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Incorporating an immersed boundary method to study thermal effects of vascular systems during tissue cryo-freezing

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A B S T R A C T

In this paper, the three-dimensional thermal effects of a clinically-extracted vascular tissue undergoing cryo-freezing are numerically investigated. Based on the measured experimental temperature field, the numerical results of the Pennes bioheat model combined with the boundary condition-enforced immersed boundary method (IBM) agreed well with experimental data with a maximum temperature discrepancy of 2.9 °C. For simulating the temperature profile of a tumor sited in a dominantly vascularized tissue, our model is able to capture with ease the thermal effects at specified junctions of the blood vessels. The vascular complexity and the ice-ball shape irregularity which cannot be easily quantified via clinical experiments are also analyzed and compared for both two-dimensional and three-dimensional settings with different vessel configurations and developments. For the three-dimensional numerical simulations, a n-furcated liver vessels model from a three-dimensional segmented volume using hole-making and subdivision methods is applied. A specific study revealed that the structure and complexity of the vascular network can markedly affect the tissue's freezing configuration with increasing ice-ball irregularity for greater blood vessel complexity.

1. Introduction

Hepatocellular carcinoma (HCC) is the most common malignancy worldwide, with the survival rate of 25–30% (Solovchuk et al., 2012; Jemal et al., 2011), especially in East Asia. It is the second most frequent cause of cancer death in men, while ranked sixth in women. Currently, the common cancer treatments include surgical resection, chemotherapy, radiofrequency ablation and cryosurgery. Compared with conventional therapies, cryosurgery can reduce pain, minimize bleeding, simplify surgical complications and thus decrease the post-surgical recovery time. Hence, cryosurgery has been applied to treat tumors yielding highly positive results.

However, clinical data suggests that conventional cryosurgery is still not efficient in the treatment of complex tumors, with high recurrence rate taking place in follow-up diagnosis (Yu et al., 2005). This mostly occurs when attempting to treat tumors having large volume or are irregularly shaped (Mazur, 1984). In addition, it has been suggested that the cooling rate of cryosurgery is insufficient to produce the intracellular ice crystals in tumor cells, especially at the tumor edge (Gage and Baust, 1998). Such limitations imply that cryosurgery cannot guarantee total lethal damage to the target region.

The heating effect between large blood vessels and cancerous tumor tissue poses another major challenge to completely freeze the target tumor. Insufficient freezing, which will lead to the untreated tumor cells around large blood vessels, is the major reason for tumor survival which results in many local recurrences (Kim et al., 2008; Deng and Liu, 2005; Jungraithmayr et al., 2004). From the heat transfer perspective, a large blood vessel (also termed a thermally significant vessel) denotes a vessel larger than 0.5 mm in diameter (Kim et al., 2008; Chato, 1980). Anatomically, tumors are often situated close to or embedded with large blood vessels, since the growth of a tumor primarily depends on the nutrients supplied by its blood vessel network. It is well known that the blood flowing through large blood vessels acts as a heat source or heat sink and can dramatically affect the temperature profiles of cooled or heated tissue (Crezee and Lagendijk, 1992).

During cryosurgery, the blood flow inside a large vessel represents a heat source that heats the nearby frozen tissue and, thereby, limits the freezing lesions during cryosurgery. Furthermore, the possibility of unexpected complication will arise if the adjacent blood vessels are correspondingly damaged. Under this condition, a part of the vital tumor cells may remain out of the cryolesion and may potentially lead to tumor recurrence after cryosurgical treatment. More specifically, tumor cell survival in the vicinity of large blood vessels is often correlated with tumor recurrence after cryosurgical therapy (Berger and Poledna, 2001). Consequently, it is difficult to implement an

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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)
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
$\mathbf{x}$	Eulerian coordinates
x, y, z	Coordinate components for the Eulerian mesh
Δx, Δy, Δz	Mesh spacing

Greek symbols

ρ	density (kg m^{-3})
ω	the blood perfusion rate per unit tissue volume (kg m^{-3} s^{-1})
β	blood vessel complexity
α	ice-ball shape irregularity

Subscripts

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

effective cryosurgery when a tumor is contiguous to a large blood vessel. Numerical simulation technique is often used to obtain the transient thermal field inside the target tissue as long as the boundary conditions, initial conditions and the thermal properties of the target are known and accurately installed.

Many numerical models have been formulated to simulate the heat transfer in bio-tissue (Kim et al., 2008; Peng et al., ; , 2011,; Zhao et al., ; Rossi and Rabin, 2007; Xue et al., 2013). Among the many of bioheat models, the one that is extensively applied is the Pennes model (Pennes, 1948). It employs a perfusion heat source term to simplify complex blood flows. The Pennes bioheat model (Kim et al., 2008) has been found to be accurate, and has been successfully employed in numerous biomedical applications, viz., thermal therapy (Okajima et al., 2009; Absalan et al., 2012), light-tissue interaction (Kim and Guo, 2007), evaluation of skin burning effect (Talukdar et al., 2014), and cryotherapy (Zhao and Chua, 2012; Ge et al., 2016) etc. However, studies have also demonstrated that the Pennes bioheat equation is better suited to model the heat exchange due to capillary blood perfusion within the tissue. However, it has limitation when it comes to evaluating the significant thermal effect of blood flow associated with relatively larger diameter vessels (Singh et al., 2014).

To consider the heating effect of blood flow, some studies have simplified the blood vessels via fractal-like tree networks or reducing them to a thermally-effective one. Miao et al. (Miao et al., 2016) developed an analytical model for equivalent thermal conductivity of the damaged network based on fractal. Dombrovsky et al. (Dombrovsky et al., 2012) developed an advanced thermal model, which coupled both energy equations of the arterial blood temperature and the tissue temperature. Huang et al. (Huang et al., 2015) proposed a sentinel convergence value (SCV)-controlled 7th order temperature-based adaptive power scheme, which is applied for hyperthermia with large counter-current blood vessels in tumors. Chua (Chua, 2013) developed a computational cryo-freezing model that incorporates a simplified mathematical description of the vascular morphology. Complex vascular network with varied blood flows were simplified and modeled as tree-like branched fractal network.

It is evident that a major limitation of the above models is that they did not consider the complex structures of blood vessels and their thermal impacts, particularly large vessels. Moreover, many of these numerical studies employ a collective perfusion term and thermal conductivity to quantify the thermal effect of blood heat transfer. Thus far, little effort has been devoted to judiciously study the influence of the structure distribution of blood vessels on heat transfer process. The relationship between the geometrical features of the vessel network and the related thermal influence is thus not well understood or pursed.

The present study employs a hybrid approach. It involves the Pennes bioheat equation to study the heat transfer problem in the perfused tissue domain while incorporating an immersed boundary condition to present the heat transfer in the vascularized domain. The method employs the Eulerian mesh points to present the whole computational domain and the Lagrangian points to present the boundary condition, which can significantly simplify the implementation of the complex boundary conditions caused by the vascular system. Through this hybrid approach, a comprehensive investigation on the thermal effects of the vascular structure of a three-dimensional (3D) model during tumor cryo-freezing process is presented.

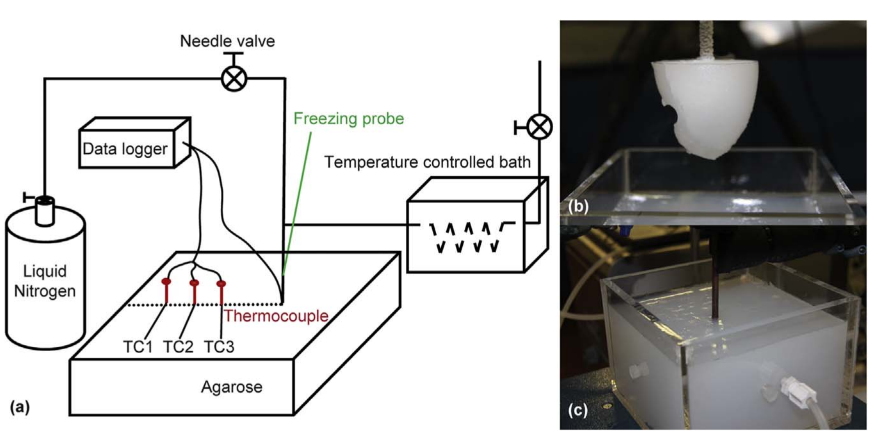

Fig. 1. Schematic and pictorial view of the experimental set-up and the layout of thermocouples.