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Diffusion of magnetic nanoparticles in a multi-site injection process within a biological tissue during magnetic fluid hyperthermia using lattice Boltzmann method

Ali Akbar Golneshan[a], Mansour Lahonian[b,*]

[a] Thermal-Fluid and Energy Department, School of Mechanical Engineering, Shiraz University, Molla Sadra Street, Shiraz, Iran
[b] Mechanical Engineering Department, School of Engineering, Kurdistan University, Pasdaran Street, Sanandaj, Iran

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ABSTRACT

In this study the lattice Boltzmann model (LBM) has been used to simulate diffusion of magnetic nanoparticles (MNPs) injected at multiple sites inside a biological tissue during magnetic fluid hyperthermia (MFH). To validate the numerical results, diffusion in infinite one and two dimensional domains have been compared with the analytical solutions. Agreement were excellent. Also diffusion of a water based nanofluid containing magnetite MNPs (ferrofluid) for mono and multi-site injection in the tissue has been studied. Moreover, the effects of ferrofluid injection volume as well as infusion flow rate of ferrofluid on the distribution of MNPs have been investigated.

1. Introduction

MFH is one of hyperthermia modalities for tumor treatment. In MFH, fine MNPs are localized at the tumor tissue and alternating magnetic field is then applied to the target region. These particles might act as localized heat sources. Iron oxides magnetite Fe_3O_4 and maghemite γ-Fe_2O_3 nanoparticles are the most studied to date (Hilger et al., 2005) due to their biocompatibility, when injected in the human tissue (Moroz et al., 2002). The heat generated by the particles subjected to an external alternating magnetic field is mainly due to the Néel relaxation mechanism and/or Brownian motion of the particles (Hergt and Andra, 1998; Rosensweig, 2002; Nedelcu, 2008). The superparamagnetic particles 10-nm are recommended in clinical application as they are able to generate substantial heat within low magnetic field strength and frequency (Lv et al., 2005). An ideal MFH treatment should selectively destroy the tumor cells without damaging the surrounding healthy tissue. A successful MFH treatment is substantially dependent on MNPs distribution in the tissue.

Two techniques are currently used to deliver MNPs to a tumor. The first is to deliver particles to the tumor vasculature (Matsuki and Yanada, 1994) through its supplying artery; however, this method is not effective for poorly perfused tumors. Furthermore, for a tumor with an irregular shape, inadequate MNPs distribution may cause under-dosage of heating in the tumor or overheating of the normal tissue. The second approach, is to directly inject MNPs into the extracellular space in tumors. MNPs diffuse inside the tissue after injection of ferrofluid. If the tumor has an irregular shape, multi-site injection can be exploited to cover the entire target region (Salloum et al., 2008a).

The relationship among MNPs distribution, infusion flow rate, injection volume of nanofluid, and tissue structure are not well understood. It is difficult to devise a treatment protocol that enables the optimum distribution of temperature elevation in the tumor. Hence, it is important to quantify the MNPs distribution and heating pattern following the injection regarding the infusion flow rate and tissue properties (Salloum et al., 2008b).

A recent experimental study in a tissue-equivalent agarose gel, has revealed that the particle concentration was not uniform after the injection and were confined in the vicinity of the injection site. Also the particle deposition was greatly affected by the injection rate and amount (Salloum et al., 2008a).

Due to difficulties in experimental studies, to understand the actual spatial distribution of the MNPs after being injected into the tumor, numerical simulations are necessary. To model this problem, LBM may be employed, since this numerical method has been demonstrated to be successful in simulation of fluid flow and heat transfer problems and other types of complex physical systems (He et al., 1998; Chen and Doolen, 1998; Succi, 2001; Ho et al., 2002; Gupta et al., 2006; Mishra and Roy, 2007; Wang et al., 2007a,b; Joshi et al., 2007a,b).

* Corresponding author. Tel.: +98 711 6133007; fax: +98 711 6287294.
E-mail address: lahonian@shirazu.ac.ir (M. Lahonian).

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LBM has many advantages over the conventional CFD methods. The advantages of the LBM include, among others, a clear physical meaning, simple calculation, simple implementation on a computer, ease in parallel computation, easy handling of complex geometries and boundary conditions, capability of stable and accurate simulation, etc. The LBM is second-order accurate in time and space, which is sufficient for most engineering applications. The LBM also shows potentials to simulate the non-linear systems (He et al., 1998; Chen and Doolen, 1998; Succi, 2001; Velivelli and Bryden, 2006; Shi et al., 2008; Mishra et al., 2009).

In this study the two dimensional, nine velocity (D2Q9) LBM is used to simulate diffusion of MNPs inside a tissue as a porous media with Neumann boundary condition, during MFH. To validate the numerical results, diffusion in infinite one and two dimensional domains are compared with the analytical solutions. Also diffusion of ferrofluid for mono and multi-site injection is studied. Finally the effects of ferrofluid injection volume as well as infusion flow rate of ferrofluid on the distribution of MNPs are investigated. To our knowledge, it is the first attempt to study the MNPs distribution inside the tissue for multi-site injection of magnetic fluid.

2. Mass diffusion in tissue

In hyperthermia treatment, the distribution of temperature elevation is an important factor determining the therapeutic outcome. The temperature distribution inside the tumor and its surrounding healthy tissue can be computed using the Pennes bio-heat equation as follow (Pennes, 1948):

$$\rho c_p \frac{\partial T}{\partial t} = \nabla.(k\nabla T) + W_b \rho_b c_{pb}(T_b - T) + (q_m + q_g) \tag{1}$$

where ρ, c_p, T, t, k, W_b, ρ_b, c_{pb}, T_b, q_m and q_g are tissue density, tissue specific heat, tissue temperature, time, tissue thermal conductivity, blood perfusion, blood density, blood specific heat, blood temperature, uniform rate of metabolic heat generation in the tissue and distributed volumetric heat source due to spatial heating, respectively. Due to the inherent simplicity of Pennes bio-heat model, this model was implemented in various biological research works such as therapeutic hyperthermia for the treatment of cancer.

The quantification of heat generated by the MNPs has suggested that the size of MNPs and properties of the magnetic field (strength and frequency) determine its heating capacity, defined as specific loss power (*SLP*). Given the *SLP* of the MNPs at a magnetic field strength and MNPs concentration distribution C, the distribution of heat generation q_g can be computed as $q_g = SLP \times C$. Clearly, the spatial distribution of the MNPs dispersed in tissue is an important factor determining the resulting temperature elevation. However, it is not clear how the spatial concentration of the particles in the tissue correlates with the particle concentration in the carrier solution before the injection (Salloum et al., 2008b).

For mass transport due to diffusion for isotropic tissues, with no blood perfusion and no interaction between cells and MNPs, the following equation is used (Nicholson, 2001):

$$\frac{\partial C}{\partial t} = D^* \nabla^2 C + \frac{S}{\varepsilon} \tag{2}$$

where C, D^*, S, ε and t are the volume average concentration of the species, effective diffusivity, mass source density, porosity of the tissue and time, respectively. The effective diffusivity, however, is related to the tortuosity of the tissue λ and the diffusivity in the absence of the porous medium, D through the following relation:

$$D^* = \frac{D}{\lambda^2} \tag{3}$$

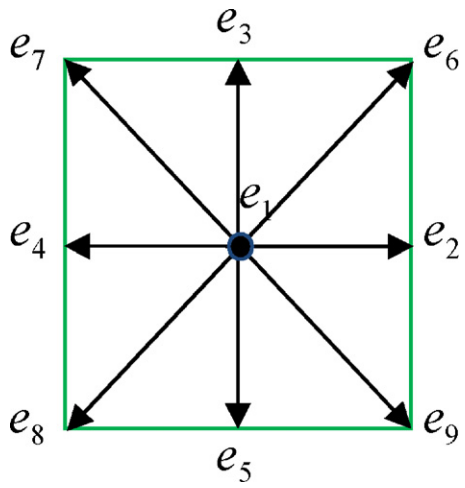

Fig. 1. Schematic plot of the D2Q9 lattice.

Therefore an increase in the tortuosity and a decrease in the porosity have significant effects in reducing the effective mass diffusivities of species.

3. Lattice Boltzmann model

According to Eq. (2), the particle velocity distribution equation of the two-dimensional nine-speed (D2Q9) lattice Boltzmann model is (He et al., 1998):

$$f_i(r + e_i\,\Delta t, t + \Delta t) - f_i(r, t) = -\frac{1}{\tau}\left[f_i(r, t) - f_i^{eq}(r, t)\right] + w_i\ \Delta t \frac{S}{\varepsilon}\frac{\tau - 0.5}{\tau} \tag{4}$$

where, the distribution functions f_i is a set of populations representing the probability of finding a particle at position r, at time t, moving along the direction identified by the propagation velocity e_i. The subscript i, the direction of the thermal population (see Fig. 1), Δt the time step, τ the dimensionless relaxation time. f_i^{eq}, the equilibrium distribution of the evolution population is:

$$f_i^{eq} = w_i C \tag{5}$$

where w_i is the weight factor which is equal to 4/9 for $i = 1$, 1/9 for $i = 2, 3, 4, 5$ and 1/36 for $i = 6, 7, 8, 9$ and the propagation velocity is defined as:

$$e_i = \begin{cases} 0 & \text{for} \quad i = 1 \\ (\pm c, \nrightarrow 0),\ (0, \nrightarrow \pm c) & \text{for} \quad i = 2, 3, 4, 5 \\ (\pm c, \pm c) & \text{for} \quad i = 6, 7, 8, 9 \end{cases} \tag{6}$$

where $c = \Delta x/\Delta t$ is the lattice velocity, Δx is the discrete lattice unit (lu) and Δt is the time step (ts). The dimensionless relaxation time is defined as:

$$\tau = 3\frac{D^*\ \Delta t}{\Delta x^2} + \frac{1}{2} \tag{7}$$

The macroscopic physical quantities such as C and $\dot{m}$ can be obtained from the distribution function. The concentration and diffusive mass flux are as follow (D'Orazio et al., 2004):

$$C = \sum\nolimits_i f_i + \frac{\Delta t}{2}\frac{S}{\varepsilon} \tag{8}$$

$$\dot{m} = \frac{\tau - 0.5}{\tau}\sum\nolimits_i f_i e_i \tag{9}$$