International Conference on Control, Engineering & Information Technology (CEIT'13)
Proceedings Engineering & Technology - Vol.1, pp. 7-12, 2013

Transmission Line Matrix Modelling of bioheat transfer in cryogenic therapy applications

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Abstract— **The transmission line matrix (TLM) method is well suited to efficiently solve the bioheat transfer with phase change in biological tissues during the freezing process. However, the accuracy of this model relies upon thermal properties which are known to be highly dependent on temperature during solidification process. To do so, a numerical algorithm based on the TLM method with a hyperbolic model and an automatic time stepping is developed to predict temperature history during freezing process taking into consideration phase change and temperature-dependant thermophysical properties. Propagation of ice ball fronts or solid-liquid interface as well as lethal temperatures isotherms are investigated. Cooling analysis of in vivo biosystems such as cryoablation and the role of blood flow and metabolic heat generation are analyzed during phase changes. Confirmation of results through comparison with known numerical and experimental solutions is achieved where possible.**

Keywords— **TLM, Modelling, Cryotherapy, Bioheat transfer, Solidification, Phase change, blood perfusion.**

I. INTRODUCTION

Cryosurgery is frequently performed as a minimally-invasive procedure that destructs undesired biological tissues as cancers by freezing [1],[2]. Cryoablation compares favorably with other techniques, such as radical surgery and irradiation of tissues because it is less traumatic and reduces blood loss and hospitalization times [3].
Freezing starts as the probes are turned on, and ice balls formed on each probe and propagate into tissue as a freeze front leading to localized tissue destruction.

An important engineering task in cryotherapy is to measure or calculate the heat transfer during freezing-induced phase change in biosystems and then correlate this with the biological outcome. The surgeon may also resort to treatment planning strategies, such as: the ability to demonstrate that the temperature distribution in a cryolesion is sufficiently low to achieve cellular destruction in the region of interest and the optimal placement of cryoprobes to maximize tissue ablation while minimizing collateral damage by delineation of the frozen region borders.

The relationship between thermodynamic parameters such as temperature, cooling rate and cell destruction is not completely established. However, quantitative estimation of these parameters is also an important tool for investigating this relationship. It was being tested that difference between estimated and measured temperatures was larger close to the cryoprobe than in peripheral regions [3]. This is due to the steep temperature gradient in this area. However, in clinical settings, the main objective is destruction of tissue and the central area is therefore of less importance, as the temperature in this region is adequate for cellular destruction.

Although phase change problems have been analyzed during the last century, there are very few exact solutions which are commonly based on numerical techniques [4–7] or approximate analytical methods [8–10]. Studies aimed at improving cryoprocedures by numerically modeling the freezing and assessing the best placement for the cryoprobes have been carried out recently by other researchers [11],[12]. Information given by isotherms is also beneficial to research on temperature distribution within frozen tissue as noninvasive spatial information is provided [13]. In cryoablation, the zone of coagulation necrosis or lethal temperature threshold lies typically within the isotherm zone of -40 ^{0}C [14] and −45 ^{0}C [15].

Basic numerical approaches that are applied in solving phase change in cryogenic problems, are the moving interface tracking technique [16], enthalpy method [17],[18], source term method[19],[20] and the apparent heat capacity approach [21],[22].

In this study, a numerical scheme based on transmission line matrix (TLM) method is developed for freezing processes such as cryoablation. Because of the simplicity and reasonable accuracy under certain conditions, Pennes' bioheat equation has been extensively used in heat transfer analysis of biological tissues under thawing and freezing conditions, it is employed in this study with temperature-dependant thermophysical properties, when the change of phase from liquid (soft) to solid state deviates from equilibrium conditions, leading to the occurrence of a latent heat. The source term method is used to represent the latent heat during phase change, this, in addition to blood perfusion and metabolic heat generation involved during in vivo cryotherapy. This numerical model was validated by comparing results to those obtained by other researchers [23].

Nomenclature

c	specific heat (J/kg.K)
C	TLM node capacitor (F)

f	Crystallized fraction
G	TLM node conductance (S)
H	Latent heat of whole phase change (J/m^3)
I	Liquid-solid Interface function
I(V)	Electric current source (A)
k	thermal conductivity (W/m.K)
L	TLM Node inductance (H)
Q	metabolic heat (W/m3)
R	TLM node resistance (Ω)
S	Source term of latent heat (W/m3)
t	Time (s)
T	Temperature (K)
V	TLM node voltage (volt)
Z	TLM node impedance (Ω)
ρ	density (kg/m3)
ω	Blood perfusion rate (1/s)
τ	Tissue relaxation time (s)
υ	Propagation speed of thermal energy (m/s)
Δx	Discretization in space (m)
Δt	Discretization in time (s)

Subscripts

a	Arterial
b	Blood
f	Fraction
l	Liquid phase
ls	Liquid-solid phase
s	Solid phase
0	Initial state

II. GOVERNING EQUATIONS AT CRYOGENIC TEMPERATURES

The phase change from liquid to solid state in a cryosurgery process will occur over a temperature range (T_l-T_s) where both the solid and liquid phases coexist; it is often referred to as the mushy zone. However, mass transfer in this phase related to formation and growth of ice crystals can be neglected for many practical situations in cryobiology where heat diffusivity is orders of magnitude higher than mass diffusivity [24]. Thermal properties of biomaterials in the subzero temperature range have a large dependence on temperature, we consider in this study that only thermal conductivity (k) and specific heat capacity of tissue (c) vary with temperature (fig.2) (i.e. conductivity rise and specific heat drop at lower temperatures).Density (ρ) is supposed constant and volume changes due to freezing are neglected (table1). Since this is a study of phase change problem, an appropriate heat equation must be formulated for each phase zone.

(i) liquid zone $(T \geq T_l)$

At temperatures above the liquid temperature T_l, the system remains in liquid (soft) form and at its original thermophysical properties (k_l and c_l).

Thermal energy equation at unfrozen tissues is represented mathematically by the Penne's bioheat equation (eq. 1), which is valid for representing heat flow in the presence of dense capillary networks and not in the presence of major blood vessels, as explained by other researchers [25]:

$$\rho c_l \frac{\partial T}{\partial t} = k_l\left(\nabla^2 T\right) + Q + \omega \rho_b c_b \left(T_a - T\right) \qquad (1)$$

Where T is temperature; ρ is density; k_l and c_l are thermal conductivity and specific heat capacity of tissue in liquid state. Index b indicates blood properties.
Metabolic heat is generated throughout the unfrozen tissue at a constant volumetric rate Q. Blood at the arterial temperature Ta is supplied to the tissue at a uniform volumetric rate per unit tissue volume ω.

(ii) Solid zone $(T \leq T_s)$

At temperatures below Ts the biosystem with new thermophysical properties (k_s and c_s) will undergo solidification. Blood circulation stops once the tissue is frozen [1],[25], and the latter two terms of (eq.1) are set to zero inside the frozen region, thus, the classical heat conduction equation is applicable in this region:

$$\rho c_s \frac{\partial T}{\partial t} = k_s\left(\nabla^2 T\right) \qquad (2)$$

Index s indicates the solid state of tissue.

(iii) Phase change zone $(T_s \leq T \leq T_l)$

Upon freezing, primary ice will form and grow (depending on the cooling rate), and a latent heat of fusion is liberated as a result of freezing process. This heat is supplied as a source term to (eq.1) for the non-isothermal phase change:

$$\rho \frac{\partial}{\partial t}\left(c_{ls} T\right) = \nabla\left(k_{ls} \nabla T\right) + Q + \omega \rho_b c_b \left(T_a - T\right) + S \qquad (3)$$

Thermal conductivity (k_{ls}) and specific heat capacity (c_{ls}) of the mushy zone are calculated by combination of solid and liquid properties [23],[24]:

$$\frac{1}{k_{ls}} = \frac{f}{k_s} + \frac{(1-f)}{k_l} \qquad c_{ls} = f \cdot c_s + (1-f) \cdot c_l \qquad (4)$$

Where *f* is the crystallized fraction that is the amount of frozen tissue over the maximum amount of tissue which can possibly freeze. In many systems, it is reasonable to assume that the crystallized fraction is just a temperature function [26] and is continuously updated with the passage of time:

$$f = \frac{T_l - T}{T_l - T_s} \qquad \text{where} \quad T_s \leq T \leq T_l \qquad (5)$$

The source term S representing latent heat of phase change is described by [24]:

$$S = H_f \cdot \frac{\Delta f}{\Delta t} \qquad (6)$$

Where latent heat of phase change (H_f) is related with the one of the whole phase change L (at the end of solidification process) by:

$$H_f = f \cdot H \tag{7}$$

Once the formulation of solidification is determined, we have to calculate the moving boundary between liquid and solid phases during cryoprocess. It presents the limit between frozen and unfrozen tissues, by assuming temperature profiles in these two regions.

Methods for the moving boundary problem are classified mainly into two groups [27],[28]: front tracking method and front capturing method. In this study, the second method is more suitable for easy calculations; it encompasses the sub-method of phase field (volume of fluid (VOF)). The interface function I at a given time t is formulated as:

$$I = \begin{cases} 0 & T \succ T_s \\ 1 & T \prec T_s \end{cases} \tag{8}$$

It is a function with a value in the range of 0 through 1.

III. Numerical Solution of the Problem

For situations when direct measurement of thermal transport becomes difficult and simplified analytical approaches are inadequate, numerical calculation becomes a valuable alternative in allowing us to predict the outcome of a cryobiological procedure.

Transmission Line Matrix (TLM) method was adapted to problems in many areas; starting by electromagnetic, thermodynamic optics, acoustics and finally hyperthermal and cryothermal procedures in biosystems. It can provide new insights into the physiological processes. Anyway, this model has proved its explicit and unconditionally stable nature when used as a physiological model that predicts pressure/flow waveforms of blood along the arterial tree in human circulation [29]. It was used also as a model for the study of tumours in living tissues [30] and injuries in skin [31]. However, the methodology for using TLM in cryogenic procedures is not well established.

This study takes the initiative to illustrate the applicability of TLM method at cryotherapy procedures. It's based on Huygens principle and could be used for modeling any phenomena which obeys this principle. It is a time and space discrete method that solves field problems using their equivalent electrical circuit [32]. It assembles a lattice of discrete points in space connected by transmission lines and defines the transmission matrix between lattice points, so that successive calculations can be performed. Transmission-lines are considered as a network of distributed models of capacitors, inductors and resistors; the physical variable is modeled as a sequence of voltage pulses travelling through this network.

The Maxwell's curl equation for electromagnetic propagation defines well such a network:

$$LC\frac{\partial^2 V}{\partial t^2} + RC\frac{\partial V}{\partial t} + RG.V = \nabla^2 V \tag{9}$$

a)Parabolic model

In TLM method; neglecting the inductance (L) term in equation (9) by assuming small time steps means that there is an infinite speed of thermal transport and then relaxation time of systems is neglected. Immediately; analogy is made between equations (1-9).

It should be noted that Pennes' bioheat equation has been extensively used in heat transfer analysis of biological tissues under thawing and freezing conditions, then analogy made between bioheat equation (1) and Maxwell's curl equation for electromagnetic propagation (9) in TLM method makes it possible and easy to define the absorption of thermal energy during a cryoprocessus as a diffusion processus as long as there is a temperature gradient. Therefore, temperature at every node in the transmission lines network becomes analogous to potential V without changing the TLM model (Fig.1) for high temperatures [30-32], resulting analogies are:

$$\mathrm{RC}.\frac{\partial V}{\partial t} \equiv \rho \frac{\partial}{\partial t}\left(\frac{c_i}{k_i}T\right) \quad , \quad RGV \equiv \frac{\omega \rho_b c_b}{k_i}T \tag{10}$$

Resistor R and capacitor C are the electric models of thermal tissue properties and can be deduced from a dimensional analysis:

$$R = \frac{1}{2k_i \Delta x}\,, C = \rho c_i\, \Delta x^3 \tag{11}$$

Indice (i) refers to any state of phases (l,s,ls). Noting that impedance C is modelled in terms of transmission lines of impedance Z (in 1 and 2 dimensions respectively):

$$Z = \frac{\Delta t}{C} \quad , \quad Z = 2\frac{\Delta t}{C} \tag{12}$$

Perfusion is modelled as a controlled current source I instead of a conductance G as shown in equation (9) to allow more stables results [32]. This current source depends at every moment on the node temperature and its thermal properties.

$$I_p \equiv \frac{\omega \rho_b c_b}{k_i}(T - T_a) \tag{13}$$

The metabolic heat generation rate Q is modelled as a constant current source and is assumed to present the initial conditions of living tissue temperature (T_0=37°C).

The source term S representing the latent heat of phase change in equation (3) is represented also as a current source depending on crystallized fraction, time and thermophysical properties according to the combination of equations (5-6-7).

$$I_S \equiv \frac{f\,H}{k_i} \cdot \frac{\Delta f}{\Delta t} \tag{14}$$

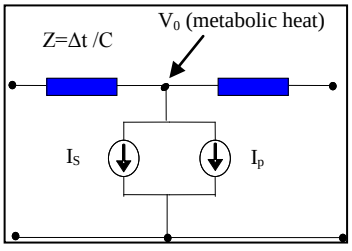

Fig.1: Typical form of 1D TLM node for bioheat transfer with blood perfusion and latent heat.

One has to notice that boundaries are supposed to be sufficiently far from the cooling surface, that they have very little influence on inner region of interest.

b)Hyperbolic model and time step changes

By considering a non-zero thermal relaxation time of tissue (τ), a non-Fourier model should be considered by taking into account the propagation term $\left(LC\frac{\partial^2 V}{\partial t^2}\right)$ of equation (9) which introduces and models the relaxation phenomena.

It's not our intension to describe the hyperbolic transmission lines model here, since this has been established [33,34]. Briefly, a finite propagation speed of thermal energy is used which depends on thermal properties of tissue:

$$v = \frac{k_i}{\rho c_i \tau} = \frac{\Delta x}{\Delta t} \qquad i = l, ls, s \qquad (15)$$

However, thermal properties (k_i , c_i) changes according different phases and are dependent in phase change especially on the crystallized fraction in space and time (eq. 4). Hence, timestep will vary since discretization in space (Δx) is constant.

Although implementation of timestep changes in TLM routines are discussed elsewhere [35]; our study focuses on the ability of TLM method to monitor different cases in a cryoprocessus such as determining local crystallized fractions and interface motion instantaneously and updating a variety of properties as a function of temperature and crystallized fraction.

TABLE (1): Thermophysical properties of biological tissues according to temperature T.

	$T > T_L = -1$ °C	$T_L = -1$ °C $> T > T_S = -8$ °C	$T_S = -8$ °C $> T$
C (J KG^{-1} K^{-1})	$C_L = 3430$	EQUATION (4)	$C_S = 1715$
K (W M^{-1} K^{-1})	$K_L = 0.5$	EQUATION (4)	$K_S = 2$
P (KG M^{-3})	1050	1050	1050
Ω C_b (W KG^{-1} K^{-1})	17	17	0
P_b (KG M^{-3})	1050	1050	1050
L (KJ M^{-3})		250	

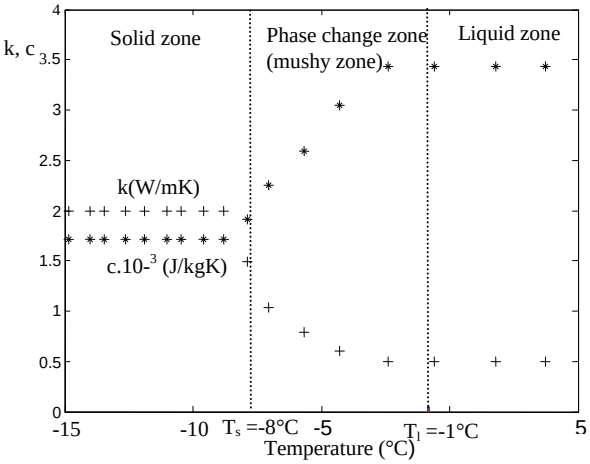

Fig.2: Schematic presentation of the temperature–dependant thermal properties in the current study.

IV. RESULTS AND DISCUSSION

TLM model numerically solved Penne's bioheat equation and gives the thermal history of cooling of in vivo biosystems such as cryoablation. In what follows, the hyperbolic model is adopted with a thermal propagation speed in order to introduce the temperature-dependant thermal properties in all freezing process phases. In order to validate this numerical study, a layer of skin tissue is considered to have a one dimensional case initially at 27 °C (in vivo temperature) and subjected to a boundary temperature T(x=0) at -196 °C (liquid nitrogen temperature). The other boundary (x=2cm) is supposed to be sufficiently far from the cooling surface and have no influence on inner region of interest.

Skin tissue properties are presented in table (1). Figure (3) shows the temperature distribution within the sample tissue. It is clear that the solidification process for the area closer to the cooling boundary occurs in a shorter time than that of the farther one. A good agreement is observed between the current study and results obtained by other researchers [23]. Figure (4) shows the temperature profiles in two different points which gives the dynamics of the problem and confirm the above result. The concept of a finite heat propagation velocity is well viewed by the sharp wave front at shorter times for both positions and near the cooling surface for x=0.6cm.

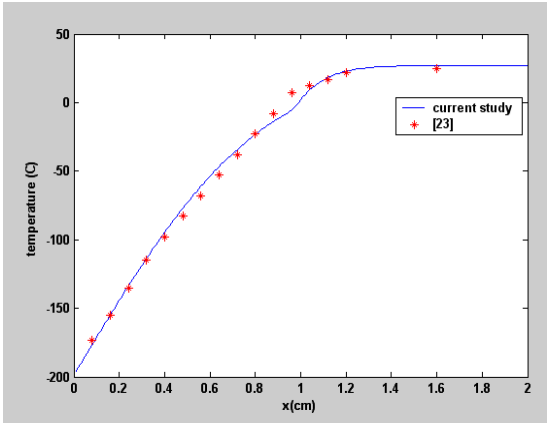

Fig.3: Temperature distribution in 1 Dimension after 50s of freezing process.

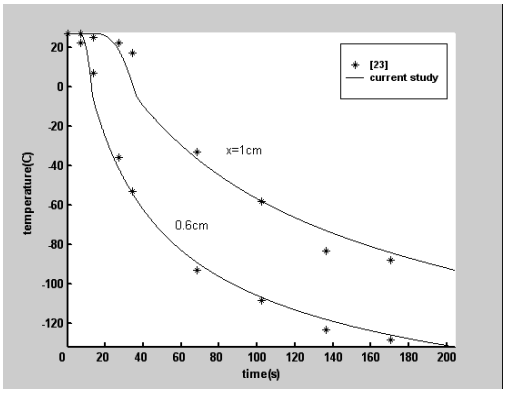

Fig.4: Temperature profiles in two different positions.

To show the effect of blood perfusion on freezing interface location, the transient solution of this one is plotted in figure (5) for two different surface cooling temperatures. Because the initial temperature gradient is more severe compared with the later times, we observe for each subplot; an increasing motion of the interface with a high slope. When time increases the temperature gradient between tissue and cooling boundary becomes smaller, thus the slope of the freezing position profile decreases. It is observed that the effect of blood energy supply on interface location is not very significant although the decreasing of interface motion with blood perfusion. Even this decreasing in profiles slopes at the presence of blood perfusion is well viewed when we decrease the cooling boundary temperature from -100 to -50 °C, we can deduce that heating due to blood perfusion during a cryoprocessus remains insignificant or negligible and considered as a second-order effect [5].

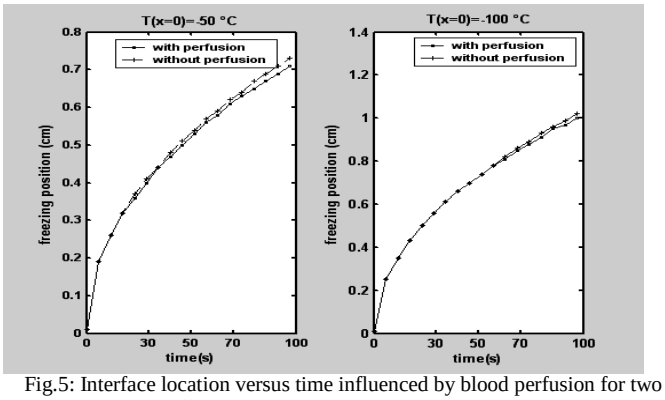

Fig.5: Interface location versus time influenced by blood perfusion for two different cooling temperatures (at T(x=0)).

It is seen based on the temperature and cooling rate profiles (Fig. 6) of the node located at x=5mm from the cooling surface; that the local area is subject initially to fast cooling rates; which is reduced at early times according to the decreasing in temperature gradient. The non existence of a cooling rate at first seconds is due to freezing-front propagation with finite velocity; the system remains in its initial form with metabolic temperature until the freezing interface arrival. Noting that the cooling rates varied greatly depending on the location within the sample.

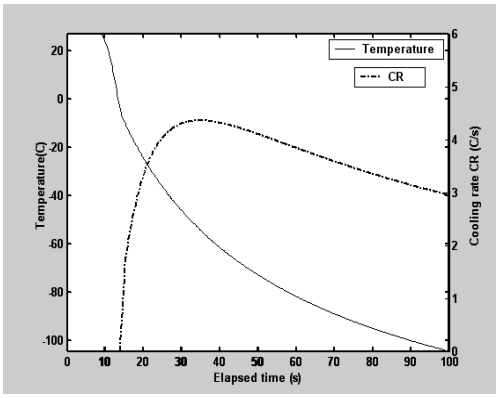

Fig.6: Temperature and cooling rate profiles at x=5mm from the cooling surface.

The latent heat generated according the liquid-solid phase-change in all freezing processes is assumed to be negligible. This is well explained in microscopic scale when there are not enough molecules left to join the formed crystal and transfer their energy into bond formation, then the temperature rise due to released latent heat will stop and will not be observed at a macroscopic scale analysis.

At a reel cryotherapy with experimental results, the system has a three-Dimensional behavior; and a 2D numerical study approach is well suited. For this purpose; the freezing of a blood perfused-tissue around one cryoprobe is considered to have a two dimensional case. Initial and outer boundary temperatures are those of the first 1D-modelling. Cryoprobe is turned on with a constant cooling temperature of -50 K.

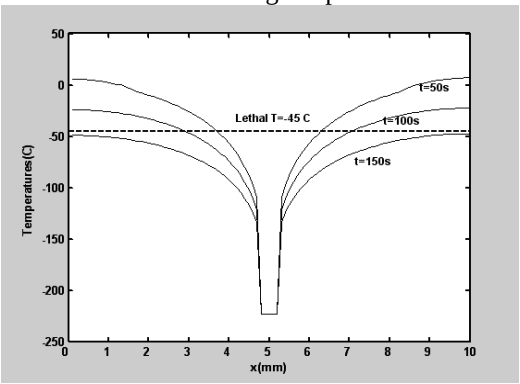

Fig.7: Temperature profiles at different times along the Cryoprobe section (y = 5mm from outer boundaries).

Fig.7 shows the time dependence of temperature profile for y = 5mm from the outer boundaries. The temperature profiles show an increase in the interval of influence of the cryoprobe as time progresses. The time requested to undergo a cryolesion which is the region under lethal temperature isotherm is related to the cryotherapy conditions, in this case; t = 150s leads to the necrosis of all treated tissue.

V. CONCLUSION

In this work, a numerical scheme based on transmission line matrix (TLM) method is developed for freezing processes of in-vivo biosystems such as cryoablation. The Penne's

bioheat transfer with phase change is studied in 1 and 2D incorporating temperature-dependant thermophysical properties with a variable time step. Biological tissues as not pure systems freeze over a wide temperature range creating a two phase zone related to non-instantaneous crystallization which occurs under slow cooling conditions. The numerical technique has been developed accordingly to predict instantaneously local temperatures, crystallized fractions, freezing interface location and assumed lethal temperature isotherms. We considered a numerical research [23] which is based on an experimental one; to validate our model because it is a recent study that focuses on the same application of our interest.

Hyperbolic model related to the relaxation time of biological tissues is a best method leading to the new developed TLM scheme used previously. It's observed that the cryotherapy outcomes are altered by the cryoprobe location and the cooling rate which depends on thermophysical properties. It is observed that effects of blood energy supply and latent heat generation of phase change are negligible in a cryotherapy results.

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