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## Mathematical study of probe arrangement and nanoparticle injection effects on heat transfer during cryosurgery

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#### ABSTRACT

Blood vessels, especially large vessels have a greater thermal effect on freezing tissue during cryosurgery. Q2 Vascular networks act as heat sources in tissue, and cause failure in cryosurgery and reappearance of cancer. The aim of this study is to numerically simulate the effect of probe location and multiprobe on heat transfer distribution. Furthermore, the effect of nanoparticles injection is studied. It is shown that the small probes location near large blood vessels could help to reduce the necessary time for tissue freezing. Nanoparticles injection shows that the thermal effect of blood vessel in tissue is improved. Using Au, Ag and diamond nanoparticles have the most growth of ice ball during cryosurgery. However, polytetrafluoroethylene (PTFE) nanoparticle can be used to protect normal tissue around tumor cell due to its influence on reducing heat transfer in tissue. Introduction of Au, Ag and diamond nanoparticles combined with multicryoprobe in this model causes reduction of tissue average temperature about 50% compared to the one probe.

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#### 1. Introduction

Cryosurgery is a medical technique to destroy abnormal or diseased tissues by exploiting cryogenic freezing temperatures. Comparing with other treatments such as surgical excision, radiation therapy and chemotherapy, cryosurgery has attractive clinical advantages. These advantages include less cost, less pain, less invasiveness, reduced bleeding, shorter recovery time, and shorter duration of hospitalization. Using this method is applicable in treating skin, liver, lung, and bone cancer [1-3].

Cryosurgery mechanism is a method using a probe usually with liquid nitrogen that lowers the temperature of cancerous tissue and destroys it. Frozen tissue volume can be affected by the probe, probe temperature, tissue contacting surface area and duration of contact. Thermal conductivity of tissue is also an effective factor. Ideal cryosurgery freezes quickly, thaws slowly, and then freezes the second cycle. The aim of cryosurgery is that to reach death cancerous tissue while preventing injury to surrounding normal tissue. In this case, time and temperature of thawing, and the number of freeze-thaw cycles are factors which affect the performance of cryosurgery [4]. One of the most significant current discussions in cryosurgery is tissue temperature distribution which some researchers investigated thermal effects of cancerous tissue in cryosurgery [5–7]. By obtaining temperature distribution

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in tissue during cryosurgery, it is demonstrated that tissue temperature and cooling rate are two significant operational factors in successful cryosurgery. It is also necessary that predict rate of cooling to destroy cancerous cells [8].

So far, several studies have been carried out to consider specific cryoprobes and multiple probes in cryosurgery simulation. Zhao et al., developed an analytical model to study performance of bifurcate cryoprobes especially for irregularly shaped tumors [9]. Zhao et al., in another research assessed the performance of a hybrid cryoprobe operating under freeze-thaw cycles [10]. Based on their observations, the proposed cryoprobe destroyed large tumors with irregular shape. As well, the mechanism of the cryoprobe can protect normal surrounding tissues. Chua used several probes to form an ice ball with irregularly shaped tumor, and the results showed that effective factors which form ice ball are the number of probes and their positions [11].

Numerous studies conducted to investigate effect of freezethaw cycles. Zhang et al. developed a numerical algorithm based on one-dimensional finite difference method to describe the process of thawing [12]. Chua et al. studied a model in accordance with thermal freeze-thaw process in a biological system [13]. This paper assessed ice front in both primary and secondary process of freezing and mandatory thawing. The results showed that double of freeze-thaw cycles can create more ice ball.

Recent developments in the field of nanotechnology have heightened the need for studying nanotechnology in cryosurgery. Loading of nanoparticle to cryosurgery is another approach to improve the temperature distribution of tissue. According to

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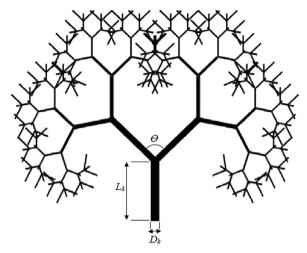
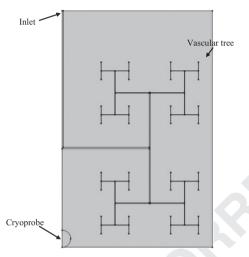


Fig. 1. The fractal model of vascular tree.



**Fig. 2.** The schematic of the model geometry (the total level of the vascular tree is 6).

recent research, injection of nanoparticles with high thermal conductivity into the cancerous tissue accelerates the freezing process, and increases the volume of the ice ball [15–19]. In addition, incorporating nanoparticles with low thermal conductivity into the surrounding healthy tissue can protect it during cryosurgery [20–22].

The blood flow and blood perfusion within the tissue act as heat sources which limit the destruction process of diseased tissues. This has been a major challenge in cryosurgical studies in the last decade. In order to control the freezing process in cryosurgery, many researchers have studied the thermal effects of blood vessels in tissues [23–26]. These studies showed that the heating caused by the blood stream in larger vessels can produce sharp temperature gradients, and this cooling is insufficient to terminate diseased tissues. Also, with increasing the radius of blood vessels and blood flow velocity, the tissue freezing rate is strongly reduced.

Literature studies the thermal effects of blood vessels in the tissue during cryosurgery but no appropriate strategy has been proposed for this problem. Therefore this study proposes a numerical simulation to overcome thermal effects of vascular networks. The associated system of equations consists of continuity, momentum and energy equations with appropriate boundary conditions. The equations are solved by finite element method (FEM) to evaluate the thermal impact of blood vessels on the heat transfer process. Allocating different location and size for probes with incorporating nanoparticles demonstrates that the impact of

**Table 1**The geometric parameters of all branching levels of the vascular tree.

K	0	1	2	3	4	5	6
Diameter (µm)	500	325	211	137	89	58	38
Length (μm)	30,000	18,900	11,907	7501	4725	2977	1876

major blood vessels at cryosurgical process diminish the effect of heat source. The performance of several nanoparticles is presented and compared to determine the best outcome. Our finding of this work will develop the cryosurgical procedures especially when cancerous cells are located near large blood vessels.

#### 2. Computational method

#### 2.1. Geometry and governing equations

The model geometry includes a normal tissue and its vascular tree. Actually, the structure of the vascular system is very complex to describe. Fig. 1a shows a three-dimensional vascular tree. In this study, the geometry of the model is considered in two dimensions. The computational domain has a rectangular geometry with a size of 66 mm in the *X* direction and 52 mm in the *Y* direction.

A considerable amount of literature has shown that arrangement of blood vessels in various organs of body is often described using fractal method. Recently, the complex vascular trees of a lung sample are studied by the fractal tree-like branched network [22]. In subsequent sections, to calculate the tissue temperature distribution the fractal tree-like model is employed. The vascular tree in fractal method is a single vessel which is split into two sections. Then each of these parts is divided into two divisions, and thus onward. Fig. 1 shows the fractal model of the vascular tree in tissue. In this three-dimensional figure, k, L and D show the level of branching, length and radius of the vessel, respectively. Likewise, the value of the bifurcation angle,  $\theta$  can vary between 75° and 90°. The detailed of fractal tree-like model for this study has been presented in Shi et al. investigation [23]. Also, branching level is assumed to be 6 and the bifurcation angle  $\theta$  is 180° in two dimensional spaces. The geometric parameters of all branching level of the vascular tree are shown in Table 1.

The cryoprobe has a circular geometry and its radius is equal to  $L_6$  (see Table 1, 1876  $\mu$ m), which is length of the 6th level in the vascular tree. This cryoprobe is located along the opposite side of the entrance of the blood vessel. Model geometry may consider symmetric, and so half of the model is investigated, which is depicted in Fig. 2.

From the numerical point of view, the finite element method is considered as an approach to solve the model numerically. That the blood flows in the blood vessels at a temperature of 310 K and at a constant rate is assumed. As well, the blood flows in the tissue are not frozen during cryosurgery. During cryosurgery, the tissue is divided into frozen, mushy and unfrozen regions since the phase transition occurs between 273 K and 263 K temperature range. The temperature of the phase change will be assumed constant at 273 K.

Equations of continuity, momentum and energy in the unsteady incompressible form govern blood vessels and normal tissue. The compressive stress and gravity are neglected in these equations. Since physical characteristics of blood and tissue are dissimilar, the heat transfer is different in these two regions [23]. Physical properties of tissue and blood are listed in Table 2.

The energy equation for the normal tissue is as follows:

$$(\rho c)_t \frac{\partial T_t}{\partial t} = \nabla \cdot (k_t \nabla T_t) + Q_{bio}$$
(1)

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