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Multiphysics simulation approach for photo-acoustics temperature monitoring in rodent's head during photothermal therapy

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ABSTRACT

A multiphysics model was developed to model the increase in temperature during phototherapy treatment (PTT) in mouse brain. The model includes also a numerical model for Photoacoustic thermometer during the hyperthermia therapy. The coupling of different physics was investigated.

Keywords: Radiative Transfert Equation, Monte Carlo simulations, Acoustic wave propagation, Bioheat equation

1. INTRODUCTION

The multiphysics model takes into account the exact morphology of rodents head, via the co-registration of a Mouse brain atlas using different imaging modalities such as magnetic resonance imaging (MRI) for tissue, Micro-computer tomography (Micro-CT) for blood vessels and (CT) for skull. Acoustic propagation was introduced as well to test the effect of Blood Brain Barrier (BBB) opening, and simulated under both assumptions of linear and nonlinear. BBB opening is introduced by the blood vessel spatial position and effective pressure inside it. Optically, Monte Carlo simulations were performed to study the energy deposition of optical excitation inside a rodents head. PhotoAcoustic pressure measurement was also introduced in the simulations. The whole process is developed to propose a complete simulation of the increase in temperature during PTT.

2. MATERIAL AND METHODS

The flow chart shown in Fig. 1 summarizes the developed for Glioblastoma treatment of brain cancer. A multiphysics model was developed to evaluate in advance the effect of different therapeutic agents for hyperthermia treatment.

2.1 Coregistration

In order to develop a realistic multiphysics model based on the exact morphology of rodents head, a co-registration step of multimodal imaging atlas' was implemented, in which, a mouse brain atlas for tissue,¹ blood vessels² and skull³ were co-registered using point reference registration method.

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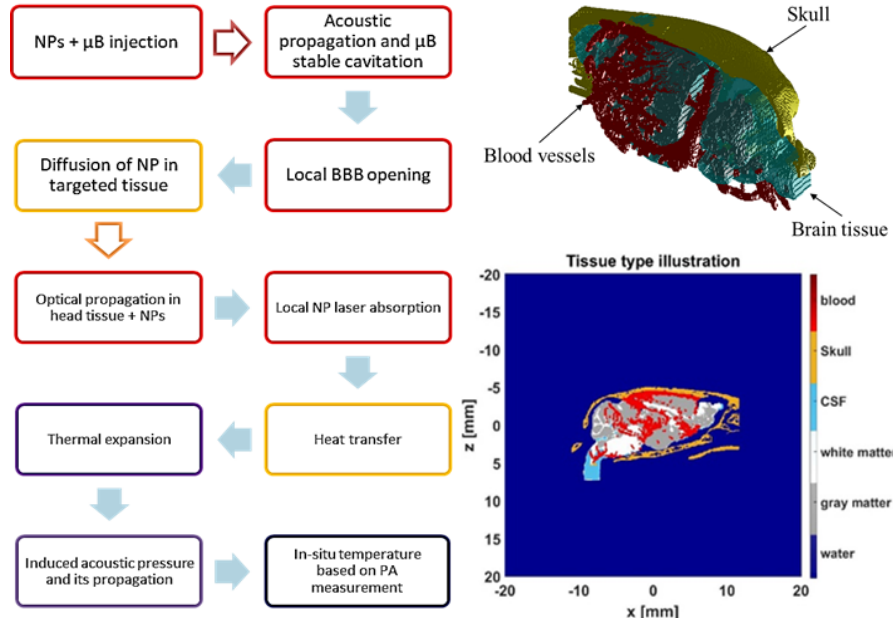


Figure 1. Flowchart of the multiphysical approach for brain cancer treatment based on exact morphology of rodents head

2.2 Governing equations

Theoretical mathematical models were solved and segregated for each included physics. On the one hand, the k-wave software⁴ was used to model the acoustic propagation of PA wave generation in heterogeneous acoustic media. BBB opening is introduced by the blood vessel spatial position and effective pressure inside it was model with the acoustic propagation equation:

$$\begin{aligned}\frac{\partial u}{\partial t} &= -\frac{1}{\rho_0} \nabla p, \\ \frac{\partial \rho}{\partial t} &= -(2\rho + \rho_0) \nabla u - u \nabla \rho_0, \\ p &= c_0^2 (\rho + d \nabla \rho_0 + \frac{B}{2A} \frac{\rho^2}{\rho_0} - L\rho), \\ A &= \rho_0 c_0^2, B = \rho_0^2 \left[\frac{\partial^2 P}{\partial \rho^2} \right]\end{aligned}$$

On the other hand, a Monte Carlo simulation approach was adopted to solve the Radiative Transfert Equation for light propagation through the tridimensional heterogeneous medium:

$$\frac{1}{c} \frac{\partial \phi}{\partial t}(x, \hat{s}, t) = q(x, \hat{s}, t) - [\hat{s} \nabla + \mu_a(x) + \mu_s(x)] \phi(x, \hat{s}, t) + \mu_s(x) \int \Theta(\hat{s}, \hat{s}') \phi(x, \hat{s}', t) d\hat{s}' \quad (1)$$

where, μ_a and μ_s are the optical absorption and scattering coefficients of the medium.

The co-registered volume integrates a voxel-based 3D model of brain tissues with its optical properties. It demonstrates that brain heterogeneity has moderate to significant impact on the optical fluence distribution in rodent's head and therefore affects the photothermal therapy results.

Once the optical fluence (J/cm^2) has been calculated, the deposited absorbed energy (J/cm^3) can be calculated as $W = \mu_a \phi$ and the thermoelastic stress confinement could be assumed to calculate the PA pressure, where the thermal conduction and stress propagation are ignored: $P = \frac{\beta c^2}{C_p} W$, where, β is the thermal expansion coefficient, c is the sound speed and C_p is the specific heat capacity. Then the acoustic propagation was simulated under both assumptions of linear and nonlinear.

Under continuous laser exposure, the deposited energy is the source term that influences the thermal behavior model in biological perfused tissues by the Pennes's bioheat equation:

$$\nabla k \nabla T + \rho_b c_b w_b (T_{a0} - T) + Q = \rho c \frac{\partial T}{\partial t} \quad (2)$$

where k , ρ and c are the biological tissue thermal conductivity, density and specific heat. Values for blood are given by ρ_b and c_b ; w_b is the tissue blood perfusion rate which represents the volume of fluid (i.e. blood) that passes per unit time and per tissue volume. Q represents the energy deposition by any external heat source such as the metabolic heat production in tissues. In this work, we consider Q is laser deposited energy. T_a is the temperature of blood in the main arteries which is assumed constant and equal to 37.3C. T is the local tissue temperature, which is a function of the spatial position and the time.

3. RESULTS AND DISCUSSION

The evolution of temperature as a function of time can be demonstrated as shown in Fig. 2 for a given case study.

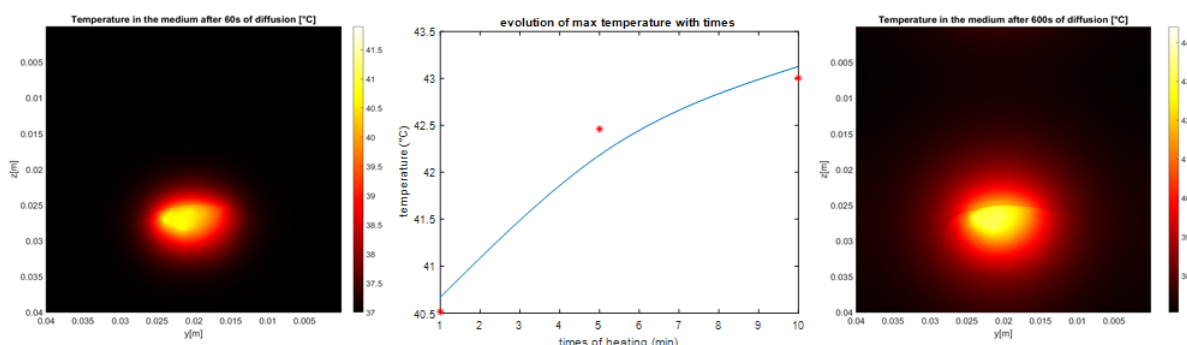


Figure 2. Evolution of temperature during photothermal therapy

4. CONCLUSION

A multiphysical model was developed to quantify and evaluate therapeutic agents efficacy in photothermal therapy in rodents head.

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