Further we assume that

$$\tau_{11} \frac{\partial^3 H_1'}{\partial t' \partial r'^2} = \frac{\tau_{12} \rho_1 c_1 R_0^2}{\tau_q^2 k_1} \frac{\partial^2 H_1'}{\partial t'^2} + \frac{R_0 \omega_{b1} \rho_b c_b}{k_1} \frac{\partial^2 H_1}{\partial t'} \quad \text{for } 0 \leq r' \leq 1, \quad t' > 0$$

and

$$\tau_{21} \frac{\partial^3 H_2'}{\partial t' \partial r'^2} = \frac{\tau_{22} \rho_2 c_2 R_0^2}{\tau_q^2 k_2} \frac{\partial^2 H_2'}{\partial t'^2} + \frac{R_0 \omega_{b1} \rho_b c_b}{k_2} \frac{\partial^2 H_2}{\partial t'} \quad \text{for } 1 \leq r' \leq \infty, \quad t' > 0$$

together with the boundary and initials conditions

$$\left. \begin{aligned} H_1(0, t') &= 0 \\ H_1(R, t') &= H_2(R, t') \\ H_2(\infty, t') &= 0 \\ H_k(r', 0) &= f_r(r'), \quad \frac{\partial^2 H_k}{\partial t'}(r', 0) = q_k(r'), \quad k = 1, 2 \end{aligned} \right\} \quad (11)$$

dropping ". " , we obtain

$$\frac{\partial^3 H_1}{\partial t \partial r^2} = a \frac{\partial^2 H_1}{\partial t^2} + b \frac{\partial H_1}{\partial t} \quad \text{for } 0 \leq r \leq 1, \quad t > 0$$

This completes the proof.

Discussion of the result

The proof of theorem shows that it is only when we specify the gradient $x_3(0)$ that the solution is guaranteed.

References

Antaki, P.J.(2005): New interpretation of non-fourier heat conduction in processed meat, ASME J. Heat Transfer 127, 189-193.

Brizel D.M., Dodge R.K., Clough R.W., Dewhirst M.W.(1999): Oxygenation of head and neck cancer: changes during radiotherapy and impact on treatment outcome, Radiother. Oncol. 53 (2), 113-117.

Liu, Kuo-chi.ChenHar-Taw(2009): Analysis for the dual-phase-lag bio-heat transfer duringmagnetic hyperthermia treatment, Int.J. Heat mass transfer 50, 1185-1192.

Liu K. C.(2007a): Analysis of the thermal behavior in multi-layer metal thin films based on hyperbolic two-step model, Int.J. Heat mass transfer 50, 1397-1407.

Liu K. C. (2007b): Numerical analysis of dual-phase-lag heat transfer in a layered cylinder with non-linear interface boundary conditions, comput. Physcommun. 177 307-314.

Liu K. C.(2008): Thermal propagation analysis for living tissue with surface heating, Int.J. Thermal sci. 47, 507-513.

Mahjood, S. and Vafai, K. (2009): Analytical characterization of heat transport through biological media incorporation hyperthermia treatment.Int.J. Heat mass transfer 52, 1608-1618.

Mitra, K., Kumar, S., Veclavarz, A., Moallemi, M.K.(1995):Experiemental evidence of hyperbolic heat conductor in processed meat, ASME J. Heat Transfer 117, 568-573.

Rau B., Wust P., Hohenberger P., Loffel J., Hunerbein M., Below C., Gellermann J., Speidel A., Vogl T., Reiss H., Felix R., Schlag P.M.(1998): Preoperative Hyperthermia combined with radio-chemotherapy in locally advanced rectal cancer: a phase II clinical trial, Ann. Surg. 227 (3) 380-389.

Tzou, D.Y. (1996): Macro-to micro scale Heat Transfer : The Lagging Behavior, Taylor and Francis, Washington, D.C.,

Van Vulpen M., DeLeeuw A.A.C., Raaymakers B.W., Van Moorselaar R.J.A., Hofman P., Legendijk J.J.W., Battermann J.J.(2004): Radiotherapy and hyperthermia in the treatment of patients with locally advanced prostate cancer: preliminary results, BJU Int. 93 (1), 36-41.

Vernon C.C., Hand J.W., Field S.B., Machin D., Whaley J.B., Zee J., Putten W.L.J., Rhoon G.C., Dijk J.D.P., Gonzalez D.G., Liu F.F., Goodman P., Sherar M. (1996): Radiotherapy with or without hyperthermia in the treatment of superficial localized breast cancer: results from five randomized controlled trials, *Int.J. Radiant.Oncol. Biol. Phys.* 35 (4), 731-744.

Wust, P.,Hildebrandt, B., Sreenivasa, G., Riess, H., Felix, R., Schlag, P. M.(2002): Hyperthermia in combined treatment of cancer, *Lancer Oncol.*3 (8), 487 497.

Zee J., Gonzalez D., Rhoon G., Dijk J., Putten W., Hart A.(2000): Comparison of radiotherapy alone with radiotherapy plus hyperthermia in locally advanced pelvic tumors: a prospective, randomized, multicenter trial, *lancet* 355 (9210),1119-1125.