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Simulation of delivering oxygen directly to the target tissues by injection ☆

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Abstract

Oxygen is vital to all animal life. Hypoxia is one of the most threatening factors to human health in emergency care clinics. However, the currently available methods to supply oxygen for patient with hypoxia are generally too slow to be effective. In this paper, we proposed a new conceptual method to directly deliver oxygen to the target tissues in the deep body, which is generally inaccessible by traditional way, through injection of solution with high oxygen content. Particularly, the cooling solution was administered to decrease the consumption rate of the oxygen and thus lengthen the endurable time for the patient, aiming to spare more valuable times for a clinical rescue. To evaluate the feasibility of this method, a mathematical model was established to characterize the multi-mode transport process, which is simultaneously coupled with fluid flow, heat transport and mass diffusion events. Preliminary simulation indicates that this method can quickly improve and maintain well the oxygen level in the target tissues inside the deep biological body. It may open a brand new technical strategy for tissue oxygen delivery, which would find significant applications in emergency rescue, especially in those clinical situations requesting immediate and volumetric oxygen supplying.

Keywords: Oxygen delivery; Circulation arrest; Bioheat and mass transfer; Emergency rescue; Hypoxia; Hypothermia resuscitation; Brain cooling; Neural system

1. Introduction

Oxygen is vital to all animal life [1,2]. People can survive for weeks without food, days without water, yet only minutes without oxygen. Without oxygen, the metabolism in cells turns from aerobic to vastly inefficient anaerobic metabolism. Only one eighth of the energy is produced at the expense of producing a lot of lactic acid. Cells do not function well in an acidic environment and tend to die. Therefore, it can never be over emphasized that time is life for those patients subject to hypoxia. If the oxygen level of the tissue or, more specifically the brain of the patient is well maintained, for minutes, it would significantly increase the probability for the patients to be successfully rescued [3–5]. The major approach currently used in emergency clinics to supply oxygen for a patient in hypoxia is to let the patient respire supplemental oxygen. However, there exist a series of problems before the oxygen can be transported from the lung into the important organs such as the brain. For example, such approach may not be able to deliver oxygen to the anoxic tissue very timely, the life of the patient therefore still subjects to loss. Clearly, if one can directly improve the oxygen level at the anoxic tissue just for minutes, the situations would be completely different [6–8].

As is well known, oxygen is mainly absorbed by hemoglobin in the blood and then transfered to the neuron cell over the whole body. Neuron homeostasis is strongly dependent on an adequate supply of oxygen by the blood. Low oxygen level is undesirable because it affects the neuron metabolism and may even induce toxic chemicals [5]. Without timely oxygen delivery, metabolism would quickly stop. Several possible results would be like [9]:

(1) The process of metabolism will slow down or just cease;
(2) The metabolism turns to depend on the materials that have already been stored in the neuron;
(3) The storage of oxygen in a neuron becomes reduced;
(4) More and more intermediate products are accumulated in a neuron, which may be poisonous;
(5) The function of neuron is entirely destroyed at last.

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Nomenclature

A	surface area of the tissue per unit volume, $= 6/d$	m^{-1}
C_1	oxygen concentration of tissue	$mol \cdot m^{-3}$
C_2	oxygen concentration of solution	$mol \cdot m^{-3}$
C_a	oxygen concentration of arterial blood	$mol \cdot m^{-3}$
C_{body}	initial oxygen concentration of tissue	$mol \cdot m^{-3}$
C_{high}	initial high oxygen concentration of injected solution	$mol \cdot m^{-3}$
c_b	heat capacity of blood	$J \cdot kg^{-1} \cdot K^{-1}$
c_{p1}	heat capacity of tissue	$J \cdot kg^{-1} \cdot K^{-1}$
c_{p2}	heat capacity of solution	$J \cdot kg^{-1} \cdot K^{-1}$
D	hydrodynamic radius, $= 4\varepsilon_v / A(1-\varepsilon_v)$	m
d	approximate diameter of the solid spherical particles	m
D_1	diffusion coefficient of oxygen in the tissue	$m^2 \cdot s^{-1}$
D_2	diffusion coefficient of oxygen in solution	$m^2 \cdot s^{-1}$
h_C	oxygen transport coefficient between tissue and solution	$J \cdot m^{-3} \cdot K^{-1} \cdot s^{-1}$
h_T	heat convection coefficient between fluid and tissue	$J \cdot m^{-3} \cdot K^{-1} \cdot s^{-1}$
M	molecular weight of the solution	$kg \cdot mol^{-1}$
Nu	Nusselt number	
Q_C	oxygen consumption rate	$mol \cdot m^{-3} \cdot s^{-1}$
$\dot{Q}_m$	flow flux of the fluid during the injection	$l \cdot s^{-1}$
Q_T	metabolic heat generation rate	$W \cdot m^{-3}$
Q_{T0}	metabolic heat generation rate when the temperature of tissue is 37 °C	$W \cdot m^{-3}$
r_0	radius of the pinhole	m
r_{int}	transient position of the moving front of the fluid	m
Sh	Sherwood number	
T_1	temperature of tissue	K
T_2	temperature of fluid	K
T_a	temperature of arterial blood	K
T_{body}	initial temperature of tissue	K
T_{low}	initial low temperature of the injected fluid	K
t	time	s
u_0	velocity of the fluid at the pinhole	$m \cdot s^{-1}$
V_I	volume of the first part	m^3
V_{II}	volume of the second part	m^3
V_{III}	volume of the third part	m^3
V_{O_2}	molar volume of oxygen	$m^3 \cdot mol^{-1}$
V_{tissue}	tissue volume	m^3
w_b	blood perfusion rate	s^{-1}

Greek symbols

α	volume of the fluid can be absorbed per unit tissue volume	
β	volume of the fluid taken away by blood per unit bulk volume per unit time	s^{-1}
ε	porosity	
ε_s	area porosity	
ε_v	volumetric porosity	
η	temperature coefficient	
λ_1	thermal conductivity of tissue	$W \cdot m^{-1} \cdot K^{-1}$
μ	viscosity of the solution	$kg \cdot m^{-1} \cdot s^{-1}$
ρ_1	density of tissue	$kg \cdot m^{-3}$
ρ_b	density of blood	$kg \cdot m^{-3}$
ϕ	temperature constant = 3.0	
ψ	association parameter for the fluid	

Subscripts

1	tissue
2	fluid

Up to now, cerebral hypothermia has been demonstrated as a principal means of neurologic protection during cardiac operations, especially for procedures requiring reduced perfusion or circulatory arrest [10–13]. The low temperature is usually achieved through a systemic body cooling, or almost entirely by ventilating cold blood during hypothermic cardiopulmonary bypass [14–16]. When circulatory arrest occurs, hypothermia is commonly adopted to prevent overheating, which is a result of decreased cooling by lowered cerebral blood flow, continuous oxygen consumption and metabolic heat generation [17,18]. The efficacy of hypothermia in preserving neurological function when instituted before and during certain no-flow cardiovascular states has been well documented both clinically and experimentally in animal modes since the 1950s. In laboratory studies, mild hypothermia (34 °C) was discovered to mitigate brain damage significantly after cardiac arrest [19,20]. Some previous results also found that a common disadvantage inherited in systemic body cooling was its substantial slow cooling rate because the conductive heat loss through the skull surface or countercurrent heat exchange was minimal [21–24]. In general, the hypothermia is performed for several hours or even more to achieve the desired temperature.

Clearly, sustenance of a mammalian living system depends on transport of oxygen to individual cells and maintaining well of the temperature in a low level [5,6,8,18]. For this reason, different kinds of oxygen supplying methods have been tried for many years. Overall, most of them fall in the category of indirect approaches. There is at present no ideal ways to deliver oxygen directly to the target tissues inside the deep human body. Here, we proposed a new technical route of supplying oxygen for target hypoxic tissues (such as brain tissue) by injecting solution with high oxygen content. This strategy will help bring lots of oxygen to the anoxic tissue via a direct way. The reason to use cooling solution for the injection lies in that low temperature can decrease the oxygen consumption in the tissues, which will also help maintain the oxygen level [1,6]. Therefore the present method has double significances for clinical practices. One is to supply the oxygen to the target as desired. The other is to prevent the temperature from increasing too much high and thus over-consumption of oxygen. For

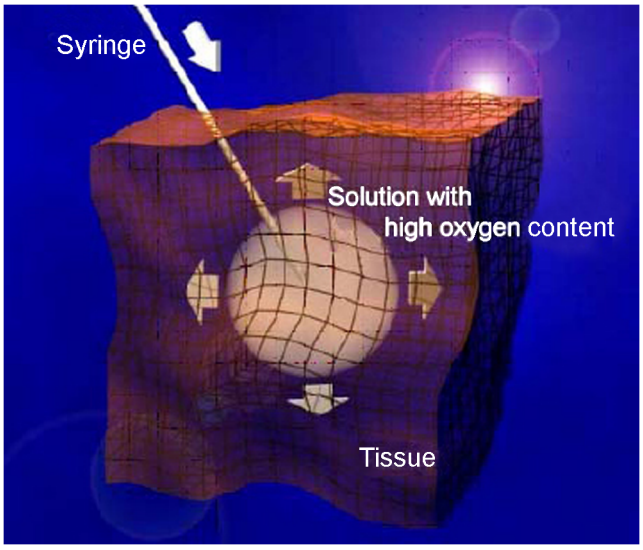

Fig. 1. Schematic for directly delivering oxygen to the target tissues in deep biological body.

the first step to understand the new approach, a comprehensive analysis on the oxygen transport behavior thus involved will be performed in this study.

2. Physical model of the simulation

Numerical investigations were performed to evaluate the feasibility of the present method. Generally, for the minimally invasive consideration, the injector should be designed as very slim to minimize the mechanical damage due to insertion, Therefore the analysis given below approximately neglects the influence brought about by the needle. Strictly speaking, oxygen transport over the tissues is a three-dimensional behavior. But completely simulating such a multi-mode process is extremely difficult. To set up a preliminary foundation for the oxygen transport in the tissue, an approximate one-dimensional model in spherical coordinate as shown in Fig. 1 will be particularly studied. The pinhole of the syringe was simplified as a spherical solution (oxygen) supplying source, and the tissue was treated as a porous medium, which consists of solid spherical particles and physiological liquid. As is well known, biological systems are comprised of porous capillary beds and cells that are heterogeneous, multi-phasic, and surface-dominated [25,26]. Therefore, treating the tissues as a porous medium, which consists of solid particles, is reasonable. Under these premises, the present problem was simplified as one with heat and fluid (oxygen) transport from a point source embedded in the porous medium.

3. Mathematical model

3.1. Postulated conditions

Before setting up the heat, fluid transport and oxygen diffusion equations, several assumptions were made as follows:

(1) The tissue is treated as a uniform porous medium, whose specific vasculature is neglected in the model. In the tissue, ε_s is isotropic and independent of the normal direction and the position of the referenced section, $\varepsilon_s(r) = \varepsilon_s$, where ε_s is defined as the area porosity, which is the ratio of surface area occupied by cooling solution to the whole surface area in referenced section. This assumption leads to $\varepsilon_v = \varepsilon_s = \varepsilon$, where ε is the porosity; ε_v is defined as the volumetric porosity, which is the ratio of volume occupied by hot fluid to the whole volume.

(2) The fluid injected into the tissues from the pinhole is divided into three parts. The first part penetrates into the tissue cell and becomes part of the tissue, whose volume V_{I} is proportional to the tissue volume V_{tissue}, i.e. $V_{\mathrm{I}} = \alpha V_{\mathrm{tissue}}$, where α is the coefficient of proportionality (m^3fluid)·(m^{-3} tissue), or the volume of the fluid can be absorbed per unit tissue volume. The second part V_{II} penetrates into the vein, and is brought out of the control volume by the flux of the blood. The volume V_{II} is proportional to the whole volume V, i.e. $V_{\mathrm{II}} = \beta V$, where β is the coefficient of proportionality or the volume of the fluid taken away by blood per unit bulk volume per unit time. The third part remains in the tissue space (among the tissue cells) and fills the pores of the tissue. The volume V_{III} is also proportional to the bulk volume V, $V_{\mathrm{III}} = \varepsilon V$.

(3) Assume that the cooling solution flows out of the surface of one small sphere, whose radius is r_0. Here, r_0 is radius of the pinhole. For the same reason as mentioned earlier, influence of the needle tube was neglected here.

(4) The speed with which the cooling solution fills the spaces among the tissues should be much larger than that for the cooling solution to transfer along the radial direction. That is to say, within the sphere area inside the moving interface of the cooling solution the solution is saturated anywhere and anytime. This is reasonable, since usually the injection speed should not be too fast during the operation for safety consideration.

(5) As soon as the solution of V_{I} enters the tissue, a thermal equilibrium is established immediately. Because α is so small that its influence on the property of tissue can be neglected, i.e. the property parameters of tissue can still be adopted from common reference data [27–29].

(6) Assume that the velocity of the cooling solution is uniform in all direction at the pinhole $r = r_0$, and is independent of time. This assumption is reasonable because the injection velocity is always not very large. Thus, the problem is successfully simplified as a one-dimensional heat and fluid transport model.

(7) Assume that the impetus for oxygen transportation in tissue or solution is through only diffusion. It is a simple and effective way to analyze the oxygen transportation in tissues.

(8) Assume that the oxygen concentration in the tissue is equal to that of the blood in the vein. In fact, the oxygen concentration in the tissue is a little higher than that of the blood in the vein. Such minor difference between them is ignored in the paper for simplicity.

What should be pointed out is that the model and postulated conditions presented above are still preliminary for simplicity. For a more comprehensive simulation, tremendous efforts are needed in the near future. Our main object here is to provide the first theoretical foundation for characterizing the basic feature of the new oxygen delivery method. Although simple, the analysis provided is still intuitive for understanding the method.

3.2. Transport velocities for the fluid and the moving interface

Before carrying out the analysis, the transient position of the moving front of the injected solution should be worked out first. Based on the previous assumption, we can easily derive the transient position of the moving front of the fluid as follows by considering the mass conservation of the whole region:

$$r_{\text{int}} = \left[r_0^3 + \frac{3u_0 r_0^2 \varepsilon}{\beta}\left(1 - e^{-\frac{\beta t}{\varepsilon+\alpha(1-\varepsilon)}}\right)\right]^{1/3} \tag{1}$$

where u_0 is the velocity of the fluid at the pinhole $r = r_0$. Considering the assumption (6), the velocity can be obtained as:

$$u_0 = \frac{\dot{Q}_m}{4\pi r_0^2} \tag{2}$$

where $\dot{Q}_m$ is the flow flux of the fluid during the injection.

Considering the mass conservation of the liquid in the region $[r_0, r]$ ($r < r_{\text{int}}$), the transport velocity of the fluid can be obtained as:

$$u = \frac{r_0^2 u_0}{r^2} - \frac{\beta(r^3 - r_0^3)}{3\varepsilon r^2} \tag{3}$$

3.3. Heat transfer equations

Heat transfer equations for fluid or tissue should be established separately. In the equations below, subscript '1' represents the tissue and subscript '2' is for the fluid.

The most widely accepted bioheat model, Pennes equation, is adopted here to simulate the heat transfer in solid tissue. Within the moving interface ($r < r_{\text{int}}$), considering the assumption (2) mentioned above, one can get the heat transfer equation for the tissue of the inner region:

$$\rho_1 c_{p1}\frac{\partial T_1}{\partial t} = \lambda_1 \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial T_1}{\partial r}\right) + \rho_b c_b w_b (T_a - T_1) + Q_T + \rho_2 c_{p2}\beta(T_2 - T_1) + h_T(T_2 - T_1) \tag{4}$$

where ρ_1 is the density of tissue, c_{p1} the heat capacity of tissue, λ_1 the thermal conductivity of tissue, ρ_b the density of blood, T_1 the temperature of tissue, T_2 the temperature of fluid, T_a the temperature of arterial blood, w_b the blood perfusion rate, Q_T the metabolic heat generation rate, h_T the heat convection coefficient between fluid and tissue. h_T is given as follows [30]:

$$h_T = \frac{Nu\,\lambda_1 A}{D} \tag{5}$$

where $A = 6/d$ is the surface area of the tissue per unit volume, d is approximate diameter of the solid spherical particles, D the hydrodynamic radius, and given by $D = 4\varepsilon_v/A(1-\varepsilon_v)$, λ_1 the thermal conductivity of tissue, Nu the Nusselt number, and approximately treated as 4.0 [30].

The heat transfer equation for the tissue of the outer region ($r > r_{\text{int}}$) can also be easily obtained. In this region, there is no coming solution inside it, so the last two items disappear from Eq. (4), i.e.

$$\rho_1 c_{p1}\frac{\partial T_1}{\partial t} = \lambda_1 \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 \frac{\partial T_1}{\partial r}\right) + \rho_b c_b w_b (T_a - T_1) + Q_T \tag{6}$$

The reason why the parameter ε does not appear in both Eq. (4) and Eq. (6) is that the value of ρ_1 and λ_1 has already included the influence brought by ε. The temperature dependence of w_b and Q_T must be considered in the simulation. This is because the injection cooling is a transient process. In this side, w_b can be approximately written as a linear form [31]:

$$w_b = w_{b0} + w_{b1} \cdot T_1 \tag{7}$$

and the Q_T [6]:

$$Q_T = Q_{T0}\phi^{(T_1-37)/10} \tag{8}$$

where Q_{T0} is the metabolic heat generation rate when the temperature of tissue is 37 °C, ϕ the temperature constant which is generally equal to 3.0 [5,7,8,14], and the constant $w_{b0} = 3.287 \times 10^{-4}\ \text{s}^{-1}$, $w_{b1} = 1.924 \times 10^{-5}\ \text{s}^{-1}\cdot{}^{\circ}\text{C}^{-1}$ [31].

Considering the mass conservation and the heat balance conditions, one can easily obtain the heat transfer equation for the moving solution as:

$$\varepsilon\rho_2 c_{p2}\left(\frac{\partial T_2}{\partial t} + u\frac{\partial T_2}{\partial r}\right) = \varepsilon\lambda_2 \frac{1}{r^2}\left(r^2\frac{\partial T_2}{\partial r}\right) + h_T(T_1 - T_2) \tag{9}$$

The initial conditions can read as:

$$T_1|_{\tau=0} = T_{\text{body}} \tag{10a}$$

$$T_2|_{\tau=0} = T_{\text{low}} \tag{10b}$$

where T_{body} is the initial temperature of tissue, T_{low} the initial low temperature of the injected fluid.

The boundary conditions for the whole region are defined as follows:

$$\left.\frac{\partial T_1}{\partial r}\right|_{r=r_0} = 0 \tag{11a}$$

$$T_2|_{r=r_0} = T_{\text{low}} \tag{11b}$$

$$\frac{\partial T_1}{\partial r}|_{r=\infty} = 0 \tag{11c}$$

At the moving interface, the temperature should satisfy these equations:

$$\left.\frac{\partial T_1}{\partial r}\right|_{r=r_{\text{int}}^-} = \left.\frac{\partial T_1}{\partial r}\right|_{r=r_{\text{int}}^+} \tag{12a}$$

$$T_1|_{r=r_{\text{int}}^-} = T_1|_{r=r_{\text{int}}^+} \tag{12b}$$

$$\left.\frac{\partial T_2}{\partial r}\right|_{r=r_{\text{int}}^-} = 0 \tag{12c}$$

3.4. Oxygen transport equations

In analogy to the heat transfer modeling, the oxygen transport equations can be obtained in the similar way [32]. Following the assumptions (7) and (8) as mentioned above, the oxygen transport can also be divided into three parts: oxygen transport in the inner region of tissue ($r < r_{\text{int}}$), oxygen transport in the outer region of tissue ($r > r_{\text{int}}$) and oxygen transport in the solution.

What should be pointed out is that, in analogy to the Pennes equation, the contribution of the arterial to the oxygen concentration in tissue can also be considered in a similar way. The blood perfusion rate w_b was introduced into the oxygen transport equations of tissue. The only difference between the heat transfer equation and the oxygen transport equation lies in that the temperature difference between the arterial and vein is replaced by the oxygen concentration difference. So, according to the assumption (8), oxygen transport equation for the tissue of the inner region ($r < r_{\text{int}}$) can read as:

$$(1-\varepsilon)\frac{\partial C_1}{\partial t} = (1-\varepsilon)D_1\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C_1}{\partial r}\right) - Q_C + h_C(C_2 - C_1) + w_b(C_a - C_1) \tag{13}$$

where C_1 is the oxygen concentration of tissue, C_2 the oxygen concentration of solution, C_a the oxygen concentration of arterial blood, D_1 the diffusion coefficient of oxygen in the tissue, Q_C the oxygen consumption rate, h_C the oxygen transport coefficient between tissue and solution which can be expressed as:

$$h_C = \frac{ShD_1A}{D} \tag{14}$$

This equation is proposed to calculate the oxygen transport coefficient between tissue and solution in analogy to the heat convection coefficient between liquid and solid phases (Eq. (5)) [30]. For the forced convection over external boundaries in the presence of a porous medium, the Sherwood number Sh is approximately treated as $Sh = 2.0$ [33], $A = 6/d$, $D = 4\varepsilon_v/A(1-\varepsilon_v)$.

The temperature dependence of D_1 and Q_C should be considered in the simulation, D_1 can be written as [34]:

$$D_1 = a \cdot e^{bT_1} \tag{15}$$

and the Q_C [1]:

$$Q_C = k' C_1 \cdot \eta^{(T_1-37)/10} \tag{16}$$

where the constant $a = 3.95 \times 10^{-10}$ m^2·s^{-1}, $b = 4.6\%$·°C^{-1}, $k' = 4.7 \times 10^{-3}$ s^{-1}, and η is the temperature coefficient and often regarded as 2.5 [5].

The oxygen transport equation for the tissue of the outer region ($r > r_{\text{int}}$) reads as:

$$(1-\varepsilon)\frac{\partial C_1}{\partial t} = (1-\varepsilon)D_1\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C_1}{\partial r}\right) - Q_C + w_b(C_a - C_1) \tag{17}$$

Considering the mass conservation of the oxygen, the oxygen transport equation for the liquid can be written as:

$$\varepsilon\frac{\partial C_2}{\partial t} + \varepsilon\frac{1}{r^2}\frac{\partial}{\partial r}\left(C_2 u r^2\right) = \varepsilon D_2\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C_2}{\partial r}\right) - h_C(C_2 - C_1) \tag{18}$$

where D_2 is the diffusion coefficient of oxygen in solution. The temperature dependence of D_2 is also considered in this simulation as follows [35]:

$$D_2 = 5.878 \times 10^{-10}\frac{(T_2 + 273.15)(\psi M)^{0.5}}{\mu V_{O_2}^{0.6}} \tag{19}$$

where ψ is an "association" parameter for the fluid, which is regarded as 2.26 [36], M the molecular weight of the solution, μ the viscosity of the solution, V_{O_2} the molar volume of oxygen.

The initial conditions can read as:

$$C_1|_{t=0} = C_{\text{body}} \tag{20a}$$

$$C_2|_{t=0} = C_{\text{high}} \tag{20b}$$

where C_{body} is the initial oxygen concentration of tissue, C_{high} the initial high oxygen concentration of injected solution.

And the boundary conditions read as:

$$\left.\frac{\partial C_1}{\partial r}\right|_{r=r_0} = 0 \tag{21a}$$

$$C_2|_{r=r_0} = C_{\text{high}} \tag{21b}$$

$$\left.\frac{\partial C_1}{\partial r}\right|_{r=\infty} = 0 \tag{21c}$$

The oxygen concentration at the moving interface should satisfy the following equations:

$$\left.\frac{\partial C_1}{\partial r}\right|_{r=r_{\text{int}}^-} = \left.\frac{\partial C_1}{\partial r}\right|_{r=r_{\text{int}}^+} \tag{22a}$$

$$C_1|_{r=r_{\text{int}}^-} = C_1|_{r=r_{\text{int}}^+} \tag{22b}$$

$$\left.\frac{\partial C_2}{\partial r}\right|_{r=r_{\text{int}}^-} = 0 \tag{22c}$$

4. Parameters of the model

In the following studies, most of the parameters in the model are chosen as their typical values. Some parameters are still not available from literature or measurement. For a preliminary analysis, those for water will be adopted. The parameters used are listed as follows:

$\lambda_1 = 0.5$ W·m^{-1}·K^{-1}, $\lambda_2 = 0.685$ W·m^{-1}·K^{-1}

$\varepsilon = 0.3$, $\rho_1 = 1.05 \times 10^3$ kg·m^{-3}

$\rho_2 = 1.0 \times 10^3$ kg·m^{-3}, $\rho_b = 1.0 \times 10^3$ kg·m^{-3}

$c_{p1} = 4.0 \times 10^3$ J·kg^{-1}·K^{-1}

$c_{p2} = 4.18 \times 10^3$ J·kg^{-1}·K^{-1}

$c_b = 4.18 \times 10^3$ J·kg^{-1}·K^{-1}, $T_a = T_{\text{body}} = 37$ °C

$d = 1$ mm, $r_0 = 1$ mm, $M = 18$ g·mol^{-1}

$V_{O_2} = 25.6\ \text{cm}^3\cdot\text{mol}^{-1}$, $C_{\text{body}} = 2.0\ \text{mol}\cdot\text{m}^{-3}$

$C_a = 5.0\ \text{mol}\cdot\text{m}^{-3}$, $C_{\text{high}} = 9.0\ \text{mol}\cdot\text{m}^{-3}$

$Q_{T0} = 2500.0\ \text{W}\cdot\text{m}^{-3}$, $\alpha = 0.01$, and $\beta = 0.01$

All the simulations are performed with the injection velocity $1\ \text{ml}\cdot\text{s}^{-1}$.

5. Results and discussion

In order to test the feasibility of the new oxygen delivery approach, the finite difference method was used to solve the above model. The total CPU time used in a practical case-study is about 5 minutes. Here, taking account of the situation of hypoxia state, the blood perfusion w_b was deliberately halved in the calculation. Depicted in Fig. 2 is the temperature distributions in tissues at different times when $T_{\text{low}} = 5\,^{\circ}\text{C}$. It was observed that tissue was quickly cooled down with the coming of the cooling solution especially during the first 10 seconds. The reason can be attributed to that the moving speed of the interface is much faster at the early stage. Such trend can also be clearly seen from the Eq. (3). Owing to the decrease of the temperature, the oxygen consumption rate can be significantly lowered in the tissue, which is very beneficial for maintaining the oxygen concentration in a high level. Further, Fig. 3 depicts the oxygen concentration distribution inside the tissues at different time point when $T_{\text{low}} = 5\,^{\circ}\text{C}$. It can be seen that the oxygen concentration level in the tissue was significantly raised by the injection. However, it is not the case at the tissue center where the oxygen concentration appears the maximum at about the first 30 seconds. This happens because the cooling not only reduces the oxygen consumption in tissue but also decrease the diffusion coefficient of oxygen in the tissue. The region near the center has a much lower temperature than that of the far region, therefore the oxygen diffusion coefficient here is also much smaller. The oxygen concentration near the center thus increases more slowly than that at the far region. After about 30 seconds later, decrease of the oxygen consumption begins to dominate the oxygen concentration distribution, and the oxygen concentration reaches its maximum at the center. What should be pointed out is that when 5 °C solution is injected into the tissue, not only the oxygen concentration increases rapidly but also the local temperature decreases evidently. This indicates that the present method serves not only for a rapid supplying of oxygen but is also a rapid way to induce hypothermia. When subjected to ischemia, the human brain can survive much longer if its temperature could be successfully reduced by 3–5 °C. In this sense, the present method provides a promising way to prolong the patient's life by inducing an immediate local hypothermia.

Similar process can also be illustrated by Fig. 4, where the oxygen concentration distribution of tissue at different time when $T_{\text{low}} = 37\,^{\circ}\text{C}$ was given. Clearly, without the temperature variation, the diffusion coefficient remains constant over the whole region. Therefore the oxygen concentration at the tissue center will always stay at its maximum value from the beginning. Overall, no mater whether the solution for injection is cold (5 °C) or warm (37 °C), improvement of the oxygen level is rather evident. The injection of the fluid with high oxygen content can increase the oxygen concentration in the tissue in a short time. A comparison between the cases for injecting cooling solution and the warm fluid can be seen more clearly in Fig. 5. It gives the oxygen concentration variations at $r = 2$ mm

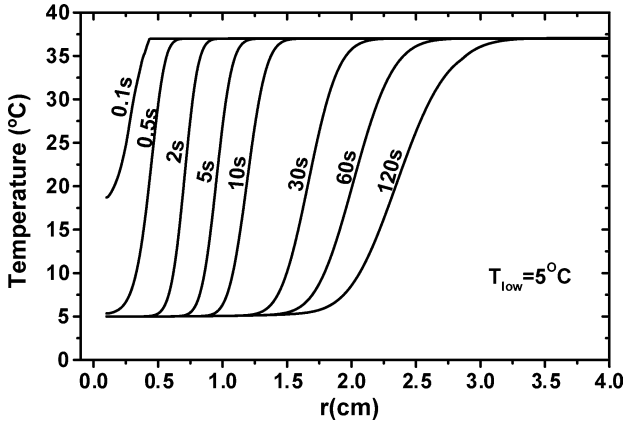

Fig. 2. The temperature distributions of tissue at different time when $T_{\text{low}} = 5\,^{\circ}\text{C}$.

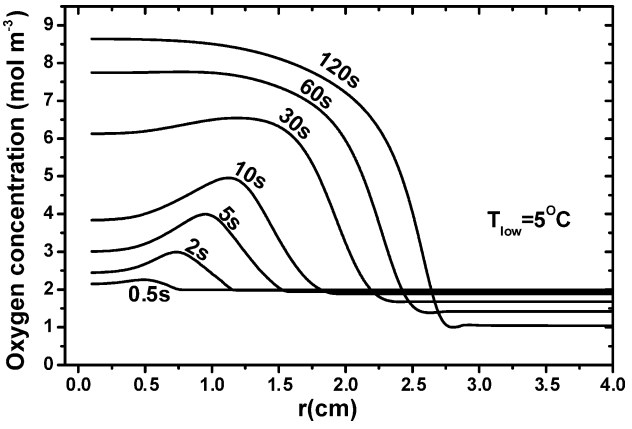

Fig. 3. The oxygen concentration distribution of tissue at different time when $T_{\text{low}} = 5\,^{\circ}\text{C}$.

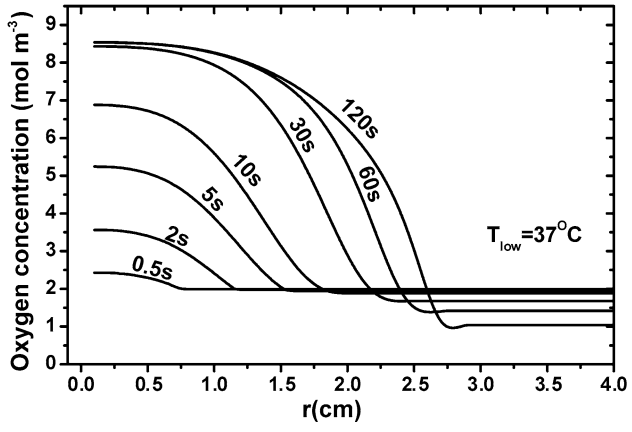

Fig. 4. The oxygen concentration distribution of tissue at different time when $T_{\text{low}} = 37\,^{\circ}\text{C}$.

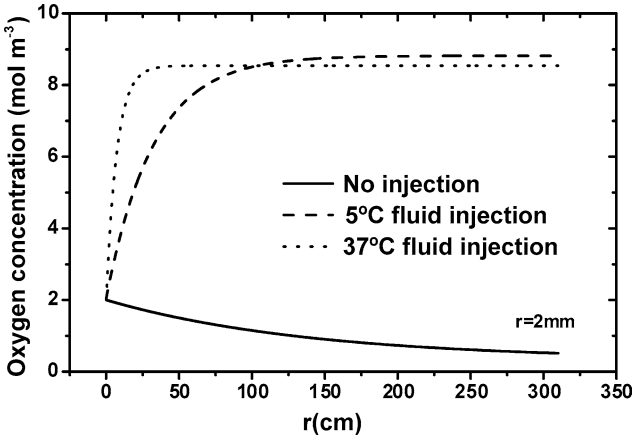

Fig. 5. The comparison of oxygen concentration variations at $r = 2$ mm under different circumstances: (1) Without injection; (2) Cooling solution injection; (3) Warm solution injection.

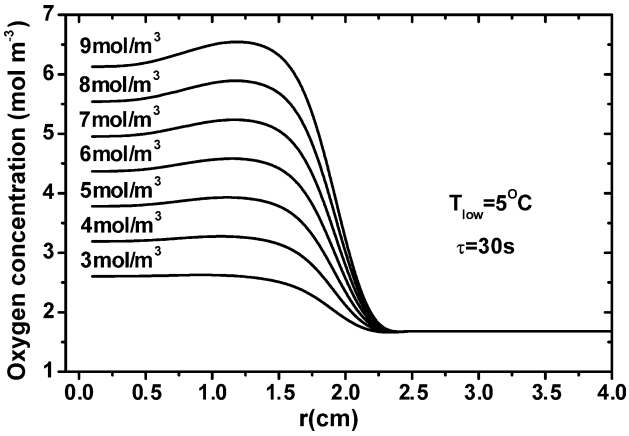

Fig. 6. The comparison of oxygen concentration distributions under different injection concentration at $t = 30$ s.

under different circumstances. The solid line depicts the oxygen concentration variation at $r = 2$ mm without any injection. The dash line gives the oxygen concentration variation with cooling solution injection (5 °C). The dot line represents the oxygen concentration variation with warm fluid injection (37 °C). It can be seen that the oxygen concentration of the tissue decreases quickly for the case without injection. The injection of solution with high oxygen content sharply improves the oxygen concentration in the tissues to be about 8.5 mol·m^{-3} within 60 seconds. Because of the influence brought about by the diffusion coefficient, the oxygen concentration with warm fluid injection increases much faster than that with cooling solution injection at first. However, the oxygen concentration with cooling solution injection will exceed that of warm fluid injection after just one minute later. Another merit for using cooling solution in the injection lies in that, it evidently decreases the oxygen consumption rate. Therefore the high-level oxygen concentration in the tissue will remain higher in a much durable time than the case injected with warm fluid. To see the influence of the oxygen concentration of the fluid, Fig. 6 gives the comparisons of oxygen concentration distributions under different oxygen concentration of the injected solution at $t = 30$ s. It can be seen that the higher the oxygen concentration of the solution, the higher the oxygen concentration for the tissue to reach. Different fluid can be used to handle various extent of hypoxia.

6. Conclusion

From the above discussion, it can be concluded that injection of cooling solution with high oxygen content into target tissue provides a very promising way for emergency rescue of hypoxia patient. The method can help increase the local oxygen concentration of tissue within a very short period. Meanwhile, injection of the cooling solution further decreases the temperature of the tissues, which then significantly lower the oxygen consumption rate. Both features will help to realize a much higher oxygen concentration and maintain well the oxygen level in tissues during hypoxia state. The present method can be used as an auxiliary way for the conventional oxygen supplying method. Owning to its extremely high efficiency in supplying oxygen, this method is expected to win a lot of treasure time for the patients to sustain longer for the rescue.

Except for the above applications, selectively supplying oxygen to the specific organs or tissues can also be very useful for some newly emerging bioengineering field such as cell transplantation or tissue culture. For example, without efficient in-situ delivery of nutrient or oxygen, the implanted stem cells or tissues may subject to death. Clearly, the concept proposed in this paper opens new opportunities for such biomedical practices. Further work will be performed along this direction in the near future.

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