

# Computational Modeling of Electromagnetically Induced Heating of Magnetic Nanoparticle Materials for Hyperthermic Cancer Treatment

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**Abstract**— We present work on the computational modeling of electromagnetically induced heating in the hyperthermic treatment of cancer using fluid-dispersed magnetic nanoparticles. Magnetic nanoparticle hyperthermia can be used as a complement to chemotherapy or for direct targeting and destruction of tumors through heat treatment. The ability of nanoscale materials to provide an extremely localized therapeutic effect is a major advantage over traditional methods of treatment. When an AC magnetic field is applied to a ferrofluid, Brownian rotation and Néel relaxation of induced magnetic moments result in power dissipation. In order to achieve appreciable volumetric heating, while maintaining safe values of frequency and magnetic field strength, and to reduce the risk of spot heating of healthy tissue, it is necessary to determine an ideal range of input parameters for the driving magnetic field as well as the complex susceptibility of the ferrofluid. We do this by the coupling of the solution of Maxwell's equations in a model of the tumor and surrounding tissue as input to the solution to the Pennes' Bioheat Equation (PBE). In this study, we solve both sets of equations via the Finite Difference Time Domain (FDTD) method as implemented in the program SEMCAD X (by SPEAG, Schmid & Partner Engineering). We use a multilayer model of the human head made up of perfused dermal and skeletal layers and a grey-matter region surrounding a composite region of tumor tissue and the magnetic nanoparticle fluid. The tumor/ferrofluid composite material properties are represented as mean values of the material properties of both constituents, assuming homogeneity of the region. The AC magnetic excitation of the system (within 100 kHz–2 MHz frequency range) is provided by square Helmholtz coils, which provide a uniform magnetic field in the region of interest. The power density derived from the electromagnetic field calculation serves as an input term to the bioheat equation and therefore determines the heating due to the ferrofluid. Results for several variations of input parameters will be presented.

## 1. INTRODUCTION

The raising of an organism's body temperature to about 5 or more degrees Celsius above its normal value is referred to as hyperthermia. Artificially induced hyperthermia may be used for therapeutic treatments and is especially effective for cancer treatment [1]. A sustained temperature above 42°C can cause cell apoptosis, and a sustained temperature above 45°C causes cell necrosis, resulting in irreversible damage to cell function, or heat-induced sensitization of cells to radiation and some cytotoxic drugs [2, 3].

Hyperthermia has fewer side effects than traditional chemotherapy or radiotherapy. The body naturally uses one type of hyperthermia, a fever, to fight many types of diseases (such as viruses and bacteria) by slowing their proliferation. Magnetic materials under the influence of an AC magnetic field are particularly convenient for hyperthermic applications. Since 1957, when investigations of the applications of magnetic materials for hyperthermia began, a wide variety of magnetic materials, field strengths, and frequencies have been used in these experiments. Human clinical trials have recently begun as a result of the increased safety and efficacy of magnetic nanomaterials for hyperthermia [4].

The subject of this research is the computational modeling of electromagnetic and thermal effects during the hyperthermic treatment of cancer using magnetic nanoparticles. These magnetic nanoparticle systems can be utilized both as drug delivery agents for chemotherapy and for direct targeting and destruction of tumors through heat treatment. This method of treatment would be much less invasive than many current treatment options. Additionally, since these are nanoscale devices, the energy deposition in the cancer cells would be extremely localized. This should cause very minimal damage to surrounding tissue, making these systems superior to traditional hyperthermic treatment. The clinical use of magnetic nanoparticles requires that enough volumetric heating power to destroy tumor cells must be produced, while maintaining safe magnetic field

strengths and frequencies. The safe and useful range of magnetic field strengths and frequencies for these applications are considered to be  $0 < H < 15 \text{ kA/m}$  and  $0.05 < f < 1.2 \text{ MHz}$ . Higher field strengths can lead to various problems such as aggregation of magnetic materials, leading to embolisms. Lower frequencies can cause stimulation of the skeletal or peripheral muscles, or even stimulation of the cardiac muscles and arrhythmias. It has also been established that exposure to fields where the product of  $H_0 f$  (where  $H_0$  is the magnitude of the applied magnetic field) is less than  $4.85 \times 10^8 \text{ Am}^{-1}\text{s}^{-1}$  is safe for use in humans. This restriction limits tissue heating power and may be relaxed depending on the diameter of the region being treated and the severity of the illness [5].

In addition to the restrictions on these input parameters mentioned in previous sections, one must also consider the delivery of the magnetic nanoparticles to the tumor region. This is of particular concern for the treatment of deep-seated brain tumors, where direct injection of the magnetic material to the tumor site is impractical. In order to cross the blood-brain barrier or blood-brain-tumor barrier, particles must be quite small ( $\sim 12 \text{ nm}$  magnetic core size to cross the blood-brain-tumor barrier) [6].

It is therefore necessary to determine a set of ideal input parameters, including  $\chi''$ , and the effect of brain tumor perfusion rates on heating of the tumor region and possible spot heating in order to aid in design of clinical trails for magnetic nanoparticle hyperthermia in the brain. The effect of various brain tumor perfusion rates will be the focus of this study.

## 2. THEORY: HEATING MECHANISMS OF MAGNETIC NANOPARTICLE FLUIDS

An electrically conductive body subject to an AC magnetic field will have induced electrical currents that give rise to heating due to the resistance of the material. Smythe found an analytical expression for the time averaged power dissipation of an inductively heated sphere [7]. If it is assumed that the particles are smaller than the domain size, and  $\mu = \mu_0$  (we use SI units throughout), the Smythe formula simplifies, so that the series expansion (after multiplication by the number of spheres in a sample,  $n = 3\pi/4\phi R^3$ , where  $\phi$  is the volume fraction of nanoparticles in the fluid) yields the time-averaged power dissipation per unit volume:

$$P = \frac{\phi\sigma(\pi RBf)^2}{5} \quad (1)$$

(1) Applies for small particles where  $f \ll fc$ , where

$$fc = (\pi R^2 \mu_0 \sigma)^{-1} \quad (2)$$

$\sigma \equiv$  electrical conductivity =  $200 \Omega^{-1}\text{cm}^{-1}$  for magnetite, so  $fc = 5 \times 10^{17} \text{ Hz}$  for  $R = 5 \text{ nm}$ , then if  $B = 0.06 \text{ T}$  and  $\phi \equiv$  volume fraction of magnetic nanoparticles in the fluid =  $0.071$  (representative typical values for clinical hyperthermia with a ferrofluid),  $P = 2.5 \times 10^{-10} \text{ Wcm}^{-3}$ . If instead,  $\sigma = 9.3 \times 10^4 \Omega^{-1}\text{cm}^{-1}$  (for iron),  $P = 1.2 \times 10^{-7} \text{ Wcm}^{-3}$ . Since appreciable heating occurs due to magnetic nanoparticle fluid hyperthermia, there must be some heating mechanism other than induction for these materials [4].

The heating processes for a magnetic nanoparticle fluid was detailed by Rosensweig based on the Debye model for dielectric dispersion in polar fluids [8]. When an alternating magnetic field is applied to a ferrofluid, the magnetic moments of the magnetic nanoparticles rotate to align with the changing field. As the magnetic field decreases, the magnetic moments rotate back to their equilibrium positions. Rotation of the particles in the viscous medium (called Brownian rotation) and rotation of the magnetic moments (Néel relaxation) both result in power dissipation due to friction. A phase lagging between the applied magnetic field and rotation of the magnetic moments due to friction results in heating. High heating rates are achieved in the regime of particle size where the Néel mechanism does not dominate the relaxation processes. The volumetric heating power ( $P$ ) of a ferrofluid is given by [8]:

$$P = f\Delta U = \mu_0\pi\chi''fH_0^2 \quad (3)$$

where  $\chi'' \equiv$  the imaginary component of the magnetic susceptibility function,  $f \equiv$  the frequency of the AC magnetic field, and  $H_0 \equiv$  the magnitude of the applied magnetic field. Since the change in direction of magnetization lags the magnetic field, (i.e.,  $\chi''$  is nonzero) work is converted into thermal energy [6]. Heat generation of magnetic nanoparticle fluids has a square dependence on  $H$ ,

leading to greater heating than ferromagnetic or paramagnetic materials at the same magnetic field strength. Heat generation for magnetic fluids is often expressed in terms of the specific absorption rate (SAR), where

$$\text{SAR} \times \text{particle density} = P \quad (4)$$

At  $f = 300 \text{ kHz}$ ,  $H = 14 \text{ kAm}^{-1}$ ,  $\text{SAR} = 209 \text{ Wg}^{-1}$  for superparamagnetic ferrofluids. At  $f = 300 \text{ kHz}$ ,  $H = 14 \text{ kAm}^{-1}$ ,  $\text{SAR} = 75 \text{ Wg}^{-1}$  for ferromagnetic magnetite [4].

The heat flow equation for tissue, including the effects of perfusion of blood and metabolic heating is given by the PBE [4, 8]:

$$\rho c \partial T / \partial t = \nabla \cdot (k \nabla T) + \rho_b c_b w (T - T_b) + Q_m + Q_s \quad (5)$$

where  $\rho$  is the tissue density,  $c$  is the specific heat for the tissue,  $k$  is the thermal conductivity of the tissue,  $\rho_b$  is the blood density,  $c_b$  is the specific heat for blood,  $w$  is the blood perfusion rate,  $T_b$  = blood temperature,  $Q_m$  = metabolic heating,  $Q_s$  = heat added to the system from a source, such as heating due to the ferrofluid in an AC field [8, 9]. In the case of magnetic fluid hyperthermia, the  $Q_s$  term is the energy deposition due to heating of the magnetic fluid in an AC magnetic field. This heating power is given by Equation (3).

### 3. MODEL

In this research, the program Semcad X [10] will be used to solve the Pennes bioheat Equation (5) for a tissue volume, such as the human head with a cancerous region with imbedded magnetic nanoparticles using the Finite Difference Time Domain (FDTD) method. Semcad uses the FDTD solver with volume mesh techniques applied to a 3D model in order to solve Maxwell's equations in PDE form in the region of interest. The electromagnetic results are then used in the thermal simulation to solve the PBE and determine the heating. In order to perform the calculation, the user must provide dielectric, magnetic and thermal properties of all materials, the excitation for the coils (for example, the current or voltage), the AC frequency, and specify a solver (such as the FDTD solver).

The current version of the model uses square Helmholtz coils to provide the AC magnetic field. Square Helmholtz coils are capable of producing a magnetic field more uniform than the more commonly seen circular Helmholtz coils [11].

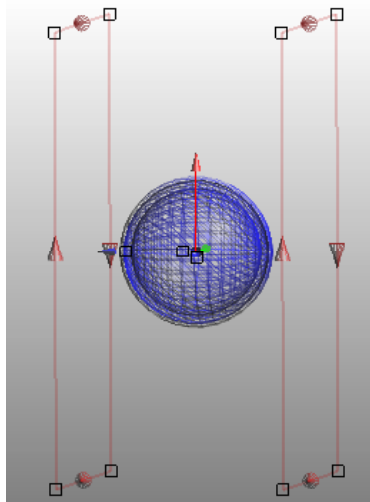


Figure 1: Square Helmholtz coils and multi-tissue layer model of the human head, including a central composite region of tumor tissue and the magnetic nanoparticle fluid. In both examples, the tumor/ferrofluid composite material properties were mean values of both material properties, assuming homogeneity of the region.

### 4. BENCHMARKING: FIELD UNIFORMITY

### 5. RESULTS

Results for  $f = 1 \text{ MHz}$  are plotted in Figure 3 for temperature vs. time inside the composite tumor region. Material properties and perfusion rates of the tissue were those detailed by Duck [12] and

are similar to those found in the current literature [13]. Conductivities and permittivities for the tissues at the various frequencies were obtained using the publicly available program atsf.exe [14].

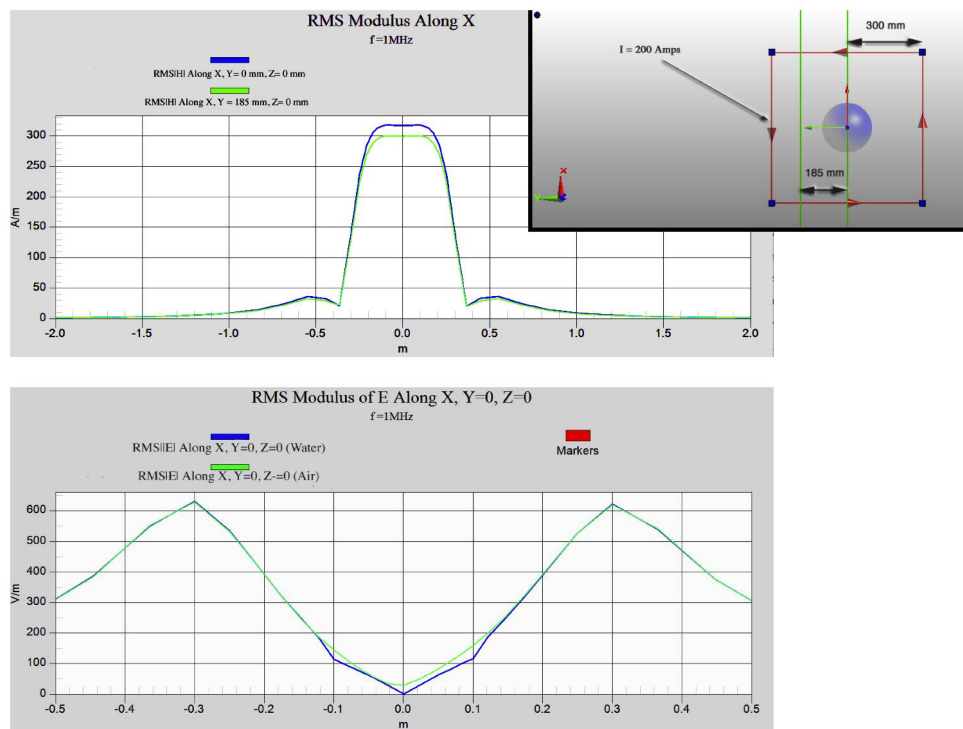


Figure 2: Calculations were first performed in order to verify uniformity of the magnetic and electric field due to the square Helmholtz coils. Above is shown  $RMS|H|$  along the  $x$  axis (see inset model diagram for coordinate system) at  $y = 0, z = 0$  (blue line) and  $y = 185 \text{ mm}, z = 0$  (green line). It can be seen that  $RMS|H|$  is uniform within 6% at 185 mm from the origin along the  $y$  axis. Below is shown  $RMS|E|$  for the square Helmholtz coils with and without loading of a dielectric sphere (the dielectric is water in this case). A slight decrease in  $RMS|E|$  field amplitude is seen in the region of interest.  $RMS|E|$  remains uniform in the region of interest. Similar results were obtained for frequencies between 30 kHz and 3 MHz.

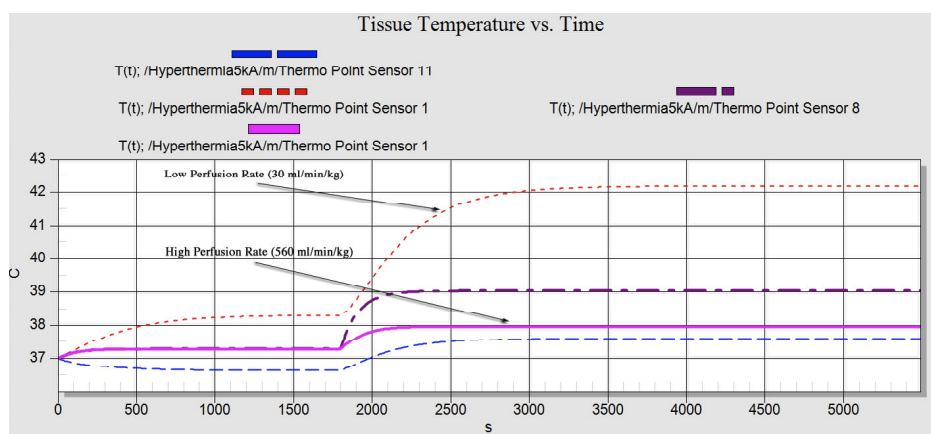


Figure 3: Temperature vs. time for heating at  $f = 1 \text{ MHz}$ . The applied field,  $H_0 = 5 \text{ kA/m}$ . The imaginary susceptibility of the ferrofluid is set to  $\chi'' = 5$ , an experimentally realistic value at 1 MHz [15]. Thermal sensors were placed on the boundary, labeled “Sensor 11” (skin layer), inside the healthy grey matter at 4 cm, labeled “Sensor 8”, and inside the composite tumor region (at the center in this case), labeled “Sensor 1”. In the calculations, the low perfusion rate for the tumor region was 30 ml/min/kg, while the high value was 560 ml/min/kg, the same value as the surrounding grey matter.

An increase in temperature in the composite tumor region for a low perfusion rate (30 ml/min/kg), due to the thermal deposition from the electromagnetic field, is suppressed when the perfusion rate of the tumor region is increased to match that of the surrounding healthy brain tissue.

## 6. CONCLUSIONS

It was shown (Figure 3) that there exists a marked increase in tissue temperature near the center of the tumor region for a low rate of tumor blood perfusion. For normal perfusion rates within the tumor region, the temperature of the composite tumor/ferrofluid remains nearly that of the skin boundary layer through out the simulation. It is necessary to further investigate this effect for various parameter input values, in order to determine how perfusion rates, i.e., the metabolic response of a patient, influence the thermal damage done to both tumor and healthy tissue in magnetic nanoparticle hyperthermia.

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