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# Numerical analysis of a clinically-extracted vascular tissue during cryo-freezing using immersed boundary method

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ABSTRACT

In this paper, the effects of the blood vessel structure and injected nanoparticles on the cryo-freezing of a clinically-extracted vascular tissue are numerically investigated. A hybrid two-dimensional (2D) finite difference analysis combined with immersed boundary method has been developed to accurately simulate the cryo-freezing process. Based on the measured experimental temperature field, the numerical results compared well with the experimental data with a maximum error of 3.04%. This improved cryo-freezing model is able to significantly simplify the mesh generation process at the boundary resulting in improved computational efficacy. For simulating the temperature profile of a tumor that is sited in a dominantly vascularized tissue, our model is able to capture with ease the thermal effect at junctions of the blood vessels. We also analyzed the effects of blood vessel complexity and nanoparticles on iceball deformation which cannot be easily quantified through clinical experiments. Results indicated that the thermal effects of large blood vessels, especially for a more complex blood vessel boundary, remarkably affect the temperature and deformation distributions. In addition, the numerical results showed that, the inclusion of nanoparticles enlarged the cryo-freezing area as they enhance the thermal conductivity and thermal capacity of tissue.

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## 1. Introduction

Cryosurgery is a significant medical therapy in the latter half of the 20th century and remains in many cases the only effective therapy for end-stage organ failure [1,2]. It has been widely applied to treat cancers of liver, lung and bone due to its fewer complications, minimally invasive advantages and low recurrence rate. However, due to the heating effect between major blood vessels and cancerous tumor tissue, insufficient cryo-freezing becomes the major reason for cancer cells survival [3,4]. The heat source brought by the vascular network, especially around the tumor, promotes the recurrence rate. The key reason for recurrence after cryoablation is the untreated tumor cells around large blood vessels [5]. Thus, developing tools like mathematical modeling, numerical simulation and experimental methods [6,7] provide highly effective ways to acquire detailed information such as the temperature field, iceball growth monitoring etc.. Studies have been conducted to investigate the thermal and kinetic behaviors between blood vessel and tumors during ablation.

Kim et al. [3,8] developed a finite element model (FEM) which was designed to solve the cryosurgical problem with or without large blood vessels. The simulation results were also experimentally validated. A good agreement with a maximum error of 4.3% was achieved. Rabin et al. [9,10] developed a new finite difference scheme that examines transient multidimensional heat transfer problems with melting/solidification processes. Key results from their validated model highlighted that common cryosurgical devices have low thermal efficiency and high coolant consumption. Chao et al. [11,12] proposed a three-dimensional FEM strategy based on a MRI -reconstructed model, which composed of thyroid gland, trachea, CCA (common carotid artery) and IJV (internal jugular vein). Considering the heat balance between the arterial blood vessel and the ambient tissue, Dombrovsky et al. [13] developed an advanced thermal model, which coupled both energy equations of the arterial blood temperature and the tissue temperature. Table 1 highlights the salient differences between our present work and several recent studies on numerical analysis of thermal effects due to large blood vessels and complex vascular systems. It worth noting that many of the models in literature are applied to a relative simple vascular system, compared with a

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**Nomenclature**

| | |
|---|---|
| $T$ | temperature (K) |
| $T_{ml}$ | lower phase transition temperatures of tissue (K) |
| $T_{mu}$ | upper phase transition temperatures of tissue (K) |
| $c$ | specific heat (J $kg^{-1}$ $K^{-1}$) |
| $k$ | thermal conductivity (W $m^{-1}$ $K^{-1}$) |
| $k_{eff}$ | effective thermal conductivity tensor (W $m^{-1}$ $K^{-1}$) |
| $k'$ | the thermal equilibration parameter (0 or 1) |
| $q''_m$ | metabolic heat rate (W $m^{-3}$) |
| $q_l$ | latent heat (kJ $kg^{-3}$) |
| $\vec{v}$ | blood velocity (m $s^{-1}$) |
| $h$ | local volumetric/interfacial convective heat transfer coefficient |
| $t$ | time (s) |
| $P$ | perimeter of blood vessel |
| $d$ | diameter of blood vessel |

*Greek symbols*

| | |
|---|---|
| $\rho$ | density (kg $m^{-3}$) |
| $\omega$ | the blood perfusion rate per unit tissue volume (kg $m^{-3}s^{-1}$) |
| $\tau_q$ | phase-lags arising due to thermal inertia (s) |
| $\tau_\theta$ | phase-lags arising due to micro-structural interaction (s) |
| $\varepsilon$ | porosity |
| $\beta$ | blood vessel complexity |
| $\alpha$ | ice ball shape irregularity |

*Subscripts*

| | |
|---|---|
| $t$ | tissue |
| $b$ | blood |
| $a$ | arterial blood |
| $m$ | metabolism |
| $f$ | frozen tissue |
| $u$ | unfrozen tissue |

**Table 1**
Comparison between the present and recent studies on numerical analysis of thermal effects with large blood vessels during cryo-freezing.

| Literature | Simulation method | Experiment validation | Key features | Error |
|---|---|---|---|---|
| Kim et al. [3, 8] | 2D/FEM | YES | Modified a FEM to simulate the freezing process with large blood vessels; Constructed a perfusion model with a bovine liver; Predict the maximum allowable distance between the cryoprobe and the large blood vessel | 0.80% (1st trial) 0.57% and 0.83% (2nd trial) |
| Jin et al. [11, 12] | 3D/FEM | NO | Developed a three-dimensional FEM strategy based on a MRI -reconstructed model; Provided a better understanding on the thermal lesions of RFA within thyroid domain | N.A. |
| Ge et al. [14] | 2D/IBM | NO | Applied IBM to the cryo-freezing simulation; Compared three bioheat models; Validated with data from literatures | 1.7% |
| Zhao and Chua [15] | 2D/FLUENT | YES | Developed a cryo-freezing model dedicated to tumors with a complex blood vessel network | 3.4% |
| Present work | 2D/IBM | YES | Analyzed the effects of blood vessel complexity and nanoparticles on iceball deformation based on a complex vascular network | 3.04% |

complex network which is existed in a liver tumor. This is because the model's the computing speed, scale, accuracy of the model and even the success of calculation are highly depends on the mesh segmentation. The coupling of the two energy equations will increase the complexity of the mesh construction, which will significantly affect the computational efficiency. In addition, the method employed in these models usually suffers from the level of complexity involved in regenerating the mesh to conform to the boundary due to direct implementation of the boundary conditions, particularly for very complex or moving boundary surface.

To address this issue of complex physical boundary, an immersed boundary method (IBM) was first proposed by Peskin [16] in 1971. It was first applied to study the flow pattern problems in heart valves. This method employs Cartesian Eulerian grid points for the solutions of the governing equations. In addition, Lagrangian points are generated to represent the boundary of immersed objects. Based on the fundamental idea of IBM, Ren et al. [17] conducted research on applying the implicit IBM to solve heat transfer problems. We [14] extended the basic of IBM to cryo-freezing problems. Due to the irregular branching pattern of blood vessels commonly in biological tissue, a judiciously developed cryo-model that considers the actual blood network mapped from CT or MRI-images can significantly enhance the accuracy of cryo-planning. This is particularly appropriate when the tumor is sited in a dominantly vascularized tissue. When applying the model to a physical problem, the cell freezing mechanism is an important impact on the cell survival, which is originally analyzed by Mazur [18]. Following Mazur' work, Dombrovsky et al. [19] conducted numerical study about modeling of repeating freezing of biological tissue. Nevertheless, our present study focuses on the thermal effects of large blood vessels on tissue cryo-freezing with the assumption of the tissue being homogenous.

This paper presents a comprehensive investigation on the thermal effects of the blood vessel network and the incorporation of nanoparticles during tumor cryo-freezing process using a series of thermal structure simulations. To the varying thermal field, the development of an improved cryo-freezing model of tumors located in a heavily vascularized tissue was proposed. A two-dimensional (2D) finite difference model combined with immersed boundary method [14] is developed to accurately simulate the freezing process. The model is validated with in-vitro cryo-freezing experiments and the results show the model is appropriate to present the process of cryoablation.

## 2. In-vitro experiment

### 2.1. Materials

Agarose phantom (composed of 1% of agarose (25 g) and 99% of water (2475 ml) by weight) was used to simulate the biological

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