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A General Set of Bioheat Transfer Equations Based on the Volume Averaging Theory

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1.1 Introduction

There has been considerable interest in developing sound and accurate thermal models that describe heat transfer within a living tissue with blood perfusion. Since the landmark paper by Pennes (1948), a number of bioheat transfer equations for living tissue have been proposed to remedy possible shortcomings in his equation. Although Pennes’ model is often adequate for roughly describing the effect of blood flow on the tissue temperature, there exist some serious shortcomings in his model due to its inherent simplicity, as pointed out by Wulff (1974), namely, assuming uniform perfusion rate without accounting for blood flow direction, neglecting the important anatomical features of the circulatory network system such as countercurrent arrangement of the system, and choosing only the venous blood stream as the fluid stream equilibrated with the tissue.

To overcome these shortcomings, a considerable number of modifications have been proposed by various researchers. Wulff (1974) and Klinger (1978) considered the local blood mass flux to account the blood flow direction, while Chen and Holmes (1980) examined the effect of thermal equilibration length on the blood temperature and added the dispersion and microcirculatory perfusion terms to the Klinger equation.

All foregoing papers concerned mainly with the cases of isolated vessels and the surrounding tissue. The effect of countercurrent heat transfer between closely spaced arteries and veins in the tissue must be taken into full consideration when the anatomical configuration of the main supply artery and vein in the limbs is treated. Following the experimental study conducted by Bazett and his colleagues (1948a, 1948b), Scholander and Krog (1957), and Mitchell and Myers (1968) investigated such an effect and successfully demonstrated that the countercurrent heat exchange reduces heat loss from the extremity to the surroundings, which could be quite significant because of a large surface to volume ratio. Keller and Seiler (1971) established a bioheat transfer model equation to include the countercurrent heat transfer, using a one-dimensional configuration for the subcutaneous tissue region with arteries, veins, and capillaries. Weinbaum and Jiji (1979) proposed a new model, which is based on some anatomical understanding, considering the countercurrent arteriovenous vessels. As pointed out by Roetzel and Xuan (1998), the model may be useful in describing a temperature field in a single organ, but would not be convenient to apply to the whole thermoregulation system. Excellent reviews on these bioheat transfer equations may be found in Chato (1980) and Charny (1992).
Khaled and Vafai (2003) and Khanafer and Vafai (2006) stress that the
theory of porous media is most appropriate for treating heat transfer in bio-
ological tissues since it contains fewer assumptions as compared to different
bioheat transfer equations. Roetzel and Xuan (1998) and Xuan and Roetzel
(1997) exploited the volume averaging theory (VAT) previously established for
the study of porous media (e.g., Cheng [1978], Nakayama [1995]), to formu-
late a two-energy equation model accounting for the thermal nonequilibrium
between the blood and peripheral tissue. In their model, the perfusion term
is replaced by the interfacial convective heat transfer term. This point should
be examined since the interfacial convective heat transfer is different from
perfusion heat transfer. Naturally, the former takes place even in the absence
of the latter.

In this chapter, we present a rigorous mathematical development based
on VAT so as to achieve a complete set of the volume averaged governing
equations for bioheat transfer and blood flow. Most shortcomings in existing
models will be overcome. We start with the case of isolated blood vessels
and the surrounding tissue, to establish a two-energy equation model for the
blood and tissue temperatures. We shall identify the terms describing the
blood perfusion and dispersion in the resulting equation and revisit the Pennes
model, the Wulff model, and their modifications.

Subsequently, the two-energy equation model is extended to the three-
energy equation model, so as to account for the effect of countercurrent heat
transfer between closely spaced arteries and veins in the blood circulatory
system. In this model, three distinctive energy equations are derived for the
arterial blood phase, venous blood phase, and tissue phase with three individ-
ual temperatures. Capillaries providing a continuous connection between the
countercurrent terminal arteries and veins are modeled introducing the perfu-
sion bleed-off rate. It will be shown that the resulting model, under appropri-
ate conditions, naturally reduces to those introduced by Chato (1980), Bejan
(1979), Weinbaum and Jiji (1985), and others for countercurrent heat transfer
for the case of closely aligned pairs of vessels. A useful expression for the lon-
gitudinal effective thermal conductivity for the tissue can be obtained without
dropping the perfusion source terms. The expression turns out to be quite sim-
ilar to Bejan’s and Wienbaum and Jiji’s expressions. Furthermore, the effect
of spatial distribution of perfusion bleed-off rate on total countercurrent heat
transfer is discussed in depth exploiting the present bioheat transfer model.

As for an application of a bioheat equation, the freezing process within
a tumor during cryoaablation therapy is investigated both analytically and
numerically. The freezing front in a tumor during percutaneous cryoaablation
can be traced exploiting a bioheat equation. It will be shown that there exists
a limiting size of the tumor that one single cryoprobe can freeze at the max-
imum. The freezing front moves radially outward from the cryoprobe and
reaches the end, where the heat from the surrounding tissue to the frozen
tissue balances with the heat being absorbed by the cryoprobe. An excellent
agreement between the analytical and numerical results is achieved for the
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time required to freeze the tumor using the cryoprobe of one single needle. The resulting analytical expression for estimating the limiting radius provides useful information for cryotherapy treatment plans.

1.2 Volume Averaging Procedure

In an anatomical view, three compartments are identified in the biological tissues, namely, blood vessels, cells and interstitium, as illustrated in Figure 1.1. The interstitial space can be further divided into the extracellular matrix and the interstitial fluid. However, for sake of simplicity, we divide the biological tissue into two distinctive regions, namely, the vascular region and the extravascular region (i.e., cells and the interstitium) and treat the whole anatomical structure as a fluid-saturated porous medium, through which the blood infiltrates. The extravascular region is regarded as a solid matrix (although the extravascular fluid is present), and will be simply referred to as the “tissue” region to differentiate it from the “blood” region.

Thus, we shall try to apply the principle of heat and fluid flow in a fluid-saturated porous medium to derive a set of the volume averaged governing equations for the bioheat transfer and blood flow. For the volume averaging (smoothing process) to be meaningful, we consider a control volume \( V \) in a

![FIGURE 1.1](image_url)

Schematic view of biological tissue.
control volume in a porous medium.

Fluid-saturated porous medium, as shown in Figure 1.2, whose length scale $V^{1/3}$ is much smaller than the macroscopic characteristic length $V_c^{1/3}$, but, at the same time, much greater than the microscopic (anatomical structure) characteristic length (see e.g., Nakayama [1995]). Under this condition, the volume average of a certain variable $\phi$ is defined as

$$
\langle \phi \rangle \equiv \frac{1}{V} \int_V \phi dV
$$

(1.1)

Another average, namely, intrinsic average, is given by

$$
\langle \phi \rangle^f \equiv \frac{1}{V_f} \int_{V_f} \phi dV
$$

(1.2)

where $V_f$ is the volume space that the fluid (blood) occupies. Obviously, two averages are related as

$$
\langle \phi \rangle = \varepsilon \langle \phi \rangle^f
$$

(1.3)

where $\varepsilon \equiv V_f/V$ is the local porosity, namely, the volume fraction of the vascular space, which is generally less than 0.1. Naturally, anatomical data are required to find the porosity. Following Cheng (1978), Nakayama (1995), Quintard and Whitaker (1993), and many others, we decompose a variable into its intrinsic average and the spatial deviation from it:

$$
\phi = \langle \phi \rangle^f + \tilde{\phi}
$$

(1.4)
We shall exploit the following spatial average relationships:

\[ \langle \phi_1 \phi_2 \rangle^f = \langle \phi_1 \rangle^f \langle \phi_2 \rangle^f + \langle \tilde{\phi}_1 \tilde{\phi}_2 \rangle^f \]  

(1.5)

\[ \langle \frac{\partial \phi}{\partial x_i} \rangle = \frac{\partial \langle \phi \rangle}{\partial x_i} + \frac{1}{V} \int_{A_{int}} \phi n_i dA \text{ or } \langle \frac{\partial \phi}{\partial x_i} \rangle^f = \frac{1}{\varepsilon} \frac{\partial \langle \phi \rangle^f}{\partial x_i} + \frac{1}{V_f} \int_{A_{int}} \phi n_i dA \]  

(1.6a, b)

and

\[ \langle \frac{\partial \phi}{\partial t} \rangle = \frac{\partial \langle \phi \rangle}{\partial t} \]  

(1.7)

where \( A_{int} \) is the local interface between the blood and solid matrix, while \( n_i \) is the unit vector pointing outward from the fluid side to the solid side. The similarity between the volume averaging and the Reynolds averaging used in the study of turbulence is quite obvious. However, it should be noted that the present volume averaging procedure is somewhat more complex than the Reynolds averaging procedure, since it involves surface integrals, as clearly seen from equation (1.6). It should also be noted that biological tissues in reality are highly compliant. To include the compliance of the tissues, the foregoing spatial averaging relationships must be modified accordingly to account for the deformation of the elementary control volume. In the present study, we neglect such effects for simplicity.

We subdivide the anatomic structure into the blood phase (fluid phase) and the tissue and other solid tissue phase (solid matrix phase), in which metabolic reactions may take place. We shall consider the microscopic governing equations, namely, the continuity equation, the Navier–Stokes equation, and the energy equation for the blood phase and the heat conduction equation for the solid matrix phase.

For the blood phase:

\[ \frac{\partial u_j}{\partial x_j} = 0 \]  

(1.8)

\[ \frac{\partial u_j}{\partial t} + \frac{\partial}{\partial x_j} u_j u_i = - \frac{1}{\rho} \frac{\partial p}{\partial x_i} + \frac{\partial}{\partial x_j} \nu_f \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) \]  

(1.9)

\[ \rho_f c_p \left( \frac{\partial T}{\partial t} + \frac{\partial}{\partial x_j} u_j T \right) = \frac{\partial}{\partial x_j} \left( k_f \frac{\partial T}{\partial x_j} \right) \]  

(1.10)

For the solid matrix phase:

\[ \rho_s c_s \frac{\partial T}{\partial t} = \frac{\partial}{\partial x_j} \left( k_s \frac{\partial T}{\partial x_j} \right) + S_m \]  

(1.11)

where the subscripts \( f \) and \( s \) stand for the fluid and solid, respectively. It is assumed that the fluid (blood) is incompressible and Newtonian, and all properties are constant.
1.3 Governing Equation for Blood Flow

Let us integrate the continuity equation (1.8) over a local control volume using the formula (1.6b) as

$$\frac{\partial \varepsilon \langle u_j \rangle}{\partial x_j} + \frac{1}{V} \int_{A_{int}} u_j n_j dA = 0 \quad (1.12)$$

where $A_{int}$ is the local interface between the blood and solid matrix within the control volume $V$, while $n_j$ is the unit vector pointing outward from the fluid side to solid side. For sake of simplicity, the porosity $\varepsilon$ is assumed to vary moderately within a porous medium.

The second term describes the volume rate of the fluid bleeding off to the solid matrix through the interfacial vascular wall, as illustrated in Figure 1.3. In most microcirculatory systems of the body, there is a net filtration of fluid from the intravascular to the extravascular compartment, such that capillary fluid filtration exceeds reabsorption. However, this would not cause fluid to accumulate within the interstitium since the lymphatic system removes excess fluid from the interstitium and returns it back to the intravascular compartment, as indicated in the figure. Thus, the second term describing the net filtration is negligibly small, such that equation (1.12) reduces to

$$\frac{\partial \langle u_j \rangle}{\partial x_j} = 0 \quad (1.13)$$

FIGURE 1.3
Capillary blood flow and extravascular flow.
Accordingly, the Navier–Stokes equation (1.9) may be integrated to give

\[ \frac{\partial \langle u_i \rangle}{\partial t} + \frac{\partial \langle u_j \rangle}{\partial x_j} \langle u_i \rangle - \frac{1}{\rho f} \frac{\partial (p)^f}{\partial x_i} + \frac{\partial \langle u_i \rangle}{\partial x_j} \nu_f \left( \frac{\partial \langle u_i \rangle}{\partial x_j} + \frac{\partial \langle u_j \rangle}{\partial x_i} \right) = -\frac{1}{\rho} \frac{\partial \langle p \rangle}{\partial x_i} + \frac{\partial \langle u_j \rangle}{\partial x_j} \langle u_i \rangle - \frac{\partial}{\partial x_j} \langle u_j u_i \rangle \]  

(1.14)

To close the foregoing macroscopic momentum equations (1.14), the terms associated with the surface integral are modeled according to Vafai and Tien (1981) as

\[ \frac{1}{V_f} \int_{A_{int}} \left( -\frac{p}{\rho} + \nu_f \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) \right) n_j dA = \frac{\nu_f}{K} \epsilon \langle u_i \rangle - b \epsilon^2 \left( \langle u_k \rangle \langle u_k \rangle \right)^{1/2} \langle u_j \rangle \]  

(1.15)

such that

\[ \frac{\partial \langle u_i \rangle}{\partial t} + \frac{\partial \langle u_j \rangle}{\partial x_j} \langle u_i \rangle - \frac{1}{\rho f} \frac{\partial (p)^f}{\partial x_i} + \frac{\partial \langle u_i \rangle}{\partial x_j} \nu_f \left( \frac{\partial \langle u_i \rangle}{\partial x_j} + \frac{\partial \langle u_j \rangle}{\partial x_i} \right) ^{-1} = -\frac{1}{\rho f} \frac{\partial \langle p \rangle}{\partial x_i} + \frac{\partial \langle u_j \rangle}{\partial x_j} \langle u_i \rangle - \frac{\partial}{\partial x_j} \langle u_j u_i \rangle \]  

(1.16)

where \( K_{ij} \) and \( b_{ij} \) are the permeability and Forchheimer tensors, respectively. These tensors, which depend on the anatomical structure, can be determined following the procedure established for anisotropic porous structure (Nakayama et al. [2004]), as sufficient information on the anatomical structure and properties is provided. For the vessels of sufficiently small diameter, the foregoing equation reduces to Darcy’s law:

\[ -\frac{1}{\rho f} \frac{\partial \langle p \rangle}{\partial x_i} - \frac{\nu_f}{K} \epsilon \langle u_j \rangle = 0 \]  

(1.17)

where \( \langle u_j \rangle = \epsilon \langle u_j \rangle \) is the Darcian velocity (i.e., apparent velocity). We may use the Darcy law for most tissue regions except for the regions where large arteries or veins are located.

1.4 Two-Energy Equation Model for Blood Flow and Tissue

1.4.1 Related Work

Pennes (1948) carried out temperature measurements in the limb and found that the maximum muscle temperature is located very close to the axis of
the limb. Using his experimental data, Pennes proposed what is known today as the Pennes bioheat equation. In his model, he assumed that the net heat transferred from the blood to tissue is proportional to the temperature difference between the arterial blood entering the tissue and the venous blood leaving from the tissue, and introduced the Pennes perfusion heat source.

The Pennes bioheat equation has been used for various bioheat transfer problems and found satisfactory for roughly describing the effect of blood flow on the tissue temperature. However, a number of researchers including Wulff (1974) and Klinger (1978) pointed out serious shortcomings in his model due to its inherent simplicity, namely, assuming uniform perfusion rate without accounting for blood flow direction, neglecting the important anatomical features of the circulatory network system such as countercurrent arrangement of the system, and choosing only the venous blood stream as the fluid stream equilibrated with the tissue.

Possible modifications have been proposed by some researchers, so as to remedy these shortcomings. Wulff (1974) and Klinger (1978) considered the local blood mass flux to account the blood flow direction, whereas Chen and Holmes (1980) examined the effect of thermal equilibration length on the blood temperature and added the dispersion and microcirculatory perfusion terms to the Klinger equation.

In this section, we exploit VAT described in the foregoing sections to obtain a complete set of the volume averaged governing equations for bioheat transfer and blood flow. Most shortcomings in existing models can be overcome.

1.4.2 Two-Energy Equation Model Based on VAT

Before actually integrating the energy equation (1.10), it may be quite instructive to focus our attention on the volume average of the convection term. Using equations (1.5) and (1.6), it is straightforward to show

\[
\varepsilon \left( \frac{\partial}{\partial x_j} \rho f c_p T \right)_f = \frac{\partial}{\partial x_j} \rho f c_p <u_j>T_f + \frac{\partial}{\partial x_j} \varepsilon \rho f c_p <\tilde{u}_j \tilde{T}> + \frac{1}{V} \left( \int_{A_{int}} \rho f c_p u_j T \right) n_j dA
\]

where the first term on the right-hand side describes the macroscopic convection, while the second term on the right-hand side takes account of the thermal dispersion (Nakayama et al. [2004]). It is the last term on the right-hand side that corresponds to the blood “perfusion” heat source. Thus, the blood perfusion heat source term is identified as an extra surface integral term resulting from changing the sequence of integration and derivation, as we obtain the macroscopic energy equation by integrating the microscopic convection term over a local control volume.
Having expanded the integrated convection term, we may readily transform both the energy equation (1.10) for the blood flow and the conduction equation (1.11) for the solid matrix into the corresponding volume averaged equations as follows:

For the blood phase:

\[
\varepsilon \rho_f c_p \frac{\partial \langle T \rangle_f}{\partial t} + \rho_f c_p \frac{\partial}{\partial x_j} \langle u_j \rangle \langle T \rangle_f = \frac{\partial}{\partial x_j} \left( \varepsilon k_f \frac{\partial \langle T \rangle_f}{\partial x_j} \right) + \frac{k_f}{V} \int_{A_{\text{int}}} T n_j dA - \varepsilon \rho_f c_p \langle \tilde{u}_j \tilde{T} \rangle_f
\]

For the solid matrix phase:

\[
(1 - \varepsilon) \rho_s c_s \frac{\partial \langle T \rangle_s}{\partial t} = \frac{\partial}{\partial x_j} \left( (1 - \varepsilon) k_s \frac{\partial \langle T \rangle_s}{\partial x_j} - \frac{k_s}{V} \int_{A_{\text{int}}} T n_j dA \right) - \frac{1}{V} \int_{A_{\text{int}}} k_f \frac{\partial T}{\partial x_j} n_j dA + \frac{1}{V} \left( \int_{A_{\text{int}}} \rho_f c_p u_j T \right) n_j dA + (1 - \varepsilon) S_m
\]

where \( \langle T \rangle_s \) is the intrinsic average of the solid matrix temperature. Note that the dispersion heat flux \( \rho_f c_p \langle \tilde{u}_j \tilde{T} \rangle_f = \varepsilon k_{\text{dis}} \frac{\partial \langle T \rangle_f}{\partial x_k} \) appears in the volume averaged energy equation (1.19) for the blood phase, which may well be modeled under the gradient diffusion hypothesis:

\[
-\varepsilon \rho_f c_p \langle \tilde{u}_j \tilde{T} \rangle_f = \varepsilon k_{\text{dis},x} \frac{\partial \langle T \rangle_f}{\partial x_k}
\]

A number of expressions have been proposed for the thermal dispersion thermal conductivity \( k_{\text{dis},x} \). Nakayama et al. (2006) obtained a transport equation for the dispersion heat flux vector, which naturally reduces to the foregoing gradient diffusion form. For a bundle of vessels of radius \( R \), they obtained the following expression for the predominant axial component of \( k_{\text{dis},x} \):

\[
k_{\text{dis},x} = \frac{1}{48} \left( \frac{\rho_f c_p \langle u \rangle_f R}{k_f} \right)^2 k_f \frac{\rho_f c_p \langle u \rangle_f R}{k_f} < 1 \text{(capillary blood vessels)}
\]

\[
k_{\text{dis},x} = 2.55 \left( \frac{\rho_f c_p \langle u \rangle_f R}{k_f} \right)^{7/8} P_r^{1/8} k_f \frac{\rho_f c_p \langle u \rangle_f R}{k_f} > 1 \text{(large arteries and veins)}
\]
Bioheat Equations Based on VAT

To close the foregoing macroscopic energy equations (1.19) and (1.20), the terms associated with the surface integral, describing the interfacial heat transfer and perfusion between the fluid and solid, must be modeled. For the interfacial heat transfer, Newton’s cooling law may be adopted as

$$\frac{1}{V} \int_{A_{int}} k_f \frac{\partial T}{\partial x_j} n_j dA = a_f h_f \left( \langle T \rangle^s - \langle T \rangle^f \right)$$ (1.23)

where $a_f$ and $h_f$ are the specific surface area and interfacial heat transfer coefficient, respectively. For the bundle of vascular tubes of radius $R$, we have $a_f = 2\varepsilon / R$ and $h_f = Nu (k_f / 2R)$, such that $a_f h_f = Nu (\varepsilon k_f / R^2)$, where $Nu$ is the Nusselt number based on the local diameter of the vascular tube. If the local porosity $\varepsilon$ and specific surface area $a_f$ are provided for the complex tissue-vascular structure, we may estimate the interfacial heat transfer coefficient using $h_f = Nu (k_f a_f / 4\varepsilon)$. Roetzel and Xuan (1998) set $Nu = 4.93$ for both arterial and venous blood vessels. We may appeal to a numerical experiment proposed by Nakayama et al. (2002) for complex porous structures.

As for modeling the blood perfusion term, we may refer back to Figure 1.3 and note that the transcapillary fluid exchange takes place between the blood and the surrounding tissue. However, the fluid lost from the vascular space will be compensated by the flow of extravascular fluids and lymph from the tissue to vascular space. It is quite reasonable to assume that extravascular fluids and all lymph in the tissue space have the same temperature as the tissue itself. Thus, we assume that the transcapillary fluid exchange takes place at the rate of $\omega$ (m$^3$/s$^3$) and model the blood perfusion term as

$$\frac{1}{V} \left( \int_{A_{int}} \rho_f c_p_f u_j T \right) n_j dA = \rho_f c_p_f \omega \left( \langle T \rangle^f - \langle T \rangle^s \right)$$ (1.24)

Note that the perfusion rate $\omega$, unlike that of Pennes, varies locally, and we assume that its local value is provided everywhere. Pennes found that his model fits the experimental data for $\omega = 2 \times 10^{-4}$ to $5 \times 10^{-4}$ (m$^3$/s$^3$). The perfusion rate varies spatially. In general, it is not an easy task to do in vivo measurements for living tissues. Charny (1992) in his review describes how to measure the perfusion rate in terms of the effective thermal conductivity.

Furthermore, the surface integral terms $k_f \int_{A_{int}} T n_j dA$ and $-k_s \int_{A_{int}} T n_j dA$ present the tortuosity heat fluxes, which are usually small, as convection dominates over conduction (see e.g., Nakayama et al. [2001]). Therefore, their effects may well be absorbed in effective thermal conductivities, as done by Xuan and Roetzel (1997). Having modeled the terms associated with dispersion, interfacial heat transfer, blood perfusion, and tortuosity, the individual macroscopic energy equations may finally be written for the blood and tissue phases as follows.
For the blood phase:

\[
\varepsilon \rho f c_p f \frac{\partial \langle T \rangle^f}{\partial t} + \rho f c_p f \frac{\partial}{\partial x_j} (u_j^f) \langle T \rangle^f = \frac{\partial}{\partial x_j} \left( \varepsilon k_f \frac{\partial \langle T \rangle^f}{\partial x_j} + \varepsilon k_{dis} \frac{\partial \langle T \rangle^f}{\partial x_k} \right) - a f h_f (\langle T \rangle^f - \langle T \rangle^s) - \rho f c_p f \omega (\langle T \rangle^f - \langle T \rangle^s)
\]

(1.25)

in which the left–hand side term denotes the macroscopic convection term, while the four terms on the right–hand side correspond to the macroscopic conduction, thermal dispersion, interfacial convective heat transfer, and blood perfusion, respectively.

For the solid tissue phase:

\[
(1 - \varepsilon) \rho_s c_s \frac{\partial \langle T \rangle^s}{\partial t} = \frac{\partial}{\partial x_j} \left( (1 - \varepsilon) k_s \frac{\partial \langle T \rangle^s}{\partial x_j} \right) + a f h_f (\langle T \rangle^f - \langle T \rangle^s) + \rho f c_p f \omega \text{Pennes} (T_{a0} - \langle T \rangle^s) + (1 - \varepsilon) S_m
\]

(1.26)

in which the left–hand side term denotes the thermal inertia term, while the four terms on the right–hand side correspond to the macroscopic conduction, interfacial convective heat transfer, blood perfusion heat source, and metabolic heat source, respectively.

The resulting equations (1.25) and (1.26) appear to be a correct form for the case of thermal nonequilibrium and are expected to clear up possible confusions associated with the blood perfusion term. The continuity equation (1.13), Darcy’s law (1.17), and the two-energy equations (1.25) and (1.26) form a closed set of the macroscopic governing equations. The present model in a multidimensional and anisotropic form is quite general and can be applied to find both velocity and temperature fields, as we prescribe the spatial distributions of permeability tensor, porosity, interfacial heat transfer coefficient, metabolic reaction rate, and perfusion rate. It is interesting to note that, when the velocity field, porosity, and metabolic reaction are prescribed, we only need to know the local value of the lumped convection-perfusion parameter, namely, \((a f h_f + \rho f c_p f \omega)\) (in addition to appropriate thermal boundary conditions) to solve the two-energy equations (1.25) and (1.26) for the blood and tissue temperatures, \(\langle T \rangle^f\) and \(\langle T \rangle^s\).

### 1.4.3 Pennes Model

It should be noted that most existing bioheat transfer models already reside in the present model based on the theory of porous media. We shall revisit some of the existing models and try to generate them from the present general model, starting with the Pennes model (1948), which in our notation runs as

\[
(1 - \varepsilon) \rho_s c_s \frac{\partial \langle T \rangle^s}{\partial t} = \frac{\partial}{\partial x_j} \left( (1 - \varepsilon) k_s \frac{\partial \langle T \rangle^s}{\partial x_j} \right) + \rho f c_p f \omega \text{Pennes} (T_{a0} - \langle T \rangle^s) + (1 - \varepsilon) S_m
\]

(1.27)
where $\omega_{\text{Pennes}}$ is the mean blood perfusion rate, while $T_{a0}$ is the mean brachial artery temperature. We compare the Pennes model against the energy equation (1.26) for the solid tissue phase and find the following relationship:

$$\rho_f c_p \omega_{\text{Pennes}} (T_{a0} - \langle T \rangle^s) = a_f h_f \left( \langle T \rangle^f - \langle T \rangle^s \right) + \rho_f c_p \omega \left( \langle T \rangle^f - \langle T \rangle^s \right)$$

(1.28)

Perhaps, Pennes considered that the blood perfusion is the predominant heat source for the tissue, and did not bother to describe the interfacial convective heat transfer between the blood and tissue via the vascular wall. Instead, he introduced $T_{a0}$ to adjust the total heat transfer, which takes place as the blood enters and leaves the tissue. We may assume $T_{a0} \approx \langle T \rangle^f$ for small vessels, and find

$$\omega_{\text{Pennes}} = \omega + \frac{a_f h_f}{\rho_f c_p f}$$

(1.29)

Thus, Pennes’ perfusion rate may be regarded as an effective one that includes interfacial convective heat transfer as well. Pennes assumed that blood enters the smallest vessels of the microcirculation at $T_{a0}$, where all heat transfer between the blood and tissue takes place. The assumption of the complete thermal equilibration with the surrounding tissue is valid only when Peclet number is sufficiently small.

### 1.4.4 Wulff Model and Klinger Model

Wulff (1974) criticized the Pennes model, pointing out that the moving blood through a tissue convects heat in any direction, not just in the direction of the local tissue temperature gradient. He assumed that the blood temperature $\langle T \rangle^f$ is equivalent to the tissue temperature within a tissue control volume and proposed a new bioheat transfer equation. The equation later generalized by Klinger (1978) runs in our notation as

$$(1 - \varepsilon) \rho_s c_s \frac{\partial \langle T \rangle^s}{\partial t} = \frac{\partial}{\partial x_j} \left( (1 - \varepsilon) k_s \frac{\partial \langle T \rangle^s}{\partial x_j} \right) - \rho_f c_p \omega \frac{\partial \langle u \rangle}{\partial x_j} \langle T \rangle^s + (1 - \varepsilon) S_m$$

(1.30)

We can obtain a similar equation by combining equations (1.25) and (1.26) setting $\langle T \rangle^f = \langle T \rangle^s$ as follows:

$$(\varepsilon \rho_f c_p f + (1 - \varepsilon) \rho_s c_s) \frac{\partial \langle T \rangle^s}{\partial t} + \rho_f c_p \omega u \frac{\partial \langle T \rangle^s}{\partial x_j}$$

$$= \frac{\partial}{\partial x_j} \left( \varepsilon k_f + (1 - \varepsilon) k_s \right) \frac{\partial \langle T \rangle^s}{\partial x_j} + (1 - \varepsilon) S_m$$

(1.31)
We can easily see that the foregoing equation reduces to the Klinger equation when the ratio of vascular volume to total volume (i.e., porosity \( \varepsilon \)) is sufficiently small. Since the porosity is generally less than 0.1, the foregoing two equations are quite close to each other.

Another interpretation on the directional effect on the tissue temperature field is possible. When the blood flow is strong enough to neglect the macroscopic diffusion, the energy equation (1.25) for the blood flow reduces to

\[
\rho_f c_{pf} \frac{\partial}{\partial x_j} \langle u_j \rangle \langle T \rangle^f = -a_f h_f \left( \langle T \rangle^f - \langle T \rangle^s \right) - \rho_f c_{pf} \omega \left( \langle T \rangle^f - \langle T \rangle^s \right)
\]  
(1.32)

Substitution of the foregoing equation into the energy equation for the tissue (1.26) yields the Klinger equation (1.30). The assumption implicit here is that the blood flow velocity is sufficiently high that the ratio of the bulk convection heat transfer to conduction heat transfer, namely, the Peclet number, is much greater than unity. Thus, the Klinger model applies to the tissue with comparatively large vessels.

1.4.5 Chen and Holmes Model

Chen and Holmes (1980) assumed that all tissue-arterial blood heat exchange occurs along the circulatory network after the blood flows through the terminal arteries and before it reaches the level of the arterioles, which prompted them to propose the following bioheat transfer model:

\[
\rho c \frac{\partial T_t}{\partial t} + \rho_f c_{pf} \frac{\partial}{\partial x_j} \langle u_j \rangle T_t = \frac{\partial}{\partial x_j} \left( \varepsilon k_f + (1 - \varepsilon) k_s \right) \frac{\partial T_t}{\partial x_j} + k_p \frac{\partial T_t}{\partial x_j} + \rho_f c_{pf} \omega_j^* (T_a^* - T_t) + (1 - \varepsilon) S_m
\]  
(1.33)

where

\[
\rho = \varepsilon \rho_f + (1 - \varepsilon) \rho_s
\]  
(1.34a)

\[
c = \frac{\varepsilon \rho_f c_{pf} + (1 - \varepsilon) \rho_s c_s}{\rho}
\]  
(1.34b)

and

\[
T_t = \left( \varepsilon \rho_f c_{pf} \langle T \rangle^f + (1 - \varepsilon) \rho_s c_s \langle T \rangle^s \right) / \rho c
\]  
(1.34c)

is the temperature of the continuum based on a volume average. Moreover, \( \omega_j^* \) is the perfusion bleed-off to the tissue only from the microvessels past the \( j \)th generation of branching, while \( T_a^* \) is the blood temperature at the \( j \)th generation of branching. Both \( \omega_j^* \) and \( T_a^* \) require the anatomical data. Chen and Holmes (1980) also took account of the “eddy” conduction due to the random flow of blood, by introducing the thermal conductivity \( k_p \), which corresponds to our dispersion thermal conductivity \( k_{dis} \). The energy equation
similar to their equation (1.33) may be obtained by combining the two-energy
equations (1.25) and (1.26) in the present model as

\[ \frac{\rho c}{\partial t} + \frac{\rho f c_p f}{\partial x_j} \langle u_j \rangle \langle T \rangle^f = \frac{\partial}{\partial x_j} \left( \varepsilon k_f \frac{\partial (T)^f}{\partial x_j} + (1 - \varepsilon) k_s \frac{\partial (T)^s}{\partial x_j} + \varepsilon k_{dis,k} \frac{\partial (T)^f}{\partial x_k} \right) + (1 - \varepsilon) S_m \] (1.35)

When the three temperature gradients on the right-hand side are close
and \( \varepsilon k_{dis,k} = k_p \delta_{jk} \), the foregoing equation reduces to

\[ \frac{\rho c}{\partial t} + \frac{\rho f c_p f}{\partial x_j} \langle u_j \rangle \langle T \rangle^f = \frac{\partial}{\partial x_j} \left( \varepsilon k_f + (1 - \varepsilon) k_s \right) \frac{\partial T}{\partial x_j} + k_p \frac{\partial T}{\partial x_j} + (1 - \varepsilon) S_m \] (1.36)

which is close to the equation of Chen and Holmes, except that \( \rho f c_p f \)
\( \omega_j^* (T_a^* - T_t) \) is missing, as in the models of Wulff and Klinger, since it should
vanish, as we add equations (1.25) and (1.26).

1.5 Three-Energy Equation Model for Countercurrent
Heat Transfer in a Circulatory System

1.5.1 Related Work

Bazett and his colleagues (1948a, 1948b) conducted a series of experimental
studies on countercurrent heat exchange in the circulatory system. They found
that the axial temperature gradient in the limb artery of human, under condi-
tions of very low ambient temperature, is an order of magnitude higher than
that under normal ambient conditions. From these experimental observations,
they proposed the concept of venous shunting to the periphery, namely, that
the countercurrent heat transfer takes place in the deep vasculature at the
same time the blood is directed to the cutaneous circulation in close proxim-
ity to the surroundings. Their experimental finding brought attention to the
important role of countercurrent heat exchange in bioheat transfer. Especially
when the anatomical configuration of the main supply artery and vein in the
limbs is treated, the effect of countercurrent heat transfer between closely
spaced arteries and veins in the tissue must be taken into full consideration.

Following the experimental studies conducted by Bazett and his colleagues
(1948a, 1948b), Scholander and Krog (1957), and Mitchell and Myers (1968)
investigated such an effect and successfully demonstrated that the countercur-
current heat exchange reduces heat loss from the extremity to the surroundings,
which could be quite significant owing to a large surface to volume ratio. These models, however, were not able to take account of either metabolic reaction or perfusion bleed-off from the artery to vein. Keller and Seiler (1971) established a one-dimensional bioheat transfer model to include the countercurrent heat transfer for the subcutaneous tissue region with arteries, veins, and capillaries. Weinbaum and Jiji (1979, 1985) proposed a model, which is based on some anatomical understanding, considering the countercurrent arterio-venous vessels. Roetzel and Xuan (1998) pointed out that the model may be useful in describing a temperature field in a single organ but would not be convenient to apply to the whole thermoregulation system. The foregoing survey prompts us to establish a multidimensional model that can be applied to the regions of extremity, where the countercurrent heat transfer happens between closely spaced arteries and veins in the blood circulatory system. Excellent reviews on these bioheat transfer equations may be found in Chato (1980), Charny (1992), and Khaled and Vafai (2003).

In this section, we shall extend the volume averaging procedure described for the heat transfer between the isolated vessels and the surrounding tissue to the case of countercurrent bioheat transfer in a blood circulatory system. The set of macroscopic governing equations consists of continuity and momentum equations for both arterial and venous blood phases and three individual energy equations for the two blood phases and the surrounding tissue phase. It will be shown that most shortcomings in existing models are overcome in the present model. Capillaries providing a continuous connection between the countercurrent terminal arteries and veins are modeled introducing the perfusion bleed-off rate, originally introduced in the pioneering paper by Pennes (1948). It has been found that the resulting model under certain conditions reduces to existing models for countercurrent heat transfer such as Chato (1980), Bejan (1979), Keller and Seiler (1971), Roetzel and Xuan (1998), and Weinbaum and Jiji (1985) for the case of closely aligned pairs of artery and vein. A general expression has been presented for the longitudinal effective thermal conductivity in the energy equation for the tissue. To examine the present model, we shall apply it to the countercurrent blood vessel configuration examined by Chato (1980). While Chato assumed the constancy of the perfusion bleed-off rate, we shall allow the spatial distribution of perfusion bleed-off rate and investigate its effect on the total countercurrent heat transfer.

1.5.2 Three-Energy Equation Model Based on the Volume Averaging Theory

A schematic view of the tissue layer close to the skin surface is shown in Figure 1.4, in which the arteries and veins are paired, such that the countercurrent heat transfer takes place. Thus, we assign individual dependent variables such as temperature to the arterial blood, venous blood, and tissue, which leads us to propose a three-energy equation model.
All dependent variables in the microscopic governing equations for the arterial blood, venous blood, and tissue phases are decomposed in this manner, and then these governing equations are integrated over the local control volume. After some manipulations following Nakayama and Kuwahara (2008) and Nakayama et al. (2008), we obtain the volume averaged set of the governing equations, which can be written assigning the subscripts $a$, $v$, and $s$ to arterial blood vessels (arteries and arterioles), venous blood vessels (veins and venules), and tissue, as follows:

For the arterial blood phase:

\[
\frac{\partial \epsilon_a \langle u_j \rangle^a}{\partial x_j} + \omega_a^\prime = 0
\]  
(1.37)

\[
-\frac{1}{\rho} \frac{\partial \langle p \rangle^a}{\partial x_i} - \frac{\nu}{K_{avij}} \epsilon_a \langle u_j \rangle^a - \omega_a^\prime u_{int} = 0
\]  
(1.38)

\[
\epsilon_a \rho_f c_{pf} \frac{\partial \langle T \rangle^a}{\partial t} + \rho_f c_{pf} \frac{\partial}{\partial x_j} \epsilon_a \langle u_j \rangle^a \langle T \rangle^a
\]

\[
= \frac{\partial}{\partial x_j} \left( \epsilon_a k_a \frac{\partial \langle T \rangle^a}{\partial x_j} + \epsilon_{kdisa} k_{disak} \frac{\partial \langle T \rangle^a}{\partial x_k} \right) - a_a h_a \langle T \rangle^a - \langle T \rangle^s - \rho_f c_{pf} \omega_a^\prime \langle T \rangle^a
\]  
(1.39)

For the venous blood phase:

\[
\frac{\partial \epsilon_v \langle u_j \rangle^v}{\partial x_j} + \omega_v^\prime = 0
\]  
(1.40)

\[
-\frac{1}{\rho} \frac{\partial \langle p \rangle^v}{\partial x_i} - \frac{\nu}{K_{vij}} \epsilon_v \langle u_j \rangle^v - \omega_v^\prime u_{int} = 0
\]  
(1.41)
\[
\varepsilon_v \rho_f c_p \eta \frac{\partial \langle T \rangle^v}{\partial t} + \rho f c_p \frac{\partial \varepsilon_v}{\partial x_j} \langle u_j \rangle^v \langle T \rangle^v = \frac{\partial}{\partial x_j} \left( \varepsilon_v k_v \frac{\partial \langle T \rangle^v}{\partial x_j} + \varepsilon_v k_{disv} k \right) - a_v h_v (\langle T \rangle^v - \langle T \rangle^s) - \rho f c_p \omega' \langle T \rangle^v
\]

(1.42)

For the solid tissue phase:

\[
(1 - \varepsilon) \rho_s c_s \frac{\partial \langle T \rangle^s}{\partial t} = \frac{\partial}{\partial x_j} \left( (1 - \varepsilon) k_s \frac{\partial \langle T \rangle^s}{\partial x_j} \right) + a_v h_v (\langle T \rangle^s - \langle T \rangle^v) + \rho f c_p \omega'_s \langle T \rangle^v + (1 - \varepsilon) S_m
\]

(1.43)

where \( \varepsilon_a \) and \( \varepsilon_v \) are the volume fractions of the arterial blood and that of the venous blood, respectively, such that \( \varepsilon = \varepsilon_a + \varepsilon_v \). The terms associated with the surface integral are modeled as

\[
\frac{1}{V_f} \int_{A_{int}} \left( - \frac{p}{\rho_f} + \nu f \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) \right) n_j dA = - \nu f K_{ij} \varepsilon \langle u_j \rangle^f
\]

(1.44)

which is simply Darcy’s law and

\[
\int_{A_{int}} \rho_f u_j n_j dA / V = \rho_f \omega'
\]

(1.45)

is the mass flow rate per unit volume through the interface \( A_{int} \), modeled in terms of the perfusion bleed-off rate \( \omega' \)(1/s). The perfusion bleed-off rate \( \omega' \) describes the volume rate of the fluid per unit volume, bleeding off to the solid matrix through the interfacial vascular wall. Thus, the momentum bleed-off rate is modeled as

\[
\int_{A_{int}} \rho_f u_j n_j dA / V = \rho_f \omega' u_{int}
\]

(1.46a)

where \( u_{int} \) is the velocity vector averaged over the interface. Likewise, the enthalpy bleed-off rate is modeled as

\[
\int_{A_{int}} \rho f c_p u_j T n_j dA / V = \rho f c_p \omega' \langle T \rangle^f
\]

(1.46b)

For the interfacial heat transfer, Newton’s cooling law is adopted as

\[
\frac{1}{V} \int_{A_{int}} k_f \frac{\partial T}{\partial x_j} n_j dA = a_f h_f \left( \langle T \rangle^s - \langle T \rangle^f \right)
\]

(1.47)

where \( a_f \) and \( h_f \) are the specific surface area and interfacial heat transfer coefficient, respectively. Furthermore, \( k_{disv} \) is the thermal dispersion conductivity tensor, as introduced in Nakayama et al. (2006).
Bioheat Equations Based on VAT

For the microcirculation of peripheral tissue in which capillaries provide a continuous connection between the terminal artery and vein (i.e., arterial-venous anastomoses), as shown in Figure 1.4, we may readily set $\omega'_a = -\omega'_v$ such that the present energy equation (1.43) for the solid tissue phase reduces to

$$
(1 - \varepsilon) \rho_s c_s \frac{\partial \langle T \rangle_s}{\partial t} = \frac{\partial}{\partial x_j} \left( (1 - \varepsilon) k_s \frac{\partial \langle T \rangle_s}{\partial x_j} \right) + a_a h_a (\langle T \rangle^a - \langle T \rangle_s^s) + a_v h_v (\langle T \rangle^v - \langle T \rangle_s^v) + \rho_f c_p \omega'_a (\langle T \rangle^a_s - \langle T \rangle^s_s) + (1 - \varepsilon) S_m \quad (1.48)
$$

1.5.3 Keller and Seiler Model

Most existing bioheat transfer models for countercurrent bioheat transfer already reside in the present model based on the theory of porous media. Let us revisit some of the existing models and try to generate them from the present general model.

Keller and Seiler (1971) noted that the axial temperature gradient in the limb is much higher than the transverse one and considered an energy balance within a control volume for the idealized one-dimensional steady case, as illustrated in Figure 1.5, for which they proposed

$$
(1 - \varepsilon) k_s \frac{d^2 \langle T \rangle_s}{dx^2} + a_a h_a (\langle T \rangle^a - \langle T \rangle_s^a) + a_v h_v (\langle T \rangle^v - \langle T \rangle_s^v) + \rho_f c_p \omega'_a (\langle T \rangle^a_s - \langle T \rangle^s_s) + (1 - \varepsilon) S_m = 0 \quad (1.49)
$$

which is almost identical to what we would get for the one-dimensional case from our multidimensional expression (1.48), except that the temperature difference in the perfusion term somewhat differs from ours. Keller and Seiler

![Figure 1.5](image)

**FIGURE 1.5**

One-dimensional model for countercurrent heat exchange.
(1971) obtained solutions assuming that the arterial blood enters the peripheral region at the isothermal core temperature and that the venous blood is completely equilibrated with the tissue at the cutaneous layer.

1.5.4 Chato Model

Chato’s countercurrent heat transfer model (1980) differs from Keller and Seiler’s (1971) model in its neglect of heat transfer between the blood and the tissue. In this way, he was able to concentrate on the two temperatures instead of three as in Keller and Seiler’s model. Chato assumed that the flow rate decreases linearly, which corresponds with the case of constant perfusion bleed-off rate. His one-dimensional model can easily be generated from our general expressions (1.39) and (1.42) along with (1.37) and (1.40), dropping the transient and conduction terms as

\[ \rho_f c_p \frac{d}{dx} \varepsilon_a \langle u \rangle^a = -a_f h_f (\langle T \rangle^a - \langle T \rangle^v) - \rho_f c_p \omega'_a \langle T \rangle^a \]  
(1.50)

\[ \rho_f c_p \frac{d}{dx} \varepsilon_v \langle u \rangle^v = -a_f h_f (\langle T \rangle^v - \langle T \rangle^a) + \rho_f c_p \omega'_a \langle T \rangle^a \]  
(1.51)

where the interfacial heat transfer coefficients are assumed to be the same. The continuity equations (1.37) and (1.40) readily provide

\[ \varepsilon_a \langle u \rangle^a = u_0 - \omega'_a x \]  
(1.52)

and

\[ \varepsilon_v \langle u \rangle^v = -u_0 + \omega'_a x \]  
(1.53)

Note that \( u_0 \) is the apparent velocity at \( x = 0 \) and that the right–hand side terms in the two equations (1.50) and (1.51) cancels out each other, as they should for this “perfect” heat exchange system. Chato (1980) obtained arterial and venous temperature profiles along the length of the vessels and demonstrated that the effect of perfusion bleed-off is to increase the heat transfer between the vessels as compared with the case of constant mass flow rate (i.e., \( \omega'_a = 0 \)).

1.5.5 Roetzel and Xuan Model

Roetzel and Xuan (1998) used the theory of porous media to simulate a transient response of the limb to external stimulus, in which the effect of the countercurrent heat exchange on the temperature response is expected to be significant. Their energy equation for the tissue in our notation runs as

\[ (1 - \varepsilon) \rho_s c_s \frac{\partial (T)^s}{\partial t} = \frac{\partial}{\partial x_j} \left( (1 - \varepsilon) k_s \frac{\partial (T)^s}{\partial x_j} \right) + a_a h_a (\langle T \rangle^a - \langle T \rangle^s) + a_v h_v (\langle T \rangle^v - \langle T \rangle^s) + (1 - \varepsilon) S_m \]  
(1.54)
Comparison of the foregoing equation against our expression (1.48) for the tissue reveals that the perfusion term \( \rho_f c_p \omega_a'(T^a - \langle T \rangle^a) \) is missing. Obviously, they did not retain the term describing the transcapillary fluid exchange via arterial-venous anastomoses, namely, 
\[
\int_{A_{int}} \rho_f c_p \omega_{a} \langle (T)^a - \langle T \rangle^a \rangle \, dA/V = \rho_f c_p \omega(T)^a.
\]
If they did, they would have obtained our expression (48), which may be rearranged in their form as
\[
(1 - \varepsilon) \rho_s c_s \frac{\partial \langle T \rangle^s}{\partial t} = \frac{\partial}{\partial x_j} \left( (1 - \varepsilon) k_s \frac{\partial \langle T \rangle^s}{\partial x_j} \right) + (a_a h_a + \rho_f c_p \omega_a') \left( \langle T \rangle^a - \langle T \rangle^s \right) + (a_v h_v - \rho_f c_p \omega_a') \left( \langle T \rangle^v - \langle T \rangle^s \right) + (1 - \varepsilon) S_m \quad (1.55)
\]

In their model, the convection-perfusion parameters, namely, \( (a_f h_f \pm \rho_f c_p \omega') \), are replaced by the interfacial convective heat transfer coefficients, \( a_f h_f \). This difference should not be overlooked since the perfusion heat sources could be quite significant for the bioheat transfer in the extremities, as Chato (1980) demonstrated using his model.

### 1.5.6 Weinbaum–Jiji Model and Bejan Model

Weinbaum and Jiji (1979) considered bioheat transfer between a paired countercurrent terminal artery and vein. They took account of the vascular structure in which vessel number density, velocity, and diameter vary significantly from the deep tissue layer toward the skin layer. Later, Weinbaum and Jiji (1985) proposed a simplified model in which an effective thermal conductivity tensor is introduced as a function of the local blood velocity. They claimed that the perfusion heat source vanishes within the capillary bed and derived a single equation to describe the steady-state tissue temperature variations, which, when the vessels are in parallel to the temperature gradient, reduces to
\[
\frac{d}{dx} \left( \left( 1 - \varepsilon \right) k_s + \frac{\pi \varepsilon_a}{2\sigma} \left( \rho_f c_p (u)^a R \right)^2 \right) \frac{d \langle T \rangle^s}{dx} \right) + (1 - \varepsilon) S_m = 0 \quad (1.56)
\]
where \( \sigma \) is a geometrical factor of the vessel structure, whereas \( R \) is the local radius of the vessel. It is seen that the longitudinal effective thermal conductivity due to countercurrent flow is proportional to the square of blood mass flow rate. It is also interesting to note that the concept of the longitudinal effective thermal conductivity in countercurrent heat transfer was already explicit in Bejan (1979) in which he presented a novel method for thermal insulation system optimization. Bejan (1979) seems to be the first to point out the relationship associated with the square of the mass flow rate and the longitudinal effective thermal conductivity by convection. His expression is a simple one:
\[
Q = -\frac{(m_f c_p)^2}{U P} \frac{d \langle T \rangle^s}{dx} \quad (1.57)
\]
where \( Q \), \( \dot{m}_f \), \( U \), and \( P \) are the heat flow from the warm end to the cold end, the mass flow rate of the hot (or cold) fluid, the overall heat transfer coefficient, and the wetted perimeter, respectively. The group \((m_f c_p) \beta^2 \epsilon_a (u)^a / (UP)\) plays the same role as \( A k_{eff} \) in the one-dimensional insulation system. Upon noting that \( m_f = \rho f \epsilon_a (u)^a \) and \( P = a \alpha_f \), Bejan’s equation (1.57) may be translated in the present bioheat transfer problem as

\[
\frac{d}{dx} \left( (1 - \epsilon) k_s + \frac{(\rho_f c_p \epsilon_a (u)^a)^2}{a_f U} \frac{d\langle T \rangle^s}{dx} \right) + (1 - \epsilon) S_m = 0 \quad (1.58)
\]

In these countercurrent heat transfer models, namely, Bejan’s and Wienbaum and Jiji’s, the perfusion heat sources are ignored. Thus, in what follows, we shall attempt to reduce the present set of governing equations to a single equation for the tissue temperature variations, without neglecting these perfusion heat source terms.

When the blood flow is strong enough to neglect the macroscopic diffusion, the energy equations (1.39) and (1.42) for arterial and venous blood flows for the one-dimensional steady state reduce to

\[
\rho c_p \frac{d}{dx} \epsilon_a (u) (T)^a = -a_f h_f ((T)^a - \langle T \rangle^a) - \rho c_p \omega_a' \langle T \rangle^a \quad (1.59)
\]

\[
\rho c_p \frac{d}{dx} \epsilon_v (u) (T)^v = -a_f h_f ((T)^v - \langle T \rangle^v) + \rho c_p \omega_a' \langle T \rangle^v \quad (1.60)
\]

where the interfacial heat transfer coefficients are assumed to be the same as in the case of Chato. However, the foregoing equations are different from Chato’s equations (1.50) and (1.51), since we do take account of the heat transfer between the bloods and tissue. Upon noting the continuity relationship \( \epsilon_a (u)^a = -\epsilon_v (u)^v \) as given by the continuity equations (1.37) and (1.40) with \( \omega'_a = -\omega'_v \), we subtract equation (1.60) from (1.59) to obtain

\[
\rho c_p \frac{d}{dx} \epsilon_a (u) (T)^a + (T)^v = -a_f h_f ((T)^a - \langle T \rangle^a) - \rho c_p \omega_a' ((T)^a + \langle T \rangle^v) \quad (1.61a)
\]

or

\[
\rho c_p \frac{d}{dx} \epsilon_a (u) (T)^a = -a_f h_f ((T)^a - \langle T \rangle^v) \quad (1.61b)
\]

as we note the continuity relationship, namely, \( d(\epsilon_a (u)^a) / dx = -\omega'_a \). Weinbaum and Jiji (1985) proposed that the mean tissue temperature around an artery–vein pair can be approximated as

\[
\langle T \rangle^s = \frac{\langle T \rangle^a + \langle T \rangle^v}{2} \quad (1.62)
\]

Following their approximation, we obtain

\[
\langle T \rangle^a - \langle T \rangle^v = -2 \rho c_p \epsilon_a (u)^a \frac{d\langle T \rangle^s}{dx} \quad (1.63)
\]
from (1.61b). Using equations (1.59) and (1.60), we may replace both interfacial and perfusion heat source terms in the energy equation (1.48) for the tissue by the blood convection terms as

\[
\frac{d}{dx} \left( (1 - \varepsilon) k_s \langle T \rangle_s \right) + a_a h_a (\langle T \rangle_a - \langle T \rangle_s) + a_v h_v (\langle T \rangle_v - \langle T \rangle_s)
\]

\[
+ \rho f c_p, \omega'_a (\langle T \rangle_a - \langle T \rangle_v) + (1 - \varepsilon) S_m \\
= \frac{d}{dx} \left( (1 - \varepsilon) k_s \frac{d}{dx} \langle T \rangle_s \right) - \rho f c_p, \frac{d}{dx} (\varepsilon_a \langle u \rangle_a \langle T \rangle_a)
\]

\[
+ \varepsilon_v \langle u \rangle_v (\langle T \rangle_v) + (1 - \varepsilon) S_m = 0
\]

\[(1.64)\]

As we note the continuity relationship \( \varepsilon_a \langle u \rangle_a = -\varepsilon_v \langle u \rangle_v \) and use equation (1.63) for the last expression in (1.64), we finally have

\[
\frac{d}{dx} \left( (1 - \varepsilon) k_s + 2 \left( \frac{\rho f c_p, \varepsilon_a \langle u \rangle_a^2}{a_f h_f} \right) \frac{d}{dx} \langle T \rangle_s \right) + (1 - \varepsilon) S_m = 0
\]

\[(1.65)\]

which we find almost identical to Bejan’s equation (1.58), as we note the overall heat transfer coefficient corresponds to

\[
U = \frac{1}{\frac{1}{h_a} + \frac{1}{h_v}} = \frac{h_f}{2}
\]

\[(1.66)\]

It is most interesting to find that the foregoing relationship for the longitudinal effective thermal conductivity holds for all cases, with or without perfusion bleed-off sources, as long as the local values are used to evaluate the effective thermal conductivity by convection.

### 1.6 Effect of Spatial Distribution of Perfusion Bleed-Off Rate on Total Countercurrent Heat Transfer

As an example for illustration, we shall consider Chato’s one-dimensional problem of countercurrent heat transfer as schematically shown in Figure 1.5. Chato (1980) assumed the constancy of the perfusion bleed-off rate \( \omega'_a \), namely, a linear decrease in the arterial flow rate, and that all of the bleed-off fluid that leaves the artery reenters the vein at the same location. We shall relax his assumption, allowing the spatial variation of \( \omega'_a \) so as to investigate its effect on the total countercurrent heat transfer. Let us assume that the perfusion bleed-off rate \( \omega'_a \) follows

\[
\omega'_a = (1 + n) \bar{\omega}_a \left( \frac{x}{L} \right)^n
\]

\[(1.67)\]
FIGURE 1.6
Effect of the exponent $n$ on perfusion rate.

along the blood vessel of length $L$, where $\bar{\omega}_a$ is the average perfusion rate such that the total amount of perfusion is given by $\bar{\omega}_a L$, irrespective of the value of $n$. The exponent $n$ may take any value equal to zero (i.e., Chato’s case) or greater than zero, such that we can compare the results against Chato’s and elucidate the effect of blood pressure on the bioheat transfer for fixed total amount of perfusion. As we substitute the foregoing equation into the continuity equations (1.37) and (1.40), we readily obtain

$$\varepsilon_a \langle u \rangle^a = u_0 - \bar{\omega}_a L \left( \frac{x}{L} \right)^{1+n}$$

(1.68)

$$\varepsilon_v \langle u \rangle^v = -u_0 + \bar{\omega}_a L \left( \frac{x}{L} \right)^{1+n}$$

(1.69)

where $u_0$ is the apparent blood velocity at $x = 0$. As illustrated in Figure 1.6, the exponent $n$ controls the distribution of the perfusion rate. For a large exponent $n$, the perfusion bleed-off takes place rather suddenly toward the end of the vessel, indicating poor blood circulation.

Upon substituting these velocity distributions into the momentum equations (1.38) and (1.41), we obtain

$$\langle p \rangle\big|_{x=0} - \langle p \rangle\big|_{x=L} = (\varepsilon_a \langle p \rangle^a + \varepsilon_v \langle p \rangle^v)\big|_L = \mu \left( \frac{\varepsilon_a}{K_a} + \frac{\varepsilon_v}{K_v} \right) u_0 L \left( 1 - \frac{E}{2+n} \right)$$

(1.70)

where

$$E = \frac{\bar{\omega}_a L}{u_0}$$

(1.71)

is the dimensionless perfusion bleed-off rate, while $\mu$ is the viscosity. Thus, the pressure difference within the body may never be large since $\varepsilon_a/K_a \ll \varepsilon_v/K_v$. 

The equation (1.70), however, indicates that the blood pressure difference increases for either small perfusion bleed-off rate $E$ or large exponent $n$, which may result from aging.

Following Chato (1980), we note that the axial conduction terms in the blood energy equations are negligibly small as compared to the convection and perfusion terms. Then, the energy equations (1.50) and (1.51) along with the foregoing velocity distributions reduce to

$$\frac{d}{d(x/L)} \left[ \langle T \rangle^a \right] = -\frac{N}{1 - E \left( \frac{x}{L} \right)^{1+n}} \left( \langle T \rangle^a - \langle T \rangle^v \right) \quad (1.72)$$

$$\frac{d}{d(x/L)} \left[ \langle T \rangle^v \right] = \frac{N + (1+n) E \left( \frac{x}{L} \right)^n}{1 - E \left( \frac{x}{L} \right)^{1+n}} \left( \langle T \rangle^v - \langle T \rangle^a \right) \quad (1.73)$$

where

$$N = \frac{a_f h_f L}{\rho_f c_p f u_0} \quad (1.74)$$

is the number of heat transfer units. The boundary conditions are given by

$$x/L = 0: \quad \langle T \rangle^a = \langle T \rangle^a_0 \quad (1.75)$$

$$x/L = 1: \quad \langle T \rangle^v = \langle T \rangle^v_L \quad (1.76)$$

A series of numerical integrations were carried out for various sets of three important dimensionless parameters, namely, the dimensionless perfusion rate $E$, the number of heat transfer units $N$, and the exponent $n$. Thus, the temperature profiles along the vessel axes are obtained for the case of $n = 0$ and presented in Figures 1.7(a) and 1.7(b) for a physiological range of $E$ and $N$ values. The results appear to be in perfect agreement with the exact expressions reported by Chato (1980). The difference between the present curves for $n = 0$ and those based on Chato’s solution is indiscernible in the figure. Naturally, a better blood circulation (i.e., larger $E$) results in warming the venous blood efficiently. The figures show that its efficiency as a heat exchanging system increases with $N$.

The temperature profiles along the vessel axes for the case of $n = 5$ are presented in Figures 1.8(a) and 1.8(b). It is interesting to note that the arterial blood temperature for the case of nonzero $n$ always stays higher than that for the case of $E = 0$ (i.e., without perfusion) even at the end of the vessel. Following Chato (1980), we shall evaluate the total heat transfer from the artery to vein in terms of

$$q_{a-v} = \rho c_p u_0 \left( \langle T \rangle^v_0 - \langle T \rangle^v_L \right) \quad (1.77)$$

or its dimensionless form, namely,

$$\frac{q_{a-v}}{\rho c_p u_0 \left( \langle T \rangle^v_0 - \langle T \rangle^v_L \right)} = \frac{\langle T \rangle^v_0 - \langle T \rangle^v_L}{\langle T \rangle^a_0 - \langle T \rangle^a_L} \quad (1.78)$$
FIGURE 1.7
Arterial and venous blood temperature profiles along the vessel axes for the case of $n = 0$ (a) $N = 0.5$, $n = 0$ (b) $N = 1.0$, $n = 0$.

The total heat transfer from the artery to the vein is plotted against the exponent $n$ for various sets of $N$ and $E$ values in Figure 1.9. The total heat transfer decreases as increasing $n$ (i.e., worsening the blood circulation), while it increases with $E$ (i.e., increasing the perfusion rate).

1.7 Application of Bioheat Equation to Cryoablation Therapy

1.7.1 Related Work

Cryotherapy is often preferred to more traditional kinds of surgical therapy because of its minimal pain, scarring, and cost. The therapy has been gaining
significant acceptance as minimally invasive therapy for treatments of various malignant cancers. In a cryosurgical treatment, a single or multiprobe metal system is placed in contact with the target tissue through the skin. We have placed the emphasis of this paper upon the treatment of malignant lung tumor, since its application to lung cancer has been practiced on a trial basis for some years in Japanese medical schools (Nakatsuka et al. [2004]).

The cryoprobe in consideration houses a small coaxial nozzle internally. A high-pressure gas supply line is connected to the probe so as to supply Argon gas, which expands through the nozzle to the probe tip and then flows backward through the internal channel leading to the cryoprobe outlet. Owing to the Joule–Thompson effect, the outer surface temperature of the probe decreases below −135°C. As the tissue temperature is lowered, an ellipsoidal ice ball forms around each probe increasing in size, eventually encompassing and invading the entire tumor. This freezing process continues for 5 to 15 minutes. Then, the thawing process takes place as supplying Helium gas. Because
FIGURE 1.9
Effect of the exponent $n$ on the total heat transfer from artery to vein.

of the difference in the inversion temperature, the probe temperature during this process goes up to about $20^\circ$C to thaw the frozen tissue. This freezing-thawing sequence is repeated several times to kill abnormal cells or tissues such as are found in malignant tumors. Cryoinjury is believed to be due to two primary mechanisms: one is the direct injury to the cells from the freeze-thaw cycle, and the other is the indirect injury that results from the biological response to the damage caused by freezing, primarily the vasculature of the tumor.

As with any medical treatment, there are risks involved, primarily that of damage to nearby healthy tissue (Butz et al. [2000]). We must know the exact time required to freeze the entire cancer without damaging its surrounding healthy tissue. However, some standards for setting clinical parameters such as freezing rate and time are quite empirical today. Therefore, improvements in cryosurgery depend upon developing reliable mathematical models and preoperational simulation tools based on them.

Perhaps, Bischof et al. (1997) is the first to predict ice ball formation around a single cryosurgical probe. They used a cylindrical model to predict the interface location and temperature profile. Rewcastle et al. (1998) proposed a finite difference model for single probe freezing and generated isotherms within the ice ball during its growth. Keanini and Rubinsky (1992) and Baissalov et al. (2001) dealt with the problem of optimization in cryosurgery by regarding the placement of cryoprobes and freezing protocol design. Wan et al. (2003) appealed to finite element methodology to simulate ice ball formation in a multiprobe cryosurgery. Rabin and Shitzer (1998) and Rossi et al. (2007) introduced fairly sophisticated numerical techniques for freezing an angioma, while Rossi and Rabin (2007) developed an elegant
experimental technique to create a two-dimensional freezing problem associated with prostate cryosurgery with urethral warming. However, none of them considered the case of lung cancer nor were concerned with the effects of the blood perfusion on the temporal evolution of ice formation, which leads to the fact, namely, that there exists the limiting size of the tumor that one single cryoprobe can freeze at the maximum. No attempts were made to estimate the limiting radius for freezing tumors.

In this section, we shall appeal to the bioheat equation derived using the volume averaging theory and solve it both numerically and analytically to simulate the ice ball evolution and to locate the freezing front as time goes by. The analytical results based on the integral method agree very well with the numerical results based on the enthalpy method. Thus, the resulting analytical expression may be exploited for estimating the time for freezing a cancer of a given size. It will also be pointed out that there exists the limiting size of the cancer that one single cryoprobe can freeze at the maximum. It is believed that the present results lend quantitative support to the current empirical standards for cryosurgical clinical applications.

1.7.2 Bioheat Equation for Cryoablation

The general bioheat equation (1.26) for the solid tissue phase may be used to attack this problem. When the ratio of blood to total lung volume is small, equation (1.26) reduces to

$$
\rho_s c_s \frac{\partial T}{\partial t} = \frac{\partial}{\partial x_j} \left( k_s \frac{\partial T}{\partial x_j} \right) + \rho_f c_p \omega (T_f - T) + \alpha_f h (T_f - T) + S_m \quad (1.79)
$$

where the second time and third term on the right–hand side correspond to the blood perfusion to the tissue and the interfacial heat transfer from the blood to tissue through the vessel wall, respectively. Similarity between our equation and Pennes' equation is obvious as we rewrite the foregoing equation as

$$
\rho_s c_s \frac{\partial T}{\partial t} = \frac{\partial}{\partial x_j} \left( k_s \frac{\partial T}{\partial x_j} \right) + \rho_f c_p \omega_{\text{eff}} (T_f - T) + S_m \quad (1.80)
$$

where

$$
\omega_{\text{eff}} = \omega + \frac{\alpha_f h}{\rho_f c_p} \quad (1.81)
$$

is the effective perfusion rate. However, $\omega_{\text{eff}}$ conceptually differs from Pennes’ perfusion rate $\omega_{\text{Penne}}$ in the Pennes equation (1.27), which is purely empirical. It should also be noted that $T_f$ in $(T_f - T)$ is the local blood temperature, whereas $T_a0$ in equation (1.27) is the mean brachial artery temperature. The interfacial convective heat transfer between the blood and tissue can never be insignificant for countercurrent bioheat transfer. Even when there is no perfusion, that is, $\omega_{\text{Penne}} = 0$, the effective perfusion rate never vanishes since $\omega_{\text{eff}} = \alpha_f h / \rho_f c_p$. Thus, equation (1.81) must always be used for countercurrent bioheat transfer for the case of closely aligned pairs of vessels.
1.7.3 Numerical Analysis Based on Enthalpy Method

The enthalpy method is often used for locating an interface in phase change problems since it allows us to use a fixed mesh. An easy approach to implement the method is to include the latent heat by artificially increasing the specific heat capacity around the freezing point, thus making it a function of temperature as illustrated in Figure 1.10.

This simplest temperature function satisfies the obvious relationship among the latent heat of solidification $h_{sf}$, artificial maximum heat capacity $c_{max}$, and artificial temperature band $\Delta T$, namely, $h_{sf} = c_{max} (2\Delta T)$. The temperature band $\Delta T$ should be set according to the mesh resolution. Naturally, a finer grid system allows us to use a smaller $\Delta T$, which provides us a sharper freezing front where $T = T_i$. In this study, $\Delta T$ was set to from 1º to 5º. The temporal development of the freezing front is found fairly insensitive to $\Delta T$ in this range.

Any standard scheme may be used to discretize the governing equation (1.80). We shall use a finite volume method as proposed by Patankar (1980) to obtain a two-dimensional finite volume expression. We consider a control volume of size $\Delta x \Delta y$ centering the node $P$ (Pole), as shown in Figure 1.11, and

![Figure 1.10](image1.png)

Effective specific heat capacity.

![Figure 1.11](image2.png)

Grid nomenclatures.
let the upper-case letters \( E \) (East), \( W \) (West), \( N \) (North), and \( S \) (South) denote its neighboring nodes. Furthermore, we let the lowercase versions of the same letters \( e \), \( w \), \( n \), and \( s \) denote four faces of the control volume, and \((\delta x)_e\), \((\delta x)_w\), \((\delta y)_n\), and \((\delta y)_s\) denote the distances between the nodes. Then, the discretized version of the bioheat equation may be written as follows (see e.g., Nakayama [1995] for details):

\[
a_P T_P = a_E T_E + a_W T_W + a_N T_N + a_S T_S + b
\]  

(1.82)

where

\[
a_E = \left( \frac{\Delta y}{\delta x_e} \right) \frac{1}{T_E - T_P} \int_{T_P}^{T_E} k(T) dT
\]  

(1.83a)

\[
a_W = \left( \frac{\Delta y}{\delta x_w} \right) \frac{1}{T_P - T_W} \int_{T_W}^{T_P} k(T) dT
\]  

(1.83b)

\[
a_N = \left( \frac{\Delta x}{\delta y_n} \right) \frac{1}{T_N - T_P} \int_{T_P}^{T_N} k(T) dT
\]  

(1.83c)

\[
a_S = \left( \frac{\Delta x}{\delta y_s} \right) \frac{1}{T_P - T_S} \int_{T_S}^{T_P} k(T) dT
\]  

(1.83d)

\[
a_P = \left( \frac{\Delta x \Delta y}{\Delta t} \right) \rho c + a_E + a_W + a_N + a_S + \rho_f c_f \omega_{eff} \Delta x \Delta y
\]  

(1.83e)

\[
b = \left( \frac{\Delta x \Delta y}{\Delta t} \right) \rho c T_p + \left( \rho_f c_f \omega_{eff} T_f + S_m \right) \Delta x \Delta y
\]  

(1.83f)

\[
\rho c = \frac{1}{T_P - T_P} \int_{T_P}^{T_P} \rho c(T) dT
\]  

(1.83g)

The superscript \( o \) indicates the value at the old time \( t \), whereas no superscript is assigned for the value at the new time \( t + \Delta t \) \( t > 0 \).

The present computer code is capable of dealing with arbitrary two-dimensional shapes of cryoprobe and tumor as illustrated in Figure 1.12. The initial and boundary conditions for the freezing process using the cryoprobe of outer radius \( R_p \) are given as follows:

\[
t = 0: T = T_f \text{ (everywhere)}
\]  

(1.84)

\[
t > 0: T|_{x^2+y^2=R_p^2} = T_p \text{ (cryoprobe outer surface)}
\]  

(1.85a)

\[
T|_{x^2+y^2=\infty} = T_f \text{ (deep tissue region)}
\]  

(1.85b)

Computations were carried out using highly nonuniform grid systems, namely, \((250 \times 500)\) to cover the right half domain \(30 \text{ mm} \times 60 \text{ mm} \) for the case of the longitudinal tumor of \(20 \text{ mm} \times 27 \text{ mm} \), and \((350 \times 700)\) to cover the right–half domain \(160 \text{ mm} \times 160 \text{ mm} \) for the case of determining the limiting radius. The results associated with the limiting radius are found to be independent of any additional expansion of the calculation domain.
nodes are laid out densely around the probe. Grid refinement tests were carried out to ensure that the results are independent of grid systems. Convergence was measured in terms of the maximum change in temperature during an iteration, which was set to $10^{-5}$.

### 1.7.4 Analytical Treatment Based on Integral Method

In what follows, we shall exploit an integral method to derive an analytical expression for the limiting radius of the tumor that one single cryoprobe can freeze at the maximum (Nakayama et al. [2008]). For the sake of simplicity in this analytical treatment, we shall assume that the probe is a circular cylinder and that the tumor is so large that heat transfer to the healthy lung tissue is negligible.

The temperature around the cryoprobe is schematically shown in Figure 1.13, where $T_p$ and $T_i$ are the temperatures of the probe and freezing front, respectively, while $T_0$ is the body temperature. Upon referring to the figure, we may introduce the energy balance relationship at the freezing front at $r = R_i$ as follows:

$$
\rho_i h_f R_i \frac{dR_i}{dt} = R_i k_i \frac{\partial T}{\partial r} \bigg|_{r=R_i} - R_i k_i \frac{\partial T}{\partial r} \bigg|_{r=R_i} - \rho_c c_c (T_0 - T_i) R_i \frac{dR_i}{dt} : r = R_i
$$

(1.86)

where the subscripts $i$ and $c$ refer as to the frozen and unfrozen regions, respectively. The first, second, and third terms on the right-hand side correspond to the conduction heat flux evaluated at the ice side, the conduction heat flux evaluated at the unfrozen side, and the sensible heat entering to the interface as the interface (freezing front) at $r = R_i$ moves radially outward from the cryoprobe.
Bioheat Equations Based on VAT

FIGURE 1.13
Temperature profile around a cryoprobe.

The freezing front moves so slowly that quasi–steady approximation may be valid. Thus, assuming that the temperature profile within the frozen region follows that obtained at the steady state, namely,

\[
\frac{T - T_p}{T_i - T_p} = \frac{\ln(r/R_p)}{\ln(R_i/R_p)} : \quad R_p \leq r \leq R_i
\]  

where we may estimate the first term on the right hand side as

\[
R_i k_i \frac{\partial T}{\partial r} \bigg|_{r=R_i} = k_i \frac{T_i - T_p}{\ln(R_i/R_p)}
\]  

To estimate the second term on the right–hand side (representing the heat flux from the unfrozen tumor to the interface), we write the bioheat equation (1.79) for the unfrozen tumor region using the cylindrical coordinate system, which, under the quasi–steady approximation, may be integrated to give

\[-k_c R_i \frac{dT}{dr} \bigg|_{r=R_i} = \rho_c c_c \omega_{eff} \int_{R_i}^{R_m} r (T - T_0) dr + S_m \int_{R_i}^{R_m} r dr = 0 \]  

Let us assume that the temperature in this unfrozen region follows

\[
\frac{T - T_0}{T_i - T_0} = \left(1 - \frac{r - R_i}{R_m - R_i}\right)^2 : \quad R_i \leq r \leq R_m
\]

The equation satisfies \(T = T_i\) at \(r = R_i\) and \(T = T_0\) at \(r = R_m\) such that the boundary condition given by (1.85b) is satisfied in an approximate sense. Then substituting this temperature profile into Equation (1.89), we have

\[
2k_c R_i \frac{T_i - T_0}{R_m - R_i} - \rho_c c_c \omega_{eff} (T_i - T_0) \left(\frac{1}{3} (R_m - R_i) R_i + \frac{1}{12} (R_m - R_i)^2\right)
\]
\[+ S_m \frac{R_m^2 - R_i^2}{2} = 0
\]

(1.91)
which forms a cubic equation for \( R_i/(R_m - R_i) \). The root of the cubic equation is quite complex. However, it is found that the following explicit expression based on Newton’s shooting method gives a quite accurate value for the root:

\[
\frac{R_i}{R_m - R_i} = R_i \sqrt{\frac{1}{6} \left( \frac{\omega_{\text{eff}}}{\alpha_c} + 3 \frac{S_m}{k_c(T_0 - T_i)} \right)} + \frac{1}{8} \left( \frac{\omega_{\text{eff}}}{\alpha_c} + 6 \frac{S_m}{k_c(T_0 - T_i)} \right)
\]

where \( \alpha_c = k_c/\rho_c c_c \) is the thermal diffusivity of the unfrozen tumor. Thus, the second on the right-hand side of Equation (1.86) may be estimated as

\[
R_i k_c \frac{\partial T}{\partial r} \bigg|_{r=R_i} = 2k_c(T_0 - T_i) \left( R_i \sqrt{\frac{1}{6} \left( \frac{\omega_{\text{eff}}}{\alpha_c} + 3 \frac{S_m}{k_c(T_0 - T_i)} \right)} + \frac{1}{8} \left( \frac{\omega_{\text{eff}}}{\alpha_c} + 6 \frac{S_m}{k_c(T_0 - T_i)} \right) \right)
\]

Upon substituting (1.88) and (1.93) into (1.86), we have

\[
(\rho_i h_{sj} + \rho_c c_c(T_0 - T_i)) R_i \frac{dR_i}{dt} = k_i \frac{T_i - T_p}{\ln \left( \frac{R_i}{R_p} \right)} - 2k_c(T_0 - T_i) \left( R_i \sqrt{\frac{1}{6} \left( \frac{\omega_{\text{eff}}}{\alpha_c} + 3 \frac{S_m}{k_c(T_0 - T_i)} \right)} + \frac{1}{8} \left( \frac{\omega_{\text{eff}}}{\alpha_c} + 6 \frac{S_m}{k_c(T_0 - T_i)} \right) \right)
\]

which reduces to

\[
dt^* = \frac{1 + Sr}{Ste} \frac{R_i^* \ln R_i^*}{1 - \ln R_i^* \left( \sqrt{\frac{1}{3} (\omega^* + 3Met)} \right)^{1/2} R_i^* + \frac{\omega^* + 6Met}{3(\omega^* + 3Met)}} dR_i^*
\]

where

\[
R_i^* = R_i/R_p
\]

and

\[
t^* = \alpha_i t/R_p^2
\]
is Fourier number, where $\alpha_i = k_i/\rho_i c_i$ is the thermal diffusivity of the ice. Moreover, the following dimensionless parameters are introduced:

$$Ste_i = \frac{c_i (T_i - T_p)}{h_{sf}} : \text{Stefan number}$$

$$Sr = \frac{\rho_i c_i (T_0 - T_i)}{\rho_i h_{sf}}$$

$$\omega^* = \frac{\omega_{eff} R_p^2}{\alpha_c}$$

$$Cr = \frac{k_i (T_i - T_p)}{k_c (T_0 - T_i)}$$

$$Met = \frac{S_m R_p^2}{k_c (T_0 - T_i)}$$

The foregoing ordinary differential equation (1.95) may readily be integrated using any standard integration scheme such as Runge-Kutta-Gill, to find the dimensionless time $t^* = \alpha_c t/R_p^2$ required for freezing the tumor of a given dimensionless radius $R_i^* = R_i/R_p$. Obviously, the quasi–steady assumption is valid when $t^* Ste_i / (1 + Sr) > 1$, which roughly gives $t > 1$ sec. Thus, the assumption holds most part of the freezing process except its initial short period.

It is interesting to note that there exists the limiting radius $R_{lim}$ of the tumor that one single cryoprobe can freeze at the maximum. Its dimensionless value $R_i^* = R_{lim}/R_p$ may be obtained setting $dR_i^*/dt^* = 0$, for which equation (1.95) yields

$$\ln \frac{R_{lim}^*}{Cr} \left( \sqrt{\frac{2}{3}} (\omega^* + 3 Met)^{1/2} R_{lim}^* + \frac{\omega^* + 6 Met}{4(\omega^* + 3 Met)} \right) = 1$$

This implicit equation gives the dimensionless limiting radius $R_{lim}^*$ for a given set of the dimensionless values, $Met$, $Cr$, and $\omega^*$. Usually, $\omega^*$ is much larger than $Met$. For such cases, the following explicit expression based on Newton's shooting method may be used to give a reasonably accurate value for $R_{lim}^*$:

$$R_{lim}^* = \left( \sqrt{\frac{2}{3}} Cr + R_0^* \right) R_0^* + \sqrt{\frac{3}{2\pi\omega^*}} R_0^* (1 - \ln R_0^*)$$

where

$$R_0^* = \frac{3Cr^2}{\omega^*} + \frac{3Cr}{\omega^*} \left( 1 - \ln \left( \sqrt{\frac{3}{2\pi\omega^*}} Cr \right) \right)$$

For the present case of $Cr = 15.4$, equation (1.99) along with (1.100) gives $R_{lim}^* = 29.9$ and 12.9 for $\omega^* = 0.031$ ($\omega = 0.004/s$) and 0.310 ($\omega = 0.04/s$), respectively.
TABLE 1.1
Thermophysical Properties

<table>
<thead>
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<th>Subscript</th>
<th>Frozen</th>
<th>Tumor</th>
<th>Lung</th>
</tr>
</thead>
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<tr>
<td>$i$</td>
<td>$k [W/mK]$</td>
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<td>0.52</td>
</tr>
<tr>
<td></td>
<td>$\rho [kg/m^3]$</td>
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<td>1.000</td>
</tr>
<tr>
<td></td>
<td>$c [J/kgK]$</td>
<td>2.000</td>
<td>4.000</td>
</tr>
<tr>
<td></td>
<td>$\alpha [m^2/s]$</td>
<td>$1.10 \times 10^{-6}$</td>
<td>$1.30 \times 10^{-7}$</td>
</tr>
<tr>
<td></td>
<td>$h_{sf} = 3.34 \times 10^5 [J/kg]$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.7.5 Limiting Radius for Freezing a Tumor during Cryoablation

Some tissue freezes over a fairly large range of temperatures. However, for the case of lung cancer, the blood comes out from the vessels during the freezing–thawing sequence. The subsequent freezing takes place around the probe surrounded by the blood as a conducting medium. To a first approximation, we may use a single temperature for the phase change. Numerical calculations based on the enthalpy method were carried out for the case, in which the cryosurgical and biological parameters are given by

$$R_p = 1 \text{ mm}, T_p = -135^\circ C, T_i = -0^\circ C,$$

$$T_f = T_0 \text{ (body temperature)} = 37^\circ C, S_m = 1,200 \text{ W/m}^3.$$  

The effective perfusion rate $\omega_{eff}$ within the tumor can be quite high since some blood vessels are connected to the tumor. Here, we assume the effective perfusion rate in the range of $\omega_{eff} = 0.004$ to $0.04/s$. Moreover, the thermophysical properties for frozen and unfrozen tissues in the lung are listed in Table 1.1, according to Yokoyama (1993).

For the case in which $T_p = -135^\circ C$, $T_i = 0^\circ C$, $T_0 = 37^\circ C$, $S_m = 1,200 \text{ W/m}^3$, $\omega_{eff} = 0.004/s$, $R_p = 1 \text{ mm}$, we have $Ste_i = 0.808$, $Sr = 0.443$, $Met = 6.24 \times 10^{-5}$, $Cr = 15.4$, and $\omega^* = 0.031$. A typical evolution of the isotherms obtained for a longitudinal tumor of 20 mm $\times$ 27 mm is presented in Figures 1.14(a) to 1.14(c). The outermost isotherm in each figure corresponds to the freezing front (i.e., $T = T_i = 0^\circ C$). Figure 1.14(c) clearly indicates that ill placement of the probe may result in a substantial damage to the surrounding healthy tissue.

Let us consider the freezing process when the probe is placed in a large tumor. The temporal evolutions of the freezing front for the cases of $\omega_{eff} = 0.004/s$ (low perfusion) and $0.040/s$ (high perfusion) are illustrated in Figures 1.15(a) and 1.15(b), respectively, along with the curve analytically
FIGURE 1.14
Temporal evolution of isotherms (Interval 5°) (a) 60 sec. (b) 300 sec. (c) 600 sec.

obtained by integrating the ordinary differential equation (1.95). The figures may also be used to know the time required to kill the circular tumor of radius $R_i$. The numerical results obtained for these two cases in the figures clearly show that the limiting radii $R_{\text{lim}}$ for $\omega_{\text{eff}} = 0.004/s$ and $0.040/s$ are around 29.9 mm and 12.8 mm, respectively, which are estimated on the basis of the analytical expression (1.99).

Finally, the curve representing the limiting radius is generated from equation (1.99) and plotted against the effective perfusion rate in Figure 1.16. We learn from the figure that a single probe, even when placed in the center of the target, is capable of freezing only the size of a tumor whose equivalent radius is less than the limiting radius $R_{\text{lim}}$. The figure indicates that, for the case of comparatively high perfusion rate, a single probe of radius 1 mm can freeze a tumor only within the radius of 20 mm or less. This is consistent with the fact reported by Nakatsuka et al. (2004). In practice, we may introduce a factor $\lambda$ and estimate the range of the killed tissue by $r \leq \lambda R_{\text{lim}}$. The factor $\lambda$ has to be chosen carefully, depending on the specific clinical and surgical constraints, such as the number of cryoprobes available, the time set for a single freezing process, and the level of malignancy.
1.8 Conclusions

In this chapter, a general set of bioheat transfer equations for blood flows and its surrounding biological tissue was derived using a VAT established in the field of fluid-saturated porous media. Unknown correlations were modeled in terms of macroscopic determinable quantities. It has been shown that the resulting two-energy equation model reduces to existing empirical models such as the Pennes model, the Wulff model, and their modifications, under appropriate conditions. Subsequently, the two-energy equation model has been extended to the three-energy equation model, so as to account for the effect of countercurrent heat transfer between closely spaced arteries and veins in the
blood circulatory system. The resulting model, under appropriate conditions, naturally reduces to those introduced by Chato, Bejan, Keller, and Seiler and Weinbaum and Jiji for countercurrent heat transfer for the case of closely aligned pairs of vessels.

As for an application of the bioheat equation, the freezing process within a tumor during cryoablation therapy was investigated both analytically and numerically. The freezing front in a tumor during percutaneous cryoablation was traced exploiting the bioheat equation. It has been found that there exists a limiting size of the tumor that one single cryoprobe can freeze at the maximum. An excellent agreement between the analytical and numerical results has been achieved for the time required to freeze the tumor using the cryoprobe of one single needle. The resulting analytical expression for estimating the limiting radius provides useful information for cryotherapy treatment plans.

1.9 Nomenclature

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
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<tbody>
<tr>
<td>$A$</td>
<td>Surface area (m²)</td>
</tr>
<tr>
<td>$A_{int}$</td>
<td>Interface between the fluid and solid (m²)</td>
</tr>
<tr>
<td>$\alpha_f$</td>
<td>Specific surface area (1/m)</td>
</tr>
<tr>
<td>$b_{ij}$</td>
<td>Forchheimer tensor (1/m)</td>
</tr>
<tr>
<td>$c_p$</td>
<td>Specific heat at constant pressure (J/kgK)</td>
</tr>
<tr>
<td>$Cr$</td>
<td>Dimensionless parameter associated with the thermal conductivity ratio</td>
</tr>
</tbody>
</table>
Interfacial heat transfer coefficient (W/m²K)
Latent heat of solidification (W/kg)
Thermal conductivity (W/mK)
Permeability tensor (m²)
Dimensionless number associated with metabolic reaction rate
Unit vector pointing outward from the fluid side to solid side (−)
Pressure (Pa)
Radial coordinate (m)
Radius of the freezing front (m)
Limiting radius (m)
Metabolic reaction rate (W/m³)
Stephan number (-)
Temperature (K)
Phase change temperature (K)
Probe temperature (K)
Body temperature (K)
Fourier number (-)
Velocity vector (m/s)
Representative elementary volume (m³)
Cartesian coordinates (m)
Thermal diffusivity (m²/s)
Porosity (-)
Kinematic viscosity (m²/s)
Density (kg/m³)
Perfusion rate (1/s)
Net filtration rate (1/s)
Effective perfusion rate (1/s)
Dimensionless perfusion rate (-)
Deviation from intrinsic average
Volume average
Intrinsic average
Artery
Unfrozen tumor
Dispersion
Fluid
Ice interface
Cryoprobe
Solid
Vein
Dimensionless
1.10 References


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