Modeling Nanoparticle Heat Transfer in Tumors

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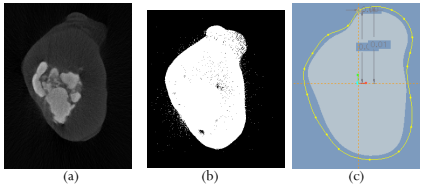
Introduction

Magnetic nanoparticle hyperthermia is gaining momentum in novel cancer research. For this treatment, tumors are injected with ferrofluid nanoparticles that generate heat through Néel and Brownian relaxation when placed in an alternating magnetic field. When nanoparticles are heated above 42°C, they effectively ablate tumor cells, causing hyperthermia- induced cell death [1]. Despite this promising ability, it remains difficult to determine the heating profile of nanoparticles in tumors. Accordingly, a virtual model of a previously conducted magnetic nanoparticle hyperthermia experiment is built and analyzed in this work using Micro CT-Scanner images of the nanoparticle infused tumors and a predetermined linear positioning relationship for the nanoparticles [2][3].

Materials and Methods

Tumor Construction

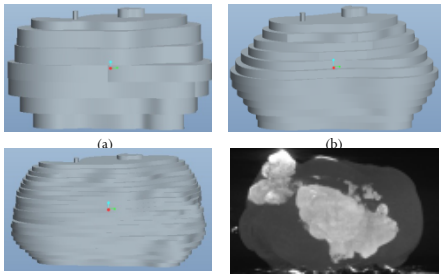
To virtually reconstruct the tumors images, MATLAB®, MagicTracer™, and Pro/ENGINEER © were used. First, representative Micro-CT Scanner .bmp tumor slice images were converted from grayscale to binary images using MATLAB®. Next, MATLAB® binary images were converted to .dxf vector files using MagicTracer™. Finally .dxf tumor images were traced, extruded, and scaled in Pro/ENGINEER ©.



(a) (b) (c)

Figure 1: Reconstruction process showing (a) Micro-CT image, (b) binary image from MATLAB®, and (c) outline from Pro/ENGINEER©

Nanoparticle distributions were determined using image intensity thresholding from MATLAB® and printed out into a table. This table was then used to calculate the Specific Absorption Rate (SAR) using Statistical Analysis Software (SAS®) and a previously determined positioning function [3].



(a) (b) (c) (d)

Figure 2: Reconstructed tumor models using (a) 8, (b) 14, and (c) 26 slices with (d) Micro-CT image shown

Heat Transfer Study

In order to conduct heat transfer studies, Pro/ENGINEER © computer aided design (CAD) models were imported into COMSOL Multiphysics® and positioned onto a block to simulate the body of the mouse. The representative mouse body is 0.03X 0.05X 0.02 meters large. Nanoparticle distributions were represented by importing SAR values from SAS® analysis to COMSOL®. Once imported, the tumor–mouse model was repositioned to center around the origin of the SAR distribution.

Governing Equation

Pennes bio-heat transfer equation is the theoretical basis for nanoparticle infusion. Assuming steady state, this equation can be represented as:

Tumor:

$$0 = K_T \nabla^2 T + SAR + \omega_{tissue}(\rho c_P)_{blood}(T_a - T_{tumor}) + Q_{M,tumor}$$

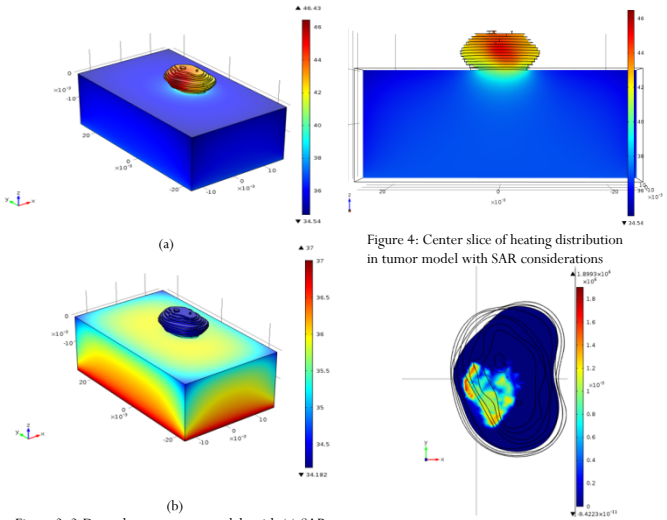
Mouse Body:

$$0 = K_M \nabla^2 T + \omega_{tissue}(\rho c_P)_{blood}(T_a - T_{tissue}) + Q_{M,tissue}$$

Table 1: Material properties, boundary conditions, and variables

Name	Value
Specific Absorption Rate (SAR)	Determined from MATLAB® and SAS® (W/m^3)
Blood profusion rate of tissue (ω_M)	0.004 (s^{-1})
Blood profusion rate of tumor (ω_T)	0.000416 (s^{-1})
Density (ρ)	1000 (kg/m^3)
Initial Temperature (T_O)	310.15 (K)
Heat Capacity at Constant Pressure (c_p)	3500 (J/(kg*K))
Metabolic Heat Generation of Body (Q_M)	3000 (W/m^3)
Metabolic Heat Generation of Tumor (Q_T)	450 (W/m^3)
Thermal Conductivity of Tumor (K_T)	0.624 (W/(m*K))
Thermal Conductivity of Mouse (K_M)	0.5 (W/(m*K))
Convective Heat Transfer Coefficient (h)	0.048/(maximum diameter) (W/m^2K)
Atmospheric Temperature (T_a)	298.15 (K)

Results



(a) (b)

Figure 3: 3-D steady state tumor models with (a) SAR heating considerations and (b) no SAR heating considerations

All surfaces of the model were considered to experience convective cooling from the environment except for the bottom face of the block. This face had a prescribed temperature of 37°C in order to remain consistent with experimental conditions [2].

Figure 4: Center slice of heating distribution in tumor model with SAR considerations

Figure 5: Sample M29I COMSOL® tumor slice showing imported SAR values

As can be seen in Figure 5 above, SAR distributions in the COMSOL® simulation of the tumor slice from Figure 1 closely match the original Micro-CT image.

Discussion

The COMSOL® simulations yielded expected heating distributions, with the highest temperatures localized towards the center of the tumor. Resultant temperature increases from body temperature (37°C) to between 42°C and 46°C show promise of effective tumor ablation by the prescribed dosage of 0.1cm^3 of ferrofluid, agreeing with experimental results. Future directions of this experiment involve developing new methodologies to analyze increasingly refined tumor models and improving data analysis speed for SAR calculations.

References

[1] Laurent, S., Dutz S., Häfeli, U., Mahmoudi M., Magnetic fluid hyperthermia: Focus on superparamagnetic iron oxide nanparticles, Advances in Colloid and Interface Science, August 2011

[2] Attaluri, A, Ma R., QinY., LiW., Zhu L., Nanoparticle distribution and temperature elevations in prostatic tumours in mice during magnetic nanoparticle hyperthermia. Int J. Hyperthermia, August 2011

[3] LeBrun, A., Conn, N., Attaluri, A., Manuchehrabadi, N., Huang, Z., Ma, R., Zhu, L., 2012 Quantification of micro CT image intensity and nanoparticle concentration in agarose gel. ASME 2012 3rd Micro/Nanoscale Heat & Mass Transfer International Conference, #MNHMT 2012-75025, April 2012, Atlanta, GA.

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