International Journal of Heat and Mass Transfer 89 (2015) 894–902

Contents lists available at ScienceDirect

International Journal of Heat and Mass Transfer

journal homepage: www.elsevier.com/locate/ijhmt

Modeling of repeating freezing of biological tissues and analysis of possible microwave monitoring of local regions of thawing

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ARTICLE INFO

Article history:
Received 28 March 2015
Received in revised form 13 May 2015
Accepted 29 May 2015

Keywords:
Biological tissues
Heat transfer
Repeating freezing
Phase change
Microwave monitoring
Computational model

ABSTRACT

Transient heat transfer problems typical of recent-day cryosurgery are considered. Relatively simple models are suggested to take into account different temperatures of freezing inside the biological cells and in the gaps between the cells. In the most complicated case of interpenetrating media, when there is a thermal contact between the cells and also between the gaps, the model one-dimensional problem is formulated and solved with a specific attention to the effects produced by repeated periods of freezing and thawing. It is shown that the latent heat of melting may lead to a significant difference between temperatures of the cells aggregates typical of tumors and the extracellular medium. It is important that the temperature inside the cell aggregate alternatively becomes less or greater than the ambient temperature. Such a temperature regime may lead to serious thermo-mechanical damage of the tumor cells not only due to ordinary thermal expansion during the freezing but also because of tensile stresses that arise at the surface of the frozen biological cells or their aggregates. Potential possibility of microwave monitoring of small local regions of thawing is analyzed on the basis of Mie theory calculations.

1. Introduction

Thermal processes accompanying repeating freezing of two-component disperse systems as applied to behavior of biological tissues during cryosurgery are considered in the present paper. Thermal, mechanical, and biochemical processes in medical applications with the use alternating freezing and thawing of human tissues have attracted increasing attention of researches mainly because of cryogenic therapy and surgery of various tumors of both superficial tissues and internal organs [1–4]. It is important that cancer cells seem to be more sensitive to freezing injury than normal cells [5].

It is known that a strong cooling of living tissues leads first to freezing the extracellular medium. With further cooling, ice crystals may be formed within the biological cells. This phenomenon has been analyzed originally by Mazur [6]. One can find a description of this analysis in more recent reviews [7,8] (see also [1,2]). It is interesting that the so-called cell survival curve plotted versus the cooling rate has a maximum (the best survival) at a certain optimal rate of cooling. On the contrary, the strongest effect of a tissue necrosis is reached in the case of relatively low or high cooling rate. At low cooling rate, time is sufficient for the cell dehydratation, when water leaves the cell and freezes in a space between the cells. At high cooling rate, the ice crystals are formed inside the cell. The growing elongated ice crystals may damage not only organelles suspended in the cytoplasm but, most importantly – the cell membrane. In the case when the medium inside the cell was not damaged, the subsequent thawing leads to recovery of the living tissue functions. As a rule, several cycles of cell freezing and thawing lead to serious damage and irreversible changes of the biological tissue.

One can distinguish at least two stages of freezing of biological tissues. At the first stage, the heat loss during the phase change in the extracellular medium does not lead to any change in temperature of this medium because of certain time needed to remove the released significant latent heat. Simultaneously, the temperature inside the cell goes on to decrease monotonically up to the lower solidification temperature. Obviously, the local thermal nonequilibrium between the cell and extracellular medium takes place at this stage. At the second stage of freezing, there is no liquid phase in both intercellular and extracellular medium and the local thermal nonequilibrium is insignificant.

The temperature difference between the cell and extracellular medium is usually small because the single cell size is less than

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http://dx.doi.org/10.1016/j.ijheatmasstransfer.2015.05.117
0017-9310/

Nomenclature

α	radius of particle or droplet
c	specific heat capacity
d	diameter of particle
E	specific coefficient of absorption or scattering
f_v	volume fraction of droplets
h_v	volumetric heat transfer coefficient
k	thermal conductivity
L	latent heat of melting
m	complex index of refraction
$\tilde{m}$	modified complex index of refraction
n	index of refraction
P	volume fraction of extracellular space
q	heat flux
Q	efficiency factor of absorption, scattering, or extinction
r	radial coordinate
R	reflectance, radius of the region
t	current time
T	temperature
ΔT	temperature difference in Eq. (2)
W	absorbed radiation power
x	diffraction parameter
$\tilde{x}$	modified diffraction parameter
Z	axial coordinate

Greek symbols

α	absorption coefficient
ε	dielectric constant
κ	index of absorption
λ	wavelength
μ	cosine of an angle
ξ	argument in Eq. (2)
ρ	density
σ	scattering coefficient or electrical conductivity
φ	spread parameter
ω	scattering albedo

Subscripts and superscripts

a	absorption
e	external
el	electrical
m	melting
n–h	normal–hemispherical
max	maximum
s	scattering or static
tr	transport
λ	spectral
1, 2	number of the medium

several tens of microns [3]. The two basic types of tumors, benign tumors and malignant tumors, are distinguished by their cell types and growth patterns. Benign tumors grow as well-defined masses that push normal cells out of the way rather than invading surrounding tissue; they tend to be restricted to a limited area (localized). A benign tumor may form a capsule of connective tissue around itself that separates the tumor from adjacent normal cells. Some cells, especially in the tumors, may agglomerate and the extracellular medium is displaced into the space between the cell agglomerates. This effect takes place in the breast tumors, where the diameter of observed dense agglomerates may be about 160 μm at the ordinary size of the tumor about one centimeter [9]. It is not a general property of all the benign tumors, but some dangerous cancers are characterized by a relatively large compact region of cancerous cells separated from the outside by a membrane [10,11]. Most likely, the above described effect of thermal nonequilibrium will be considerable in the case of relatively large agglomerates of the tumor cells. One can also expect that this effect is more pronounced in the region of relatively slow cooling and at the periphery of the cooled region.

Naturally, the reliable computational data for the temperature and phase state of biological tissues can be obtained only with the use of detailed experimental data for thermal properties of the tissues in a wide temperature range taking into account certain changes in the medium morphology including possible appearance of fine cracks in the frozen tissue. The thermal properties of human tissues at low temperatures have been considered in some books and journal papers [1,12–14]. At the same time, as was noted in [14], this information is insufficient and the experimental studies should be continued.

In the present paper, some general methodological problems are considered without an attempt of a direct application of the computational results to one or another human tumor. The objective of the paper is as follows: (1) to develop an approximate two-temperature model for calculations of transient heat transfer in human tissues during a periodic freezing and thawing employed presently as an effective regime in medical practice, (2) to study computationally the conditions of a temporary strong thermal nonequilibrium at local regions of the cooled or heated biological tissues, (3) to suggest possible principal approach to the microwave monitoring the local volumetric phase changes taking into account specific spectral properties of a composite two-phase medium formed during the freezing–thawing process.

2. Heat transfer models

One can imagine three typical morphologies of the composite tissue for the subsequent use of different heat transfer models. The most general (and maybe the most realistic) model is based on assumption of continuous interpenetrating structure of two components: the cell medium and the extracellular medium. It is assumed that there is a thermal contact between the elements of every medium. In some special cases, two other models can be more adequate to the real conditions. The cells may be suspended in the extracellular medium without direct thermal contact between the cells or, on the contrary, the volumes of extracellular medium may be isolated from each other by more densely packed cells. The mathematical formulation suggested in the present paper includes all of the above described variants. To derive coupled energy equations, it is natural to employ a general theory of heat transfer in porous media [15]. Note that the model of this type has been recently suggested in [16] to take into account the volumetric heat transfer between arterial blood and ambient human tissues.

In this section, we consider the simplest case of a 1-D model problem for the axisymmetric volume of a two-component medium having in mind that one of these components is a conventional cellular medium with some average properties and another component is an extracellular medium, which is also treated as a homogeneous one. The formulation of transient heat conduction problem without taking into account the blood perfusion and metabolic heat generation is as follows:

$$\rho_1[c_1 + L_1 f(T_1)]\frac{\partial T_1}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}\left(rk_1\frac{\partial T_1}{\partial r}\right) + \frac{h_v(T_2 - T_1)}{1-p} \tag{1a}$$