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Determination of the 3D temperature distribution during ferromagnetic hyperthermia under the influence of blood flow

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ABSTRACT

A numerical simulation of tissue heating during thermo-seed ferromagnetic hyperthermia was performed to determine the temperature distribution of treated tumor tissues under the influence of three large blood vessels at different locations. The effects of the blood velocity waveform, blood vessel size, Curie point of the thermo-seeds and the thermo-seed number on temperature distributions were analyzed. The results indicate that the existence of a blood vessel inside the tumor has a significant cooling effect on the temperature distribution in a treated tumor tissue, which is enhanced with an increase in blood velocity. However, the pulsatile blood flow does not have apparently different effects on the outcomes of uniformly heating target tissues in comparison with the steady blood flow during the hyperthermia process. It is also concluded that a higher Curie point temperature and an increase in the number of thermo-seeds can result in profound increases in the temperature variations of the tumor tissue. In addition, tissue-equivalent phantom experiments were conducted to confirm the cooling effects of the blood vessels, and to validate the effectiveness and accuracy of the proposed heat transfer model for the ferromagnetic hyperthermia.

1. Introduction

Ferromagnetic hyperthermia has attracted a great deal of attention in the field of hyperthermia tumor treatments and many experimental results have confirmed that the technique has promising potential for clinical applications (Paulus et al., 1996; Rehman et al., 2002; Stea et al., 1990). It is known that cancer cells are more sensitive to high temperatures, compared with ordinary cells (Atkinson et al., 1984). In this technique, the treated tumor tissue is heated to a desired temperature by implanted ferromagnetic seeds, whose temperature is increased to the Curie point using AC magnetic field-induced excitation (Corazza and Dughiero, 2001; O'Hara et al., 1995; Roemer, 1997). Compared with other tumor hyperthermia techniques, such as microwave thermal therapy, thermo-radiotherapy, or ultrasound hyperthermia, ferromagnetic hyperthermia can be more easily controlled to obtain a uniform desired temperature distribution according to the shape of the treated tissue. This is because the Curie point and size of the thermo-seeds can be customized as needed for the therapy temperature (Turker, 2003). Moreover, the ferromagnetic hyperthermia treatment can be repeated several times with minimal side-effects, using the same implanted seeds.

To kill cancer cells without irreversible damage to the surrounding normal tissue, the targeted tumor tissue should be uniformly heated to a desired temperature of 42–45 °C by precise adjustment of the thermal dose (Field and Dewhirst, 1998). During the heating process, accurate real-time prediction of the 3D temperature distribution is crucial for thermal dose adjustment. In the recent years, many significant contributions have been made to determine the temperature distribution of the treated tumor tissue. Brezovich et al. (1984) found that nickel–copper implants could produce substantially better temperature homogeneity, especially in tumors with unpredictable rates of blood perfusion or when the implant arrangement was not perfectly regular. Chen and Roemer (1992) analyzed the three-dimensional temperature distributions generated by interstitial ferromagnetic implants and indicated that a desired temperature distribution can be obtained by choosing a specific Curie point of the seeds and using appropriate seed spacing. Van Wieringen et al. (1997) investigated the effects of heat production of self-regulating thermo-seed on the temperature changes of a cylindrical area around the thermo-seed. Tompkins et al. (1994) numerically simulated the temperature distribution of the human prostate tumor tissue without large blood vessels when the thermo-seeds with different Curie points were implanted. But they did not consider the effect of blood flow. Raaymakers et al. (2000) modeled the temperature distributions affected by discrete vasculature and carried out experiments in an agar–agar

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phantom. Shih et al. (2003) demonstrated the effects of thermally significant blood vessels on thermal lesion sizes during thermal therapies. Dughiero and Corazza (2005) carried out numerical simulation to predict the temperature distribution when the effects of large blood vessel were considered. The research results show that the blood flow through the blood vessel in the treated target tissue has a profound cooling effect, which is worth further investigation.

Most investigations directly regard the blood flow as a steady blood flow within an idealized rigid artery, whereas the behavior of the blood flow in an artery is actually pulsatile. Khalil et al. (2005) performed a numerical study to explore the influence of pulsatile laminar flow on radial temperature variation in a single blood vessel. Oana and Scott (2001) discussed the difference in blood flow effects between a sinusoidal waveform blood velocity and an assumed, non-pulsating blood velocity. The results indicated that the cooling effect of pulsatile blood flow depended to some extent on the blood vessel size, i.e. the blood flow velocity. Horng et al. (2007) evaluated the effect of sinusoidal blood flow on the cylindrical target region when the heat power is added axisymmetrically. Craciunescu and Clegg (2001) assumed a sinusoidal velocity waveform to simulate the effect of pulsatile blood flow on temperature distribution and heat transfer within rigid blood vessels. However, the human pulsatile blood flow waveform of a resting person is not an ideal sinusoidal shaped waveform (Mills et al., 1970).

The purpose of the present study was to acquire a good knowledge of the cooling effects of human pulsatile blood flow on accurate prediction of the temperature variations in treated tumor tissues during thermo-seed hyperthermia. Numerical simulations of the heat transfer process in the targeted tissue were performed. We focused on the effects of the pulsating blood flow, location of the blood vessel, and blood flow rate on tumor tissue heating. The effects of the Curie point of the ferromagnetic thermo-seeds and the seed number on the temperature distribution were also investigated. We performed phantom experiments to validate the cooling effects of the blood vessels and the proposed heat transfer model.

2. Numerical simulations

2.1. Physical model

Considering the subsequent planned experimental research on tissue phantoms, the treated tumor tissue was modeled as a 5 cm diameter sphere, centered in a 10 cm cubic block of normal tissue. We proposed a three dimensional spherical tumor tissue model with three different blood vessel positions, as shown in Fig. 1(a)–(c). In these three cases, a large blood vessel was located inside the treated tumor tissue, beside the treated tumor tissue, and outside the treated tumor tissue. An array of ferromagnetic thermo-seeds was implanted into the treated tumor tissue. In the simulations shown, the treated tumor tissue was defined as a homogeneous tissue with a straight, rigid blood vessel passing through. The ferromagnetic thermo-seeds with constant Curie point temperature were arranged inside the treated tumor tissue in differing arrays.

2.2. The pulsatile blood flow

The physiological blood flow velocity waveform of a resting person is shown in Fig. 2. It was simplified as an ideal sinusoidal velocity waveform in most existing researches. In this paper, the physiological blood flow velocity curve is approximately fitted as a pulsatile waveform at the inlet of the blood vessel, as shown in Fig. 2.

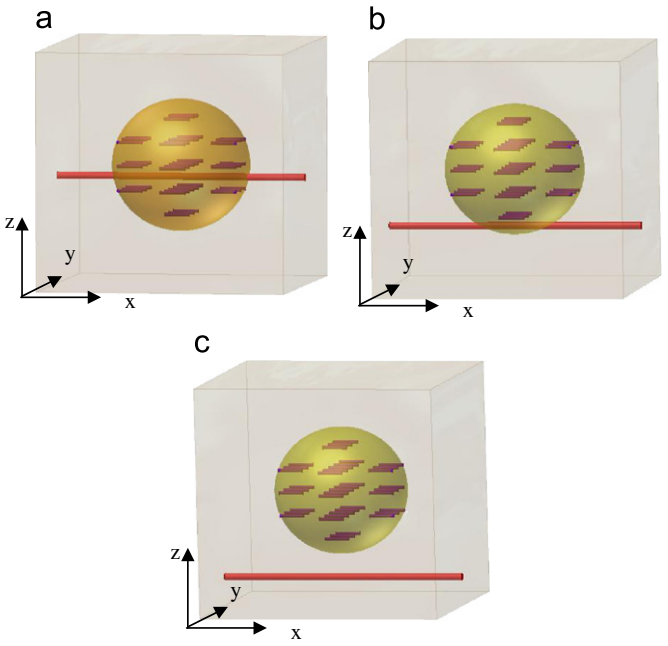

Fig. 1. Numerical simulation model of the temperature distribution in tumor tissue with the blood vessel located (a) inside, (b) beside, and (c) outside the treated tumor.

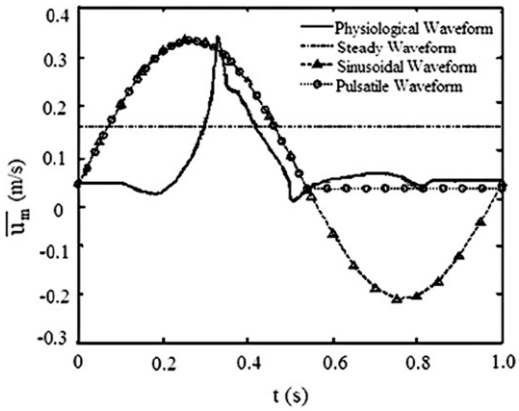

Fig. 2. Blood flow velocity waveforms.

The proposed pulsatile blood flow waveform is described as a function of time, which is given by

$$\overline{u_m}(t) = \begin{cases} 0.333 - 0.272[1 + \cos(2\pi t + 1.466)], & 0 \le t \le 0.54 \\ 0.021, & 0.54 < t \le 1 \end{cases} \quad (1)$$

2.3. Power absorption of ferromagnetic thermo-seeds

In the process of tumor ferromagnetic hyperthermia, the temperature of the ferromagnetic thermo-seed will remain constant after it increases to a constant value under the influence of an AC magnetic field. This constant value strongly depends on the thermo-seed material properties, tissue properties, and magnetic field parameters.

The power absorption in ferromagnetic thermo-seeds is mainly resulted from induced eddy current loss and hysteresis loss of ferromagnetic materials. With the assumption of homogeneous and isotropic thermo-seed materials, the power absorption of the ferromagnetic thermo-seed can be calculated when the induced magnetic field is parallel to the axis of the cylindrical