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Estimation of the optimum number and location of nanoparticle injections and the specific loss power for ideal hyperthermia

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ABSTRACT

Hyperthermia is one of the most appealing methods of cancer treatment in which the temperature of tumor is elevated to reach a desired temperature. One of the methods of increasing tissue temperature is injection of nanoparticle fluids to tumor and applying alternative magnetic field, which is called magnetic nanoparticle hyperthermia method. The total number of injection points, as well as the their location within a tissue play a significant role in this method. Furthermore, the power of heating of a magnetic material per gram or specific loss power (SLP) is another important factor which needs to be investigated. As the uniform temperature of 43 °C is effective enough for a tumor regression in certain specific tissues, the inverse method is applied to find out both the number of injection points and their location. Furthermore, the effective amount of heat generated by nanoparticles is investigated by this technique. Two-dimensional cancerous brain tissue was considered, zero gradients on boundary conditions were assumed, and diffusion equation and Pennes equation, which is regarded as energy equation, were solved, respectively. Conjugate gradient technique as a one way of inverse methods is applied, and unknowns are investigated. The results illustrate that three-point injection with the best injection sites cannot induce a uniform temperate distribution of 43 °C, and although four-point injection can create a uniform temperature elevation, the amount of it cannot reach the 43 °C. Finally, the optimum locations of five-point injection which are ((0.80,3.24), (0.80,0.84), (2.00,2.00), (3.20,3.24), (3.32,0.84)) (all dimensions are in mm) in the studied domain with special loss power of 420 W/g, all of which are obtained after 36 iterations, demonstrate that these conditions can meet the requirements of the magnetic fluid hyperthermia and can be considered for the future usage of researchers and investigators.

1. Introduction

Thermal therapy or hyperthermia is a method for cancer therapy in which a specific tissue is subjected to the prescribed high temperature which leads to destruction of cancer cells with minimum damage to other tissues (Habash et al., 2006). In general, the main target of hyperthermia is increasing the temperature of particular cells. Magnetic fluid hyperthermia (MFH) is one of the most effective types of hyperthermia in which tumor is heated by internal heat sources. Magnetic particles in the form of thermoseeds or magnetic nanoparticles are injected into a tumor, and then, exposed to an alternating magnetic field with proper amplitude and frequency. Due to hysteresis and viscous losses, these magnetic particles ultimately increase the temperature of cancerous tissue (Johannsen et al., 2004). In temperature above 42 °C, the tumor turns out to the phenomenon known as acidosis, which decreases PH of a cancerous cell and eventually results in the tumor regression (Jalali et al., 2014; Katz and Willner, 2004).

In recent years, many materials have been examined in order to use as thermoseeds in various kinds of hyperthermia (Atsumi et al., 2006). One of the initial studies on the particle injection was carried out by Jordan et al. (1999). They used two different ferrofluids in their study which are magnetite particles with aminosilan type shell and with dextran type shell. The first one had largely positive surface charges and the second one had a neutral to negative surface charge. The temperature of about 45 °C in the tissue was their achievement. Cobalt-palladium thermoseeds, Self-regulating thermoseeds type, used by Deger et al. (2003) to examine the effect of interstitial hyperthermia combined with radiation on prostate cancer. There weren't any major side effect during this treatment and the temperature of intra-prostate was reported about 44 °C. The results showed that the combination of hyperthermia with conformal radiotherapy may be another curative treatment option for the prostate cancer. Park et al., 2002, in a report, studied the duplex stainless steel thermoseeds and their heating features, especially their effect on rabbit liver in the induction of

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Nomenclature

C	nanoparticles concentration
C_p	Specific heat capacity
d	direction of the descent
D	diffusion coefficient
D^*	effective diffusion coefficient
J	sensitivity matrix
k	thermal conductivity
P	vector of unknown parameters
q_m	cellular metabolism
q_g	heat produced by nanoparticles
Q	injection rate
s	source term
S	objective function
T	temperature
V	injection volume
W	calculated quantities
L	characteristic length of square domain
x,y	x- and y-coordinate system
Y	desired quantities

Greek symbols

α	porosity
β	search step size
γ	conjugation coefficient
λ	tortuosity
ω_b	blood perfusion

Subscripts

b	blood

Superscripts

k	number of iterations
T	transpose of the vector

hyperthermia. Their study included both in vivo and in vitro studies with thermoseeds of two different shapes, L-shaped and I-shaped. By using magnetic induction field, they could reach the temperature about 55 °C. Therefore, these kinds of thermoseeds with magnetic induction field could be considered effective in the induction of interstitial hyperthermia.

Despite various advantages, thermoseeds have their negative implications. They should be planted in cancerous tissue by surgery. If the cancerous tissue has a complex shape, the planting of these seeds will be practically impossible and overpriced. Furthermore, using these seeds cannot cause a uniform temperature distribution (Salloum et al., 2009). Over the last four decades, there has been a sharp increase of interest in using nanoparticles in laboratory studies. Use of nanoparticles in MFH has been highly regarded by the researchers in the recent decade (Baghban and Ayani, 2017; Tartaj and Serna, 2003). The major advantages of magnetic nanoparticles in comparison with magnetic thermoseeds are high surface-to-volume ratio and different crystal structures, which increase the heat generated in the tumor. From 2001 on, numerous researchers have focused on using magnetic nanoparticles in MFH. The diffusion and its transport mechanism of brain tissue was carefully examined by Charles Nicholson. This study can be regarded as a turning point in the development of molecular diffusion within a tissue, especially brain tissue (Nicholson, 2001). Another outstanding study in this field was carried out by Brusentsov et al. (2002). They developed magnetic dextran-ferrite #363 (DF) nanoparticles for a special kind of hyperthermia in which AC magnetic field externally was applied. They also concluded that to achieve complete tumor regression, it is crucial to use both AC magnetic field and DF nanoparticles. Laurent et al. (2011) investigated MFH by Superparamagnetic nanoparticles both experimentally and numerically, and temperature of this type of nanoparticles was estimated more than other types. Golneshan and Lahonian (2011) examined numerically nanoparticle concentration in a cancerous tissue by lattice Boltzmann method, and the results were compared with analytical ones. They were able to achieve a nearly uniform distribution of nanoparticles with four-point injection in the tumor. The effect of some relative factors such as surface coating on nanoparticles were scrutinized by Liu et al. (2012). They showed that by optimization of both surface coating and particle size in nanometer, specific absorption rate (SAR) reached the highest rate. Vallejo-Fernandez and O'Grady (2013) examined the effect of the distribution of anisotropy constants on hysteresis losses for MFH applications. They analytically proved that in order to have an exact model for MFH, the effect of both particle size and thermal conductivity distribution should be considered. Deatsch and Evans (2014) contextualized studies about the effect of nanoparticle concentration on heating efficiency and showed that there was a negative relationship between magnetic relaxation time and nanoparticle concentration. Smolkova et al., 2015 in 2015 studied about iron oxide nanoparticles. Their main purpose was getting a relationship between magneto-structural properties of those nanoparticles and their heating efficiency for better performance of MFH. Moreover, in our recent research, an inverse algorithm was used to estimate the external power of source term in a multilayer skin tissue (Baghban and Ayani, 2015), and also, non-Fourier heat conduction during hyperthermia in a biolayer spherical living tissue was investigated (Mohajer et al., 2016).

Injected points of ferrofluids are important factors on the nanoparticle concentration within the tissue. As a matter of fact, the non-uniform concentration of nanoparticles cannot create a uniform temperature distribution, and it not only decreases the efficacy of MFH but also may change the shape of cancerous cells into complex ones, which are much more resistant against MFH. A quick glance at the review papers shows that no one works on the location of the injection points on the hyperthermia. To overcome the foregoing problems, in this study, the precise injection points and the necessary amount of special loss power (SLP) for the uniform temperature of 43 °C are obtained by using the inverse method. Maximum five points of injection are evaluated for a two-dimensional tissue. Overall, the inverse method should determine unknowns, including precise injection point coordinates and SLP. For reaching this purpose, first, governing equations that used in this study should be clarified, these are completely discussed in Section 2. Then in Section 3, the inverse method with all assumptions are explained. After that, the results will be discussed and the best conditions for this method will be illustrated.

2. Governing equations and geometry design

The whole human body has numerous complex tissues that are different from one place to another one. Physical properties of each tissue including conductivity, average temperature, and porosity are unique and different to each other. Therefore, a specific tissue should be considered for the inverse method. In this study, cancerous brain tissue was considered. The main aspect that should be mentioned is that the brain tissue as itself has a completely complex shape which makes it very difficult for the numerical modeling. Therefore, modeling of the brain is obtained by considering the following hypotheses:

1. Extracellular fluid is stagnant (Davson, 1993).
2. Brain tissue is regarded as a porous medium without considering