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THEORETICAL EVALUATION ON THE THERMAL EFFECTS OF EXTRACELLULAR HYPERTHERMIA AND INTRACELLULAR HYPERTHERMIA

Zhong-Shan Deng, Jing Liu

Cryogenics Lab, P. O. Box 2711, Technical Institute of Physics and Chemistry,
Chinese Academy of Sciences, Beijing 100080, China

INTRODUCTION

Although not currently a routine cancer treatment therapy, hyperthermia is developing rather rapidly as an alternative way as part of conventional treatment for some cancers. This treatment takes advantage of the high sensitivity of tumor cell to heat. Up to now, a variety of heating methods have been established to induce temperature rises either locally in target tissue region, or over the whole body. Among them, magnetic nano-particles offer some attractive possibilities in tumor hyperthermia, which have controllable sizes ranging from a few nanometers up to tens of nanometers. The magnetic nano-particles can be made to resonantly respond to a time-varying electromagnetic (EM) field, with advantageous results related to the transfer of energy from the exciting field to the nano-particles. This heat then efficiently conducts into the surrounding diseased cells and tissues.

A major concern involved in magnetic nano-hyperthermia is about the controversy that whether intracellular hyperthermia is superior to extracellular hyperthermia [1]. The potential of time-varying EM heating effects in a scale length smaller than the biological cell diameter was first addressed by Gordon et al. and termed as “intracellular hyperthermia” [2]. Since experimental validation of the thermal effects of intracellular hyperthermia is still not feasible with the current experimental technique, this problem has been studied theoretically. However, different researchers have suggested different results, and the controversy still goes on [1-3].

In order to understand the exact micro-mechanisms of EM heating involved in intracellular hyperthermia and extracellular hyperthermia, an energy analysis is presented in this study to simulate the corresponding heat transfer problems thus involved. Different from intracellular hyperthermia, the main characteristic of the extracellular hyperthermia is to heat up the target tissue by EM energy absorption only in the extracellular medium. A series of numerical calculations for both intracellular hyperthermia and extracellular hyperthermia are performed. The results will answer the question from the heat transfer mechanism whether intracellular hyperthermia is superior to extracellular hyperthermia in the thermal sense.

METHODS

Magnetic nano-particle induced hyperthermia can produce theoretically predictable temperature response on the basis of well-defined variables of electrical field equation and heat transfer equation. In this study, the electrical field is solved from macro-scale (characterized by the size of the target tissue) to determine the distribution of EM energy absorption, and the extracellular and intracellular heating is solved from micro-scale (characterized by the biological cell’s size, typically 5-20μm) in which the cell is approximately taken as sphere. The computation domains for electrical field and heat transfer are depicted in Figure 1.

Model for EM Field

One can obtain the potential φ inside the tissue through solving the source free Laplace equation:

$$\nabla \cdot \left[\varepsilon(\mathbf{X}) \cdot \nabla \varphi(\mathbf{X}) \right] = 0 \tag{1}$$

The electric field strength is determined by:

$$\mathbf{E}(x,y,z) = -\nabla \varphi(x,y,z) \tag{2}$$

Heat generation due to the EM dissipated power in intracellular medium not embedded with magnetic nano-particles is determined by:

$$Q_{r1}(x,y,z,t) = \sigma \left| \mathbf{E}(x,y,z) \right|^2 / 2 \tag{3}$$

Heat generation due to the EM dissipated power in extracellular or intracellular mediums embedded with magnetic nano-particles is determined by [4]:

$$Q_{r2} = \left[\frac{3nr^3 \chi''}{4\mu_0 fR^2} + \left(1 - \frac{4}{3} n\pi r^3\right) \frac{\sigma_2}{2} \right] \cdot \left| \mathbf{E}(x,y,z) \right|^2 \tag{4}$$

Heat transfer Model for Cell

After the heat generation is determined, the temperature distributions in extracellular and intracellular mediums can thus be solved from the heat transfer model of cell.

Since the characteristic time for heat-penetration throughout the biological cell is about 10^{-7} s [3], only steady-state heat transfer process is analyzed in this study. The classical Fourier's Law is used to model heat transfer in intracellular medium:

$$k \cdot \frac{1}{r} \cdot \frac{\partial^2 (rT)}{\partial r^2} + Q_m + Q_r = 0 \tag{5}$$

In extracellular medium, the effect of blood perfusion is considered, and the heat transfer equation reads as:

$$k \cdot \frac{1}{r} \cdot \frac{\partial^2 (rT)}{\partial r^2} - \rho_b c_b \omega_b \left(T - T_a\right) + Q_m + Q_r = 0 \tag{6}$$

RESULTS AND DISCUSSION

The main difference between extracellular and intracellular hyperthermia consists in whether the intracellular medium containing magnetic nano-particles.

Figure 2 shows the cellular temperature distributions for extracelluar and intracellular hyperthermia, in which the area of intracellular medium is r<7.5μm. Figure 3 and Figure 4 depict the effect of the concentration of intracellular nano-particles and the frequency on cell temperature, respectively.

The results indicate that the cell temperature for intracellular hyperthermia is obviously higher than that for extracellular hyperthermia, and the maximum temperature difference under moderate heating condition can reach about 4°C. It suggests that intracellular hyperthermia is superior to extracellular hyperthermia, at least in the thermal sense.

Further results and detailed discussion will be presented at the conference.

ACKNOWLEDGMENTS

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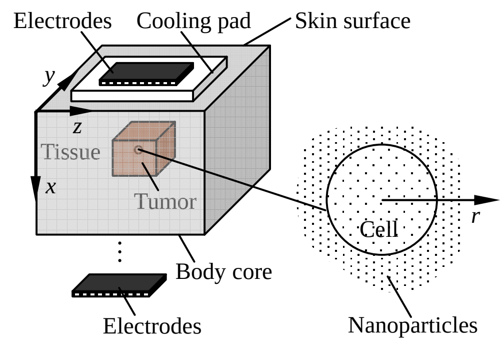

Figure 1. Schematic illustration of computation domain and EM induced intracellular hyperthermia configuration (not to scale)

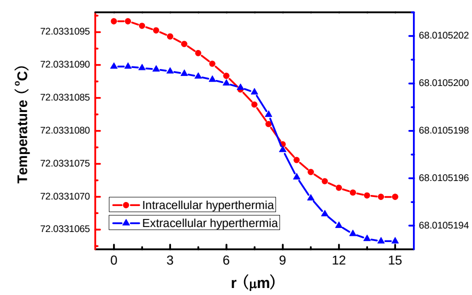

Figure 2. Temperature distribution in the intracellular and extracellular mediums

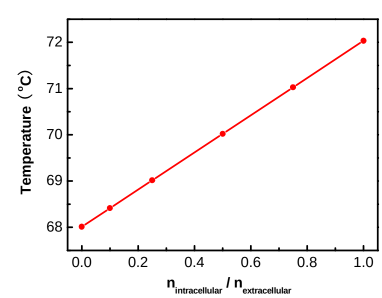

Figure 3. The effect of the concentration of intracellular nano-particles on cell temperature

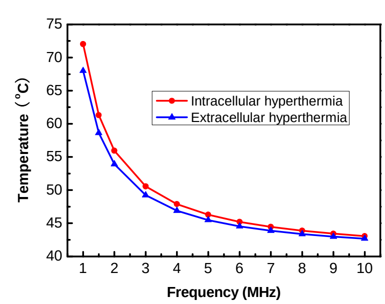

Figure 4. The effect of the frequency used for hyperthermia on cell temperature