Numerical Simulation and Evaluation of Magnetic Particle Hyperthermia System and Conditions

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Introduction

Magnetic particle hyperthermia (MPH) is a novel, minimally invasive, therapeutic modality, used as a cancer treatment, that employs a magnetic fluid (also termed ferrofluid) as the heating source. A magnetic fluid is a stable colloidal suspension of magnetic nanoparticles (MNPs) that can be injected directly into the tumor or delivered to the tumor via passive or active targeting upon intravenous administration. Once accumulated to the tumor area, MNPs are exposed to an external alternating magnetic field (AMF) that causes reversal of their magnetic moments, activating mechanisms of energy deposition in the form of heat (1).

Objectives

The main objective of the present work is the development and evaluation of numerical models for the description of the phenomena that take place in a MPH *in vitro* system. In particular, we aim at the estimation of the spatial distribution of the magnetic field and the spatiotemporal temperature distribution by taking into account all the appropriate field and heat transfer boundary conditions.

Material/Methods

In order to simulate the physical phenomena, two numerical models were developed in COMSOL Multiphysics. In the first model the "Azimuthal Induction Currents" interface provided in "AC/DC" Module, was used in order to obtain the magnetic field distribution corresponding to a 2-turn circular and 8-turn squared coil geometries, while in the second model the transient analysis of the "General Heat Transfer" interface provided in "Heat Transfer" Module was employed to calculate the MNPs volumetric power dissipation (by importing Rosensweig's model (2)) and obtain the time-dependent heating curves. The ferrofluid concentration used was 4 mg/ml for an aqueous solution of 10 nm magnetite MNPs, dispersed in 1 ml of water, while the AMF amplitude and frequency were 30 mT and 765 kHz, respectively, for the 2-turn coil, and 60 mT and 365 kHz, respectively, for the 8-turn coil.

Results

The solution of the electromagnetic problem provides the magnetic field distribution for the experimentally applied current amplitude and frequency. The role of coils geometry is also presented since COMSOL takes into account the coil geometrical characteristics, ignored in the analytical expressions. Moreover, the solution of the Heat Transfer problem gives the spatial distribution of temperature in the various subdomains of the MPH system like the ferrofluid, the vial, the coil and the surrounding air while the time-dependent heating curves are obtained after 30 minutes of treatment and are compared to the corresponding experimental ones observed under the same conditions. The spatiotemporal distribution of the MNPs volumetric power dissipation is also estimated for the non-adiabatic conditions, studied in the present work, validating Rosensweig's model (2).

Conclusion

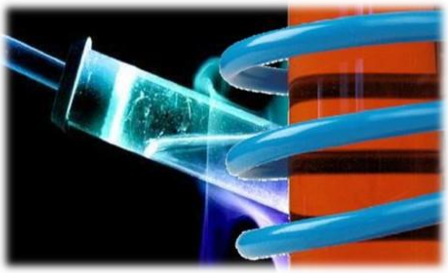
Proper use of simulations can lead to better understanding of complex physical processes, further progress in the development of novel MPH equipment designs, replacement of invasive temperature measurements and establishment of updated hyperthermia treatment protocols. In silico testing and evaluation of material properties and innovative methods can substantially accelerate their approval for clinical use and result in better treatment quality.

References

(1) Dutz, S. and Hergt, R. (2014) Magnetic particle hyperthermia—a promising tumour therapy?. Nanotechnology., 25(45), 452001.

(2) Rosensweig, R. E. (2002) Heating magnetic fluid with alternating magnetic field. J. Magn. Magn. Mater., 252,370-374.

NUMERICAL SIMULATION AND EVALUATION OF MAGNETIC PARTICLE HYPERTHERMIA SYSTEM AND CONDITIONS



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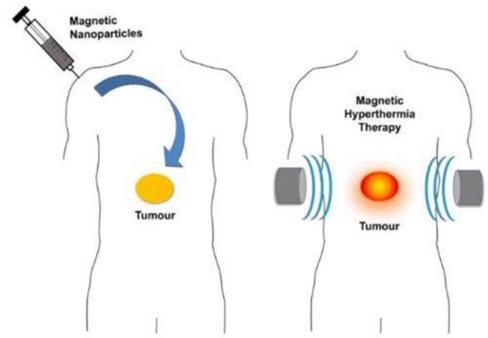
Introduction

Magnetic Particle Hyperthermia



- **Magnetic particle hyperthermia**: novel, **minimally invasive**, therapeutic modality, used as a **cancer treatment**, that employs a **magnetic fluid** (also termed ferrofluid) as the **heating source**.
- Magnetic fluid: stable colloidal suspension of **magnetic nanoparticles** injected **directly** or delivered to the tumor via passive or active (functionalized) targeting upon **intravenous** administration.
- Nanoparticles: tiny particles of **iron oxide** suspended - very finely distributed - in **water**. As soon as applied, they **agglomerate** and remain like an **implant** in the tissue to be treated.
- Alternating magnetic field causes the particles to generate **heat**.

✓ Cancer cells more **susceptible** than healthy at **41-45°C temperature region**, **rise** within this **region** leads to **suppression** of cancer cells growth and tumor **shrinkage.**

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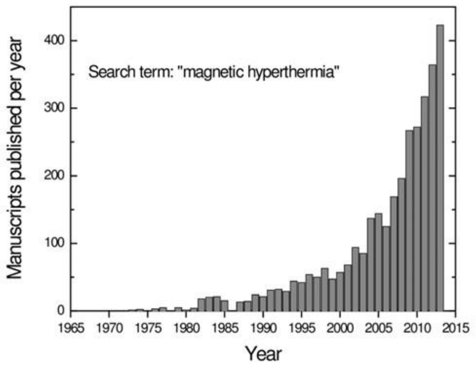
Introduction

Magnetic Particle Hyperthermia



Applied Physics Reviews 2.4, 041302 (2015)

- 1957: Was first proposed by Gilchrist et. al.
- 2011: MagForce (Berlin, Germany). obtained the first and only European Union regulatory approval of a nanotechnology therapy for treatment of brain tumors.

- NanoTherm® therapy combines the use of a ferrofluid (i.e. aqueous SPIONs), which is injected directly into the tumor site, and an AMF applicator, which is set to operate at a fixed frequency, of 100 kHz with an amplitude range, from 2 to 15 kA/m.
- Magnetic hyperthermia is used as an adjuvant therapy to RT and ChT.

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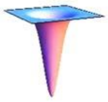
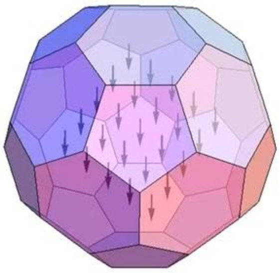
Introduction

Physical mechanisms of power dissipation in the tissue environment

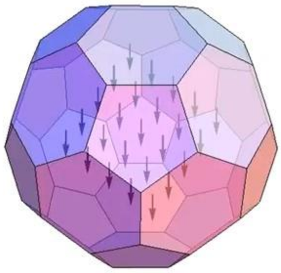
- When an external magnetic field that provides sufficient energy is applied to the system, the magnetic moment of a nanoparticle may be displaced from its preferred orientation. Consequently, as the magnetic moment returns to the equilibrium state (relaxation), thermal energy is released.



AMF



Néel relaxation



Brown relaxation

Rosensweig's model (Adiabatic system)

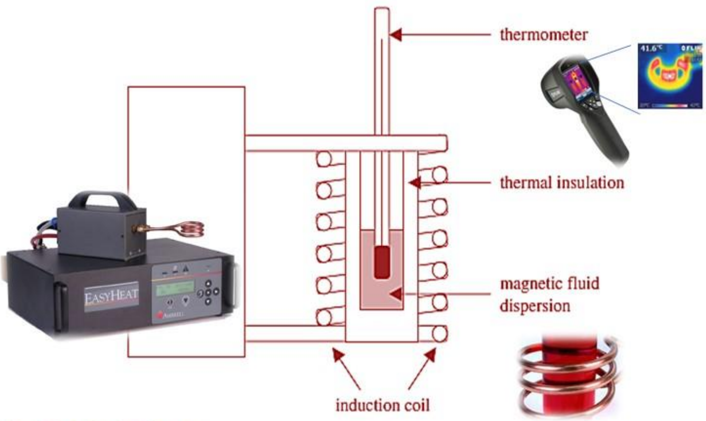
$$P = \pi\mu_0\chi_0 H_0^2 f \frac{2\pi f\tau}{1+(2\pi f\tau)^2} \quad [W/m^3]$$

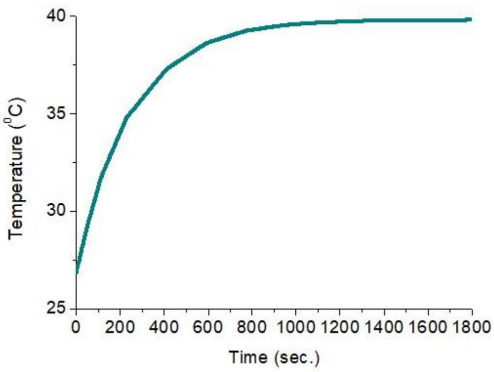
Introduction

In Vitro Testing

Frequency: 100-1000 kHz

Magnetic Filed Intensity Amplitude: 10-100 kA/m





- The main objective of the present work is the development and evaluation of numerical models for the description of the phenomena that take place in a MPH in vitro system.

METHODS AND RESULTS

NUMERICAL SIMULATION AND EVALUATION OF
MAGNETIC PARTICLE HYPERTHERMIA SYSTEM
AND CONDITIONS

Methods and Results

PROCEDURE & CONDITIONS

- In order to simulate the physical phenomena, two numerical models were developed in COMSOL Multiphysics v. 3.5a.

Parameters examined

- Effect of coil geometry
- Boundary conditions
- Time-dependent heating curves
- Nanoparticles distribution in ferrofluid
- Efficiency

✓Amplitude : 30 mT, 60 mT

✓Frequency : 765 kHz, 400 kHz

✓Magnetic Nanoparticles diameter : 10 nm

✓Material: Magnetite (Fe_3O_4)

✓Concentration: 4 mg/mL

✓Solution: 1 mL Water

✓Volume fraction (φ): 0.07%

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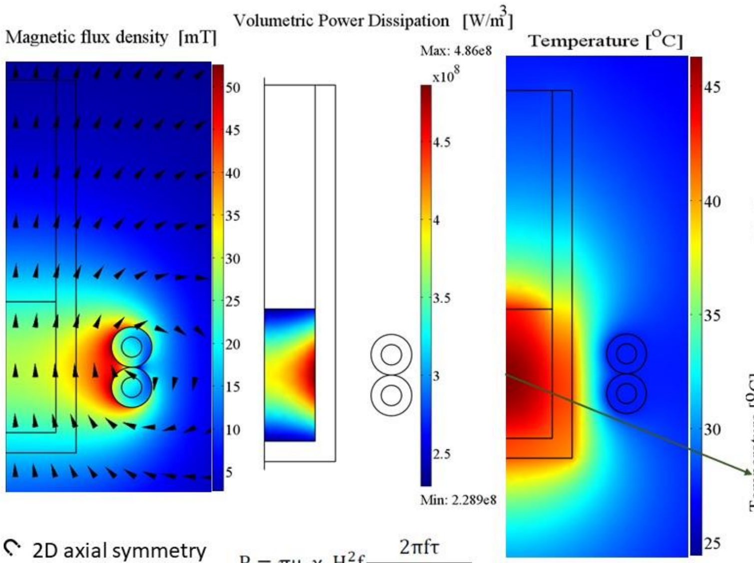
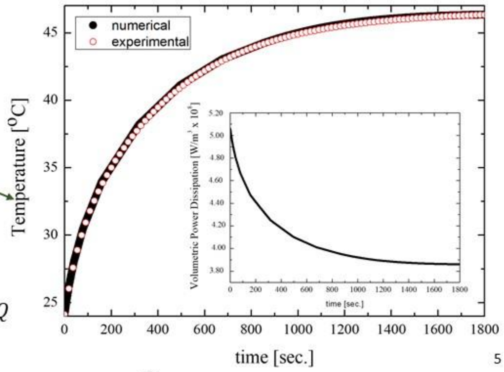
Methods and Results

2-TURN CIRCULAR COIL



- 2D axial symmetry
- Convective Heat Flux (Natural and Forced)
- Radiation
  i. surface to surface
  ii. surface to ambient
- Dirichlet



- 2D axial symmetry
- Magnetic Insulation
- Continuity

$$P = \pi\mu_0\chi_0 H_0^2 f \frac{2\pi f\tau}{1+(2\pi f\tau)^2}$$

$$\rho C_p \frac{\partial T}{\partial t} + \nabla\cdot(-k\nabla T) = Q$$

$$Q = P \times \varphi$$

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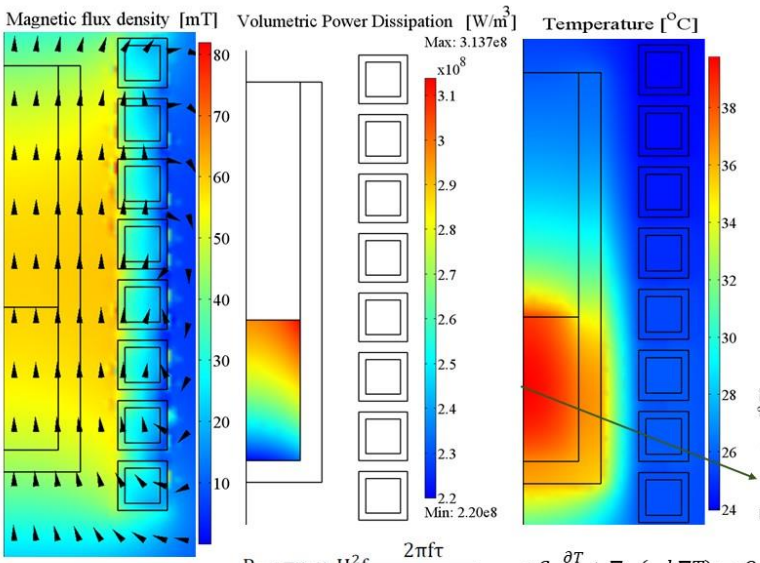
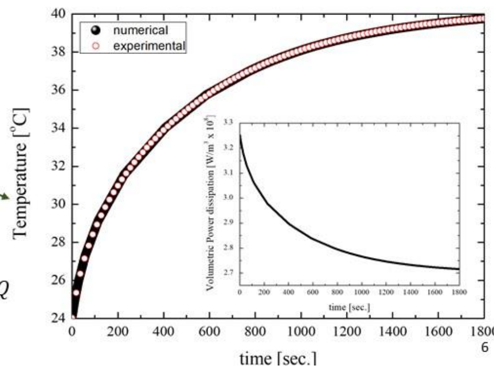
Methods and Results

8-TURN SQUARED COIL



- 2D axial symmetry
- Convective Heat Flux (Natural and Forced)
- Radiation
  i. surface to surface
  ii. surface to ambient
- Dirichlet



- 2D axial symmetry
- Magnetic Insulation
- Continuity

$$P = \pi\mu_0\chi_0 H_0^2 f \frac{2\pi f\tau}{1+(2\pi f\tau)^2}$$

$$\rho C_p \frac{\partial T}{\partial t} + \nabla\cdot(-k\nabla T) = Q$$

$$Q = P \times \varphi$$

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To Sum Up

Numerical Simulation and Evaluation of Magnetic Particle Hyperthermia System and Conditions

Conclusions

- The role of coils geometry in field homogeneity is presented since COMSOL takes into account the coil geometrical characteristics, ignored in the analytical expressions.
- The time-dependent heating curves are in good agreement with the corresponding experimental ones observed under the same conditions validating our method.
- The assumption of nanoparticles homogeneous spatial distribution in the water was also verified by the good agreement between theoretical and experimental results.
- The appropriate dose is chosen so as not to attenuate magnetic nanoparticles thermal performance but also to be absorbed to the maximum possible from the tissues and yield the best possible heat.
- Proper use of simulations can lead to better understanding of complex physical processes, further progress in the development of novel MPH equipment designs, replacement of invasive temperature measurements and establishment of updated hyperthermia treatment protocols.
- In silico testing and evaluation of material properties and innovative methods could substantially accelerate their approval for clinical use and result to better treatment quality.

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Magna
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