Vascular Cooling Effect on Temperature Distribution for Hollow Microspheres in Magnetic Induction Hyperthermia: Numerical simulation and analysis

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Abstract. Magnetic Induction hyperthermia is a type of treatment that uses electromagnetic energy to form high temperature area in tumour and kill tumour cells. Magnetic agents can generate heat to increase the temperature. However, researches have shown that the tumour is adjacent to complex vessel systems. Vascular cooling may have great impact on temperature distribution in tumour. Therefore, pre-temperature simulation including vascular cooling effect must be considered to help the clinicians decide the treatment plan. Our previous work has used numerical methods to simulate temperature distribution of avascular model. In this work, we use numerical methods, containing FDM, FVM, BADI and DADI, to simulate the vascular agar model. After comparing the simulation results and vitro heat results, BADI has the smallest error. What’s more, limited by vitro experimental conditions, many vascular parameters cannot be changed in vitro experiments. So we use BADI to simulate the temperature distribution under different conditions containing blood flow rates, vessel diameters and vessel locations. Simulation results show that the blood flow rates and vessel diameters have less impact compared to vessel locations and the blood flow rates affects the least.

1. Introduction
Tumor Hyperthermia is a type of treatment that uses electromagnetic or ultrasonic energy to raise the temperature of the body or local tissues to a specified temperature within a specified time to kill tumor cells. Temperature beyond 42\textdegree{}C can kill tumor cells. Magnetic Induction Hyperthermia (MIH) uses a ferromagnetic medium as a heat source to be implanted in the tumor tissue and heat the ferromagnetic medium through an external alternating magnetic field, forming a local high temperature area in the target tumor which cause cell apoptosis or necrosis [1].

Conformal hyperthermia is the key to MIH. It demands that the high temperature region should be consistent with the tumor. Current temperature measurement methods are limited and the temperature field in tumor can’t be monitored all the time. So pre-temperature simulation of the treatment area must be introduced into Hyperthermia Treatment planning (HTP). By using HTP, proper treatment plan could be obtained by adjusting the position, magnetic agent consumption and magnetic field parameters [2]. The commonly used equation of temperature distribution simulation is based on the biological heat transfer equation proposed by Pennes [3] (Equation (1)).

$$\rho c_T \frac{dT}{dt} = w_b c_b (T_b - T) + \nabla \cdot (k_T \nabla T) + Q_m + Q_r$$

(1)
where $T$ is the tissue temperature, $\rho_t$ is the tissue density, $c_t$ is the specific heat capacity of tissue, $w_b$ is the blood perfusion rate, $c_b$ is the specific heat capacity of blood, $T_b$ is the temperature of the blood, $k_t$ is the thermal conductivity, $Q_m$ is the metabolic heat power and $Q_r$ is the heat power of magnetic agents.

This equation explores the mechanism of isotropic heat dissipation and perfusion, and the results show that the effect is proportional to the average perfusion rate and the local temperature. However, the Pennes heat transfer equation has defects. First, the model is a macro model to calculate the temperature of tissue which does not consider the accurate heat exchange between the tissue and the real vascular system. Second, the equation does not consider the direction of blood flow. Researches have proposed many improved models in response to the above problems. Wulf et al. replaced the non-directional perfusion term with unidirectional flow in the Pennes model, which can explain the interaction between blood and tissue [4]. Chen et al. proposed the effective conductivity model, describing the blood perfusion convection represented by the effective conductivity term, which is another extension of the Pennes model [5].

In this paper, the impact of large blood vessels is simulated and analyzed by using numerical heat transfer simulation algorithms. In our previous work [6], heat transfer algorithms containing the explicit format of finite-difference method (FDM), Brian ADI (BADI), Douglas ADI (DADI) and finite-volume method (FVM) are used to calculate heat distribution of the avascular agar model. In this paper, firstly, in section 2, FDM, FVM, BADI and DADI are introduced to calculate the temperature distribution of the agar inserted with large catheter where water flows. This calculation is used to simulate the impact of large vessels. The simulation results are compared with the vitro heat experiments and analysis is performed. Limited by vitro experimental conditions, many vascular parameters cannot be changed. So, in section 3, we choose the algorithm with the smallest error to simulate the large vessel cooling effect under different conditions containing blood flow rates, vessel diameters and the distance between vessel and magnetic agents. The degree of the influence of blood vessels on the temperature field distribution are analyzed and discussed, which can provide reference for parameter adjustment of HTP and has certain clinical guiding significance.

2. Comparison of numerical simulations and vitro experiments

2.1. Biological heat transfer model

The agar cube model is inserted with catheter and the hollow microspheres which were developed in [7]. The microspheres are placed at the cube centre (figure 1).

![Figure 1. Agar model with catheter.](image)

In this paper, considering the vascular heat transfer, we assume the blood flow is laminar flow [8], the vessel is along $z$ direction and the blood velocity only has $z$ direction. The equation of blood velocity is shown as

$$v = 2v_0(1 - \frac{r_b^2}{R_b^2})$$  \hspace{1cm} (2)

where $v_0$ is the average velocity, $r_b$ is the distance between the point and central axis at blood vessel direction.

The heat transfer equation in the vessel is shown as Equation (4).

$$\rho_b c_b \left( \frac{\partial T_b}{\partial t} + v \nabla T_b \right) = \nabla \cdot (k_b \nabla T_b)$$  \hspace{1cm} (3)

where $v$ is the velocity vector which is $(0,0,v)$ in this model.
2.2. Numerical heat transfer algorithms

The cube is divided into plenty of micro cells to calculate heat transfer. Similar to [9], for the blood part, the derivation processes of FDM, FVM, BADI and DADI are as follows.

For FDM, we can get:
\[ \rho_b c_b \frac{T(i,j,k,t + \tau) - T(i,j,k,t)}{\tau} + \rho_b c_b v \frac{T(i,j,k+1,t) - T(i,j,k,t)}{h} + T(i,j,k+1,t) + T(i,j,k-1,t) - 6T(i,j,k,t) \]

For FVM, equation (3) is integrated on both sides and point P(i, j, k) can be represented by surrounding points: \( W(x - \Delta x, y, z) \), \( E(x + \Delta x, y, z) \), \( S(x, y - \Delta y, z) \), \( N(x, y + \Delta y, z) \), \( B(x, y, z - \Delta z) \), \( T(x, y, z + \Delta z) \). After derivation, we can get:
\[ \rho_b c_b h^3 \Delta t (T_P - T_P^0) + \rho_b c_b v h^2 (T_T - T_P) \]
\[ = k h \Delta t (T_E - T_P) - (T_P - T_W) + (T_N - T_P) - (T_P - T_S) + (T_T - T_P) - (T_P - T_B) \]

BADI and DADI take different time increase to calculate the temperature increase after \( \Delta t \). BADI takes the time increase of \( \Delta t / 2 \) with equation (6) for the blood part. DADI uses the average of two adjacent moments to represent the partial differential of the spatial range with equation (7).

\[ \frac{U_{i,j,k} - T_{i,j,k}^n}{\Delta t} + \rho_b c_b v \frac{\partial T_{i,j,k}^n}{\partial z} = k_b \left( \frac{\partial^2 U_{i,j,k}}{\partial x^2} + \frac{\partial^2 T_{i,j,k}^n}{\partial y^2} + \frac{\partial^2 T_{i,j,k}^n}{\partial z^2} \right) \]

\[ \frac{V_{i,j,k} - T_{i,j,k}^n}{\Delta t} = \rho_b c_b \left( \frac{\partial^2 U_{i,j,k}}{\partial x^2} + \frac{\partial^2 T_{i,j,k}^n}{\partial y^2} + \frac{\partial^2 T_{i,j,k}^n}{\partial z^2} \right) \]

\[ \frac{T_{i,j,k}^{n+1} - T_{i,j,k}^n}{\Delta t} = \rho_b c_b \left( \frac{\partial^2 U_{i,j,k}}{\partial x^2} + \frac{\partial^2 T_{i,j,k}^n}{\partial y^2} + \frac{\partial^2 T_{i,j,k}^n}{\partial z^2} \right) \]

2.3. Vitro heat experiment

We prepare the agar cube with a side length of 60cm. A catheter with diameter of 4mm is inserted into agar to simulate vessel. 200mg hollow microspheres are injected into the centre of agar. Two points are focused to measure temperature by optical fibre. The positions of vessel, microspheres and agar to simulate vessel. 200mg hollow microspheres are injected into the centre of agar. Two points are shown in figure 2(a). We use injection pump (figure 2(b)) to generate water flow at 40cm/s to simulate blood flow. The water temperature at the inlet is 10°C. The biological characteristics of the agar we made are \( \rho = 1500kg \cdot m^{-3} \), \( c = 3800J/(kg \cdot K) \) and \( k = 0.5W/(m \cdot K) \). The agar is placed in the magnetic field of 540kHz, 60Gs to conduct the heat experiment.
2.4. Comparison of simulation and experimental results

Figure 3 shows the temperature distribution graph of the agar without or with vessel at the central horizontal section. It demonstrates that the vessels could influence the temperature increase. The temperature changes of point a and b are shown in figure 4. The comparison shows that BADI has the smallest temperature error with the vitro experiment. Considering the calculation and experimental error, the error between the BADI theoretical value and the actual measurement is within the allowable range (±0.5°C), which validates the feasibility of the model we build and BADI numerical algorithms.

Figure 2. (a) Position illustration (b) Injection pump.

Figure 3. Central horizontal temperature distribution graph (a) non-vessel (b) vessel

Figure 4. Temperature changes of point a and b (a) point a (b) point b.
3. Vascular cooling effect under different vascular parameters

Due to the limitation of in vitro experimental conditions, in this part, the vascular cooling effect is analysed under different simulation conditions like blood flow rate, blood temperature, the diameter of vessel and the distance between the vessel and the microspheres. BADI is used to conduct simulations.

According to [9], the blood flow rate is about tens of centimetres per second and the vessel diameter is about a few millimetres. So we change the simulation condition with diameter of 2, 4, 6, 8 mm and 20, 30, 40, 50, 60 cm/s. Besides, for changing the distance between the vessel and the microspheres, the simulated distance is set to be 16 cm, 20 cm and 24 cm. The benchmark condition is vessel diameter of 4 mm, blood flow rate at 40 cm/s, vessel location of 20 mm between vessel centre and cube centre and magnetic field of 540 kHz, 60 Gs. This condition has been simulated in section 2. We only change one of the factors related to vascular cooling to conduct the comparison. Figure 5 shows the temperature changes of point a and b under different blood flow rates. Figure 6 is under different blood flow rates. Figure 7 is under different distances.

![Figure 5](image1.png)  
Figure 5. Temperature change under different vessel diameters (a) point a (b) point b.

![Figure 6](image2.png)  
Figure 6. Temperature change under different blood flow rates (a) point a (b) point b.

![Figure 7](image3.png)  
Figure 7. Temperature change under different vessel locations (a) point a (b) point b.
After changing the one of the vascular parameters, we can know the degree of influence under different conditions. Firstly, the closer the point is to the blood vessel, the lower the temperature. Secondly, the blood flow rate does not have as much influence on temperature as vessel diameter and vessel location. However, when the distance between this point and the blood vessel is large enough, the effect of changing these parameters is little, which can be learned from point b.

4. Conclusion

In this paper, a numerical calculation model for the temperature field distribution of the vascular cooling effect is established. Comparing vitro heat results and results of numerical algorithms including FDM, FVM, BADI and DADI, we find BADI has the smallest error. Due to the limitations of vitro experimental conditions, we use BADI to simulate the vascular cooling effect on different vessel diameters, blood flow rates and vessel locations. The simulation results show that the location of vessel has the greatest impact on temperature distribution. The closer the treatment area is to the vessel, the lower the temperature. The vessel diameter influence less and the blood flow rates has the least influence. But changing these parameters cannot affect the distant place.

In future, in the process of making MIH plan, we could import CT data to conduct multi-parameter coupling adjustment to obtain the best conformal temperature field distribution. After importing the vascular model, we can adjust the magnetic field and magnetic induction agents to make the simulated temperature distribution of treatment area meet the demands of tumor hyperthermia.

References

[1] Perigo E A, Hemery G, Sandre O, et al. Fundamentals and advances in magnetic hyperthermia. Applied Physics Reviews, 2015, 2(4): 041302.
[2] Rijnen Z, Bakker J F, Canters R A M, et al. Clinical integration of software tool VEDO for adaptive and quantitative application of phased array hyperthermia in the head and neck. International Journal of Hyperthermia, 2013, 29(3): 181-193.
[3] Pennes H H. Analysis of tissue and arterial blood temperatures in the resting human forearm. Journal of applied physiology, 1948, 1(2): 93-122.
[4] Wulff W. The energy conservation equation for living tissue. IEEE transactions on biomedical engineering, 1974 (6): 494-495.
[5] Chen M M, Holmes K R. Microvascular contributions in tissue heat transfer. Annals of the New York Academy of Sciences, 1980, 335(1): 137-150.
[6] Zhang, Y., Zhang, X., Zhang, L., & Tang, J. (2018, October). Comparison of Five Numerical Simulation Algorithms in Temperature Prediction for Hollow Microspheres in Magnetic Induction Hyperthermia. In 2018 11th International Congress on Image and Signal Processing, BioMedical Engineering and Informatics (CISP-BMEI) (pp. 1-5). IEEE.
[7] Wu, J. , Wang, H. , Zhang, H. , Wei, L. , & Tang, J. (2017). Stainless steel hollow microspheres for arterial embolization hyperthermia. Journal of Medical and Biological Engineering, 37(11), 1-10.
[8] Wang Q, Deng Z S, Liu J. Theoretical evaluations of magnetic nanoparticle-enhanced heating on tumor embedded with large blood vessels during hyperthermia. Journal of Nanoparticle Research, 2012, 14(7): 974.
[9] Kolios M C, Sherar M D, Hunt J W. Blood flow cooling and ultrasonic lesion formation. Medical Physics, 1996, 23(7): 1287-1298.