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Comparative Analysis of Temperature Fields during cryosurgery: Study using the Porosity-based Bioheat Models and Pennes Model

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Abstract - Cryosurgery plays a crucial role in cancer treatment by utilizing an advanced and minimally invasive surgical technique with significant potential for efficiently eradicating both carcinoma and non-carcinoma tissues through freezing methods. Optimizing this technique is crucial for minimizing both inadequate ablation and collateral damage to healthy tissue during the procedure. Biological tissues, by virtue of their porous nature, offer a network of interconnected spaces between dispersed cells. This intricate network facilitates the efficient delivery of vital nutrients and minerals throughout the tissue. The current study develops a mathematical model integrate bioheat equations that account for varying porosity and apply Pennes equation with variable perfusion, utilizing an effective heat capacity formulation to Capture the intricate details of the phase transitions during freezing and thawing. The transient temperature distribution, propagation of lethal front, and the resulting ablation size within tissue is investigated within the tissue, focusing on understanding the impact of blood vessel sizes, blood velocities, and porosities.

Keywords**:** Cryosurgery, Porous medium, bioheat transfer, Local thermal non-equilibrium model (LTNE), Pennes equation, Local thermal equilibrium (LTE).

1. Introduction

Cancer poses a significant financial burden on worldwide healthcare systems, leading to increased mortality and disability-adjusted life years. Among various cancer treating technique cryosurgery is particularly noteworthy as a promising, minimally invasive, and precise treatment option for tumours.

Cryosurgery strives for complete tumour eradication while minimizing harm to surrounding healthy tissue. This is achieved by reaching temperatures that induce tissue death (necrosis) within the tumour. The precise temperature needed for this effect, known as the lethal threshold. In vivo studies, suggest a range of lethal temperature around -40 to -50°C [1-4]. The techniques like X-ray, ultrasound, and CT scans effectively monitor ice ball growth, but their limitations lie in detecting temperatures below 0°C, which falls outside their practical range for this application. Resolving temperatures as low as −35°C is only possible using MRI technique[5]. Because of this, scientists have been using a variety of mathematical models to gauge how much tissue damage cryosurgery would cause by freezing.

The initial bioheat equation introduced by H. Pennes in 1948 has led to the proposal of numerous bioheat models by researchers[6]. The Pennes model has substantial limitations, including the assumption that blood from the arteries retains a constant temperature of approximately 37°C and that venous blood is in equilibrium thermally with the tissue ignoring the direction of blood flow and assuming uniform perfusion rates within the tissue. To overcome these limitations, researchers have developed and applied a range of models to thermal therapies [7-8]. Compared to the widely used Pennes model, the LTNE model Xuan & Roetzel 1997 [9] emerges as a promising alternative. Its strength lies in its ability to capture the interplay between accuracy and complexity by incorporating the effects of porous media in tissues. Khaled and Vafai [10] Examined many applications of diffusion and the transfer of momentum by convection in porous materials. The study concluded that the porous medium model is appropriate for simulating heat transfer in biological tissues since it relies less on assumptions compared to other bioheat models. Khanafer and Vafai[11] studied the evolution of the diffusion equation by using the method of local volume-averaging. Their work centred on the practical applications of the diffusion equation, which include magnetic resonance imaging and medicine delivery. Their objective was to create distinctive models using porous media for use in biological contexts. Andreozzi et al [12]. proposed a biological tissue-specific local thermal nonequilibrium model. This model intended for thermal ablation

systems with several antennas. To accommodate for tissue and blood's different water content, they modified a porous media-based model to include water vaporization independently. Porous media theory, conceptualize biological tissue as a two-phase domain, consisting of a "tissue phase" and a "blood phase" that coexist within the same space.

Based on the literature review above, it seems that there isn't a study that compares three models the Pennes model, the LTE model, and the LTNE model using commercial software (COMSOL multiphysics), in the current study comparison is done among the three bioheat models. The parameters changed for the study were porosity and perfusion (which changed as a parabolic function) in the tumour tissue but remains the same in the healthy tissue. Further the results are found by looking at spatial distribution of temperature fields with respect to time and the temporal evolution of lethal front.

2. MATHEMATICAL MODEL

To formulate the problem, the following model configuration and governing equations have been used which thoroughly discuss herein.

2.1 Model Geometry and properties parameters

Figure 1a shows a sketch of the cylinder-shaped healthy and the sphere-shaped tumour tissue inside it. Figure 1b shows the 2D axisymmetric model that was used to save computer power. The 1.50 cm diameter sphere in the middle represents the tumour, and the 8-cm-diameter, 16-cm-long cylinder on the outside represents the healthy liver tissue. This distance is large enough to neglect the end effect. Using a cryoprobe with a width of 0.15 cm and a length of 1 cm, which works at 77 K, cooling is done inside the tumour sphere. The table 1 includes the biological properties of tumour and healthy tissue.

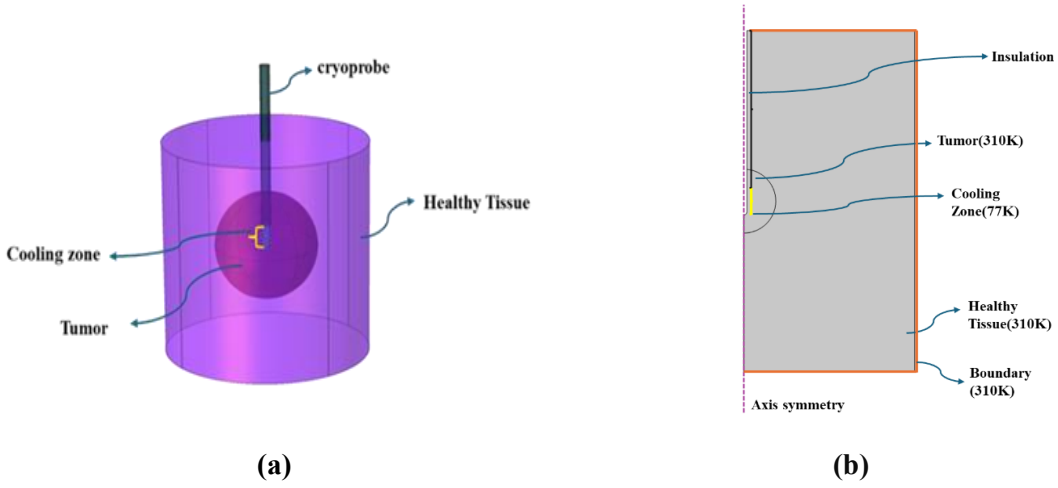

Fig. 1 Displays the spherical tumour tissue undergoing cryosurgery with the cylindrical healthy tissue (a) represent physical model and (b) Shows a numerical model.

Table 1: Biological characteristics of the tumour and healthy liver tissue [13-16]

k_t	Tissue Conductivity	W m^{-1} $°C^{-1}$	k_f = Frozen = 2
			k_u = Unfrozen = 0.5
c_t	Tissue Specific heat	J kg^{-1} $°C^{-1}$	c_f = Frozen = 1800
			c_u = Unfrozen = 3600
ρ_t	Tissue Density	Kg m^{-3}	ρ_f = Frozen = 998
			ρ_u = Unfrozen = 1000,
k_b	Blood Conductivity	W m^{-1} $°C^{-1}$	0.49
c_b	Blood Specific heat	J kg^{-1} $°C^{-1}$	3600
ρ_b	Blood Density	Kg m^{-3}	1050
μ	Viscosity of the blood	Pa s^{-1}	0.003
Q_m	Metabolic heat generation	W m^{-3}	Tumour = 42,000
			Liver = 4200
Q_f	Latent heat of fusion	MJ m^{-3}	250
T_{mu}	Upper limit of the phase transition	°C	-1
T_{ml}	Lower limit of the phase transition	°C	-8
u_b	blood velocity	m/s	$4 * 10^{-3}$
d	diameter of blood vessel	m	$3 * 10^{-5}$
ω_{int}	interfacial perfusion	1/s	0.047
ω_{min}	minimum perfusion		0.017
ω_{max}	maximum perfusion		0.056
ε_{int}	interfacial porosity		0.31
ε_{min}	minimum porosity		0.07
ε_{max}	maximum porosity		0.23

3.2 Governing Equations

The three different bioheat models applied to the porous biological model. They include the variable perfusion Pennes bioheat equation, the modified porosity LTNE model and the LTE model.

Pennes bioheat model based on equations considering variable perfusion.

In 1948, Harry Pennes developed the bioheat equation based on an experimental investigation of the human forearm [6]. Pennes' model has included modifications to the transient heat conduction equation to consider the influence of metabolic heat generation and blood circulation on heat transmission in living tissue. The whole tissue in the model is based on the assumption that the temperature of the arterial blood is 37°C.

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

$$Q_{perf} = \rho_b c_b \omega_{var} (T_a - T) \quad (2)$$

$$\omega_{var} = \left(\frac{\omega_{int} - \omega_{min}}{r_1^2}\right) \cdot (r^2 + z^2) + (\omega_{min} * 2) \quad \text{(for tumour tissue)} \quad (3)$$

$$\omega_{var} = \omega_{max} \text{ (for healthy tissue)} \quad (4)$$

Here t denote the time and T indicate the temperature. The subscripts t, b, and a signify tissue, blood, and artery respectively. The variables ρ, c, k denotes density, specific heat, and thermal conductivity, respectively. The variable ω_{var} represents the variable blood perfusion rate. The blood temperature closely approximates the body temperature, which is maintained at 37°C. In addition, the tissue temperature T_t is adjusted to 37°C at the boundary of the cylinder and at the starting time of 0 seconds.

Local Thermal Non-Equilibrium equations (LTNE) considering variable porosity.

In 1998, Roetzel and Xuan [9] introduced a bioheat model consisting of two equations to describe the transport of heat in porous media. To replicate biological tissue, they partitioned it into different sections for tissue and blood. The

tumour region features spatially varying porosity and perfusion, defined by a quadratic function derived from in vivo rabbit liver tumour experiments [17]. Yaun determined that the heat transfer coefficient has a value of 170 W m^{-2} K^{-1} [18]. The expression of differential equations is as follows:
Regarding the tissue phase:

$$(1-\varepsilon_{var})(\rho c)_t \frac{\partial T_t}{\partial t} = (1-\varepsilon_{var})\,\nabla \cdot (k_t \cdot \nabla T_t) + ha\,(T_b - T_t) + (1-\varepsilon_{var})\,Q_{m,t} \quad (5)$$

Regarding the blood phase:

$$(\varepsilon_{var})(\rho c + u_b \cdot \nabla T)_b \frac{\partial T_t}{\partial t} = (\varepsilon_{var})\,\nabla \cdot (k_b \cdot \nabla T_b) + ha(T_b - T_t) + (\varepsilon_{var})\,Q_{m,b} \quad (6)$$

$$\varepsilon_{var} = \left(\frac{\varepsilon_{int} - \varepsilon_{min}}{r_1^2}\right) \cdot (r^2 + z^2) + (\varepsilon_{min} * 2) \text{ (for tumour tissue)} \quad (7)$$

$$\varepsilon_{var} = \varepsilon_{max} \text{ (for healthy tissue)} \quad (8)$$

$$a = \frac{4 * \varepsilon_{var}}{d} \quad (9)$$

In the model, a denotes the volumetric transfer region within blood and tissue, ε_{var} is the variable porosity, u_b is the blood velocity vector and *h* is interfacial heat transfer coefficient.

Local Thermal Equilibrium equation (LTE)

According to the notion of Local Thermal Equilibrium, the temperature of the tissue is equal to the temperature of the blood (T_t=T_b=T) [19].

$$[(1-\varepsilon_{var})(\rho c_p)_t + \varepsilon_{var}\,(\rho c_p)_b]\,\frac{\partial T}{\partial t} + \varepsilon_{var}\,(\rho c_p)_b\,u_b \cdot \nabla T = [(1-\varepsilon_{var})k_t + \varepsilon_{var} k_b]\,\nabla^2 T + (1-\varepsilon_{var})\,Q_t + \varepsilon_{var}\,Q_b \quad (10)$$

In the LTE model, the initial conditions and boundary conditions are similar to LTNE model.

2.3 Numerical Simulation and validation

In order to solve the governing equations for our investigation, we use the finite element program COMSOL Multiphysics, taking into account suitable initial and boundary conditions. A time-dependent implicit solution, namely the Backward Differentiation Formula (BDF) solver, is used with a tolerance factor of 0.1. This study investigates temperature fluctuations in both spatial and temporal dimensions, together with the lethal front propagation resulting from 15 minutes of freezing and 10 minutes of thawing in cryosurgery. The current model is validated against the work of Yuan et al. [20], and a grid independence test is conducted. The grid size for the current study comprises 51,383 triangular grid elements.

3. Results and Discussion

In the current work, numerical analysis among three model has been investigated to understand temperature variation inside the tumour and the healthy tissue. The results are shown based on temperature distribution and lethal front propagation with the variation of porosity and perfusion inside the tissue during cryosurgery.

3.1 Variation of Temperature inside the tissue with space and time

To get more insight, the temperature variation at different radial positions (r = 0.5 cm, 1.0 cm, 1.5 cm, 2 cm) at a depth of z = 0 cm during freezing and thawing have been discussed in table 2 and Fig.3. The results demonstrate a significant temperature difference between the modified Local Thermal Non-Equilibrium (LTNE) models or Local Thermal Equilibrium (LTE) model with respect to the modified Pennes model at the different locations inside the tissue the reason of this high temperature difference is that modified Pennes equation assumes a constant blood temperature throughout the simulation and neglects the direction of blood flow. while solving the modified LTNE model it uses two equations for the distinct region one is for solid phase i.e tissue and other is for liquid phase i.e blood as there is non equilibrium between the blood and tissues the temperature of the blood is not constant rather change as the colling occurs also the addition of an interfacial heat transfer coefficient in the assists in the heat transfer . Further in the LTE model there is thermal equilibrium between blood and tissue but includes blood flow in the arteries. Due to these distinctions,

the LTNE or LTE models exhibit a more pronounced temperature drop compared to the Pennes model. But the temperature difference between the modified LTNE and LTE model is seems to be less because as the colling starts and when the tissue goes below the lower phase change temperature the behaviour of both the equation becomes almost similar as the velocity term becomes zero ..

Table 2: Temperature difference observation at the end of freezing process by various bioheat models

Location	**Temperature difference in ºC at the end of Freezing (15min)**		
r(cm)	***Modified LTNE vs Modified LTE***	***Modified LTNE vs Modified pennes***	***Modified LTN vs Modified pennes***
0.5	0.38	60.8	61.19
1	0.45	32.78	33.23
1.5	0.34	49.58	49.92
2	0.13	42.085	42.21

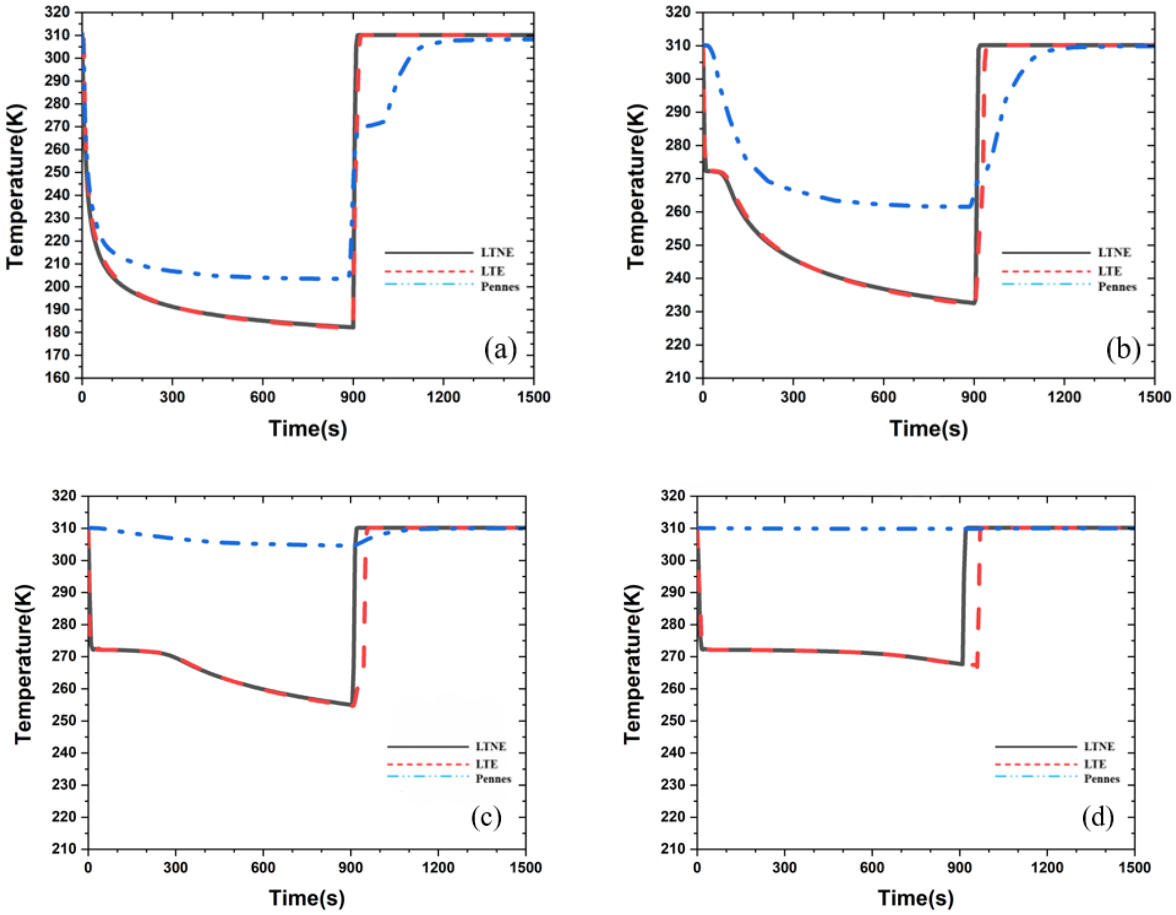

Fig. 2 Displays the Temperature vs time at various location in the tumour and tissue at (a) r = 0.5 cm (b) r = 1 cm (c) r = 1.5 cm (d) r = 2 cm

3.2 Study of lethal temperature in bioheat models

This study analyse the propagation of a lethal temperature of -40°C at a specific location (r = 1 cm, z = 0 cm). The results revealed a significantly faster lethal temperature attainment in the modified Local Thermal Non-Equilibrium (LTNE) and Local Thermal Equilibrium (LTE) models compared to the modified Pennes model. The lethal temperature was reached at 845 seconds and 810 seconds for the modified LTNE and LTE models, respectively. Conversely, the modified Pennes model did not achieve the lethal temperature within the 15-minute (900 seconds) freezing duration at this location. This observation can be attributed to the differing roles of blood flow in each model. The modified Pennes model assumes constant blood temperature and neglects blood flow direction, leading to a slower rate of heat transfer. In contrast, the LTNE and LTE models account for blood flow dynamics, facilitating faster heat dissipation and achieving the lethal temperature sooner and also due to this the ablation diameter is also higher in these cases. In the figure 3 magenta colour contour shows the location of lethal front at the end of freezing process.

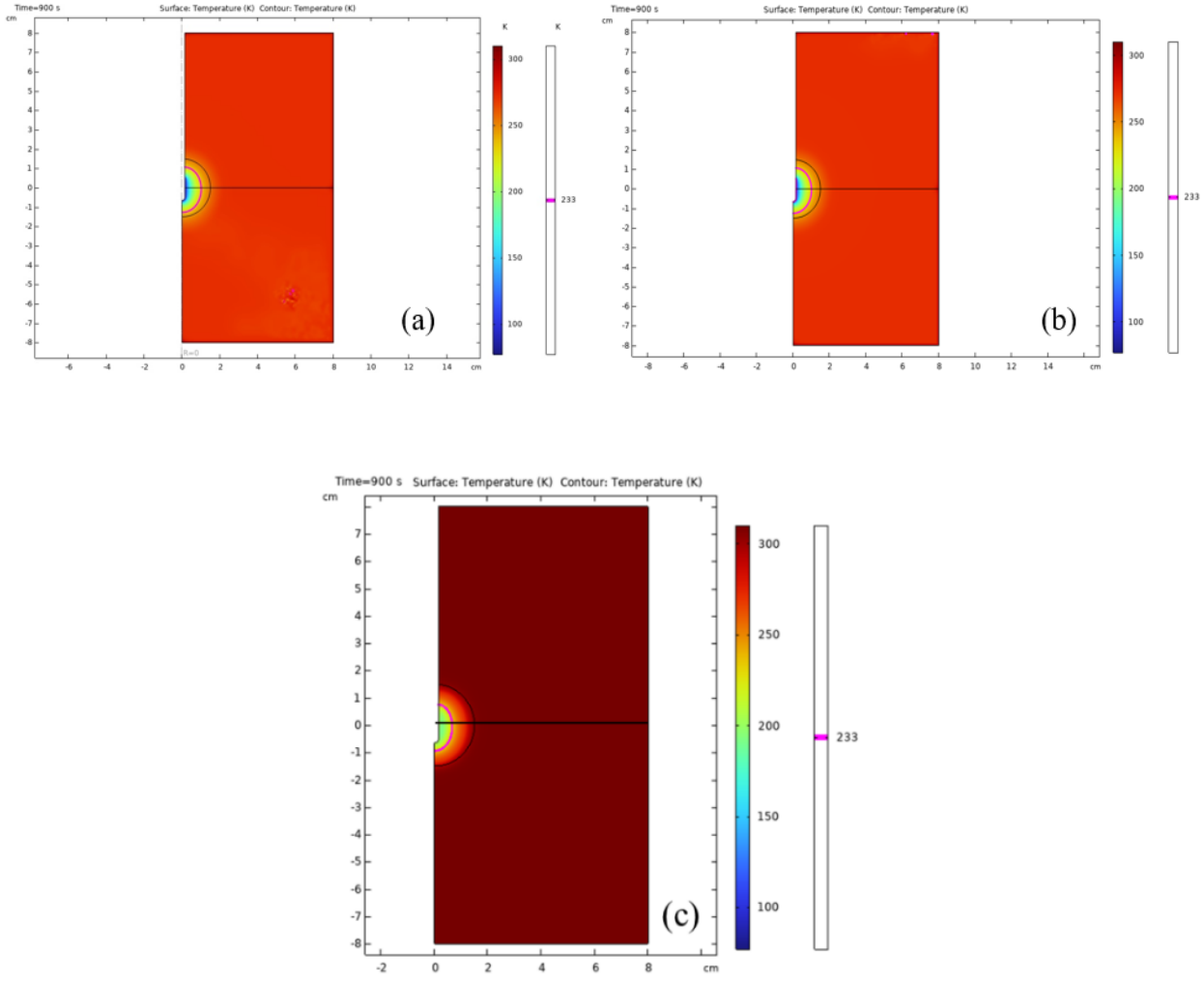

Fig. 3 Shows the lethal Temperature contour at the end of freezing process for modified (a) LTE(b) LTNE c) Pennes Bioheat models

The observation also shows that the lower phase change temperature is reached much faster in modified LTNE and LTE model and due to this reason, the tissue become solid, and its conductivity gets increased approximately become twice as compared when it's in liquid state this help in increasing the heat transfer inside the domain and also assist in the propagation of lethal front at much faster rate.

4. Conclusion

This study investigated the impact of bioheat models on temperature variation, lethal front development, and ablation diameter within the tissue. The results highlight the crucial role of blood velocity and the interfacial convective heat transfer term in the Local Thermal Non-Equilibrium (LTNE) model, as opposed to the perfusion term in the Pennes model. Notably, the Pennes model assumes a constant blood temperature, neglecting its dynamic blood flow nature. In contrast, the two-equation non-equilibrium model (LTNE) incorporates both blood and tissue temperatures, allowing for their simultaneous variation during the heat transfer process. This approach provides a more realistic representation of heat transfer within the tissue compared to the Pennes model. Our findings suggest that incorporating blood velocity and interfacial heat transfer phenomena into bioheat models is better for predictions of thermal behaviour and lethal front propagation in tissues undergoing cryotherapy**.**

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