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A Fractional Analysis of Hyperthermia Therapy on Breast Cancer in a Porous Medium along with Radiative Microwave Heating

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Abstract: Cancer is a prominent source of mortality and morbidity globally, but little is known about how it develops and spreads. Tumor cells are unable to thrive in high-temperature environments, according to recent research. Hyperthermia is the name for this therapy method. This study provides insights into hyperthermia therapy on breast cancer in the presence of a porous material with fractional derivative access when using radiative microwave heating. The mathematical model is formulated by PDE, while the time-fractional Caputo derivative is applied to make our equation more general as compared to the classical model. To produce a more efficient analysis of blood temperature distributions inside the tissues of the breast, the unsteady state is calculated by using the Laplace transform technique. The Laplace inversion is found by Durbin's and Zakian's algorithms. The treatment involves mild temperature hyperthermia, which causes cell death by enhancing cell sensitivity to radiation therapy and blood flow in the tumor. The variations of different parameters to control the temperate profile during therapy are discussed; we can also see how a fractional parameter makes our study more realistic for further experimental study.

Keywords: fractional derivative; hypothermia therapy; breast cancer; transfer of bioheat; biological tissues; radiations

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1. Introduction

Breast cancer is the most familiar cancer in women around the world. Being a medical problem, it has been extensively studied medically throughout history. In fact, the investigation into breast cancer has helped to pave the way for findings in other kinds of cancer analysis. The most frequent types of cancer include prostate cancer, brain cancer, breast cancer, skin cancer, and lung cancer, among others. It has been extremely difficult to learn about the natural history of breast cancer. The term "cancer" refers to a set of disorders in which normal cells segregate extensively, that is, the development of such cells is faster than normal cells, and therefore the transmission process of these cells to other areas of the body begins sooner or later, and this process is known as metastasis [1]. The mortality rate of cancer is more than AIDs, malaria, and tuberculosis worldwide, according to the National Cancer Registry (NCR) of South Africa [2]. The statistics relevant to cancer deaths amounted to 8.2 million in 2010. Keeping this increase in mind, the researchers estimate

that the rise in the mortality rate due to cancer will reach approximately 13 million deaths by 2030 [3].

It is critical to understand the various cancer treatments. Breast cancer has evolved in a variety of ways since its detection. Other results and therapies, on the other hand, have remained the same for years. Cancer has changed in a variety of ways over time, and, as a result, cancer medicines have evolved as well. Cancer treatments occur in several types. The type of therapy you receive will depend on the type of cancer you have and how advanced it is. Many patients will receive only one cancer treatment at a time, but the majority will receive a combination of therapies, such as chemotherapy combined with surgery and/or radiation therapy. Cancer treatments are very necessary for the purposes of restraining tumor expansion or assassinating the tumor cells in the body, so cancer can be treated with biomarker testing, chemotherapy, hormone therapy, hyperthermia therapy, immunotherapy, photodynamic therapy, radiation therapy, stem cell transplant, surgery, and targeted therapy, amongst other remedies [4,5]. Side effects are a concern, as each treatment of cancer has side effects such as vomiting, hair loss, fatigue, and nausea. Conflict effects take place during chemotherapy treatment; chemotherapy treatment is not actually able to discriminate between tumor and normal cells, consequently killing both of them [3]. Furthermore, a lot of dietary supplements and components have been inspected as possible prevention operators for cancer. Few studies can be cited [6–8] about diet, which includes the ketogenic diet, which was considered as a possible adjuvant to cancer treatment. It is well known that a ketogenic diet is a high–moderate-protein, low-carbohydrate diet that attracts the body to use fat rather than glucose for adenosine triphosphate (ATP) generation [9].

However, acceptable biological data have accumulated in recent years, and these statistics are now mathematically represented. The purpose of these mathematical models is to bring these data together. Such mathematical models are very crucial and helpful for the formulation of new therapies and can also give observations into the structures of existing treatments. A mathematical model is well known for its ability to analyze the transmission of non-infectious contaminations and offer valuable judgments on contaminations' behavior and control [10,11]. A mathematical model has been an essential instrument in understanding the actions of diseases and in decision-making mechanisms about a medical treatment approach for breast cancer control in various countries over the years [12]. Recently, reproductions of mathematical models concerned with the tumor-like dynamics and feedback to treatment along with irradiation and alone have been taken in the literature [13]. Nani and Freedman [14] illustrated a mathematical model about cancer treatment by immunotherapy. They also discussed the advantages and disadvantages in that particular article.

Hyperthermia is a therapy method in which an oncologist uses heat in various ways to treat malignant and benign tumors. There are varieties of extraneous heat sources, including magnetically excitable thermo-seeds, infrared radiation, microwaves, and radiofrequency [15]. Hyperthermia therapy was studied by Habash and his coworkers, and he observed the time duration and temperature of the therapy [16]. In that article, they examine the various outcomes of hyperthermia therapy, which are listed below.

i. Thermal ablation or high-temperature hyperthermia, i.e., temperature is greater than or equal to 46 °C for 4 to 6 min, ($T \geq 46$ °C for 4–6 min).
ii. Comfortable-temperature hyperthermia, i.e., temperature is between 41° and 46° for 15 to 60 min, ($41° < T < 46°$ for 15–60 min).
iii. Hyperthermia at a low temperature for a long time, i.e., temperature is less than or equal to 41° for 6 to 72 min, ($T \leq 41$ °C for 6–72 min).

To perform various types of hyperthermia treatment, it is necessary to use the intensity of a volumetric heat source. The type of hyperthermia to be employed depends on whether or not the malignant cells are localized. In a clinical therapeutic application, whole-body hyperthermia (WBH), hyperthermia, or regional hyperthermia may be used to eradicate malignant cells [17,18]. In localized hyperthermia, a high temperature is necessary during

the curing of a tiny location in the body where cancer cells are located to seriously harm the tumor cells, but, in regional hyperthermia, the therapy is applied to a broad area of the complete body tissue or organ but not entirely. Body hyperthermia is a treatment for glioblastoma that employs a novel method of treatment. According to Bhownik [19], heat transfer in multilayer tissues is a complex process. Diverse methods for conduction, such as diffusion, circulation, and blood perfusion, are necessary for microvascular cells. The study of heat transfer and significant damage in multi-layered tissues is fascinating, and therapeutic hyperthermia therapy can advantage of it. Microwaves, on the other hand, have grown increasingly popular for heating. Many industrial melting, sintering, and forming issues have been resolved [20]. Microwaves have been demonstrated to be useful in medical therapy as a means of removing heat in hypothermic treatment. As detected and published in reference [21], tumor cells can be removed by removing heat from the tissue for a certain period and at a higher temperature.

In their investigations on hyperthermia therapy, many researchers have investigated the impact of surface temperature control and circulatory systems on tissue temperature distribution during microwave heating [22,23]. The temperature difference in a spherical region, which could lead to a hotspot in the central part of the brain, was investigated by Kritikos et al. [24]. The problem was solved using the Fourier transform method, which demonstrated that the temperature rise for a large man's head is small. For the microwave heating of a half-space, the mathematical formulation considered various temperature profiles that were identical, as well as power-law and exponential microphysical features (thermal conductivity, specific heat); according to Hill and Income [20], the differential equation was numerically solved to obtain the solution to the transient state difficulties. On the other hand, EI-dabe et al. [25] investigated the thermal state of living tissue when exposed to microwaves. To investigate a one-dimensional multilayer model, the researchers used Maxwell equations in conjunction with a biothermal model. The influence of spatial and temperature-dependent blood circulation on the temperature field of biological tissue during microwave heating was investigated by Oke et al. [26]. As a result, their solutions showed that several results are feasible when blood perfusion is temperature-dependent; however, when the temperature is based on spatial variables, a single solution was generated. Popoola and Ayeni [27] found that the microwave heating of malignant tumors in theory generates a boundary value problem with various solutions. In their study, they prescribed an initial gradient using the finite-difference technique and shooting processes, which led to the finding of a unique solution.

Fractional calculus, as we all know, is a more generalized version of calculus. Unlike integer order calculus, which focuses on integers, fractional calculus considers all non-negative real numbers. As a result, it is obvious that utilizing a fractional approach and the study of a model, particularly those related to cancer, may be conducted more extensively and the results obtained with greater efficiency. In this article, we use the fractional approach to study the problem more generally and extensively. Keeping in mind the preceding discussion, we discovered that the effect of radiative heat flow and the permeability of the porous medium of biological tissues were mainly overlooked in the literature when using a fractional method. We intend to use a fractional approach to examine the effect of hyperthermia therapy and radiative heat flux intensity on breast tissues concerning porous-medium permeability in this study. According to the literature, the effects of differences in blood thermal conductivity, porosity, thermal radiation, heat source, and blood perfusion on temperature distribution during the microwave heating of hyperthermia therapy using a fractional derivative are an unresolved subject, which is why this study was conducted.

2. Mathematical Modeling and Solution

The body tissue that is initially at a steady $\theta_0 = 37$ °C temperature is heated by an external heat source during hyperthermia therapy. Thermal conduction in tissues, blood circulation and perfusion, and metabolic heat output are all components of the heat

transmission mechanism in living tissues. Pennes [28] developed a model to explain the tissue's standardized arterial blood temperature, while the venous blood temperature is equivalent to the local tissue temperature. In a one-dimensional multi-layer model, the microwave heating equations are as follows [25]:

$$\rho_b C p_b \frac{\partial \theta}{\partial t} = k_b \frac{\partial^2 \theta}{\partial y^2} + \omega_b \rho_b C_b (\theta_b - \theta) + Q(\theta)|E|^2 \tag{1}$$

Furthermore, the porous media benefit to be used is by [29–31] since it requires fewer assumptions than other existing bioheat transfer models.

$$\rho_b C p_b \frac{\partial \theta}{\partial t} = k_b \frac{\partial^2 \theta}{\partial y^2} + \omega_b \rho_b C_b (\theta_b - \theta) - \frac{\partial q}{\partial y} + \frac{\varepsilon}{k} + Q(\theta)|E|^2 \tag{2}$$

The following boundary conditions apply:

$$\theta(y,0) = 37\ ^\circ\mathrm{C},\ \ \theta(0,t) = 37\ ^\circ\mathrm{C},\ \ \theta(a,t) = 45\ ^\circ\mathrm{C}, \tag{3}$$

For radiation, the Rosseland diffusion approximation is used.

$$q = \frac{-4\sigma}{3\delta} \frac{\partial \theta^4}{\partial y} \tag{4}$$

$$\theta^4 \cong 4\theta_b^3 \overline{\theta} - 3\theta_b^4 \tag{5}$$

$$\frac{\partial q}{\partial y} = \frac{-16\sigma\theta_b^3}{3\delta} \frac{\partial^2 \theta}{\partial y^2} \tag{6}$$

As a result, Equation (2) becomes:

$$\rho_b C p_b \frac{\partial \theta}{\partial t} = k_b \left(1 + \frac{4}{3} R\right) \frac{\partial^2 \theta}{\partial y^2} + \omega_b \rho_b C_b (\theta_b - \theta) + \frac{\varepsilon}{k} + Q_m (\theta - \theta_0) \tag{7}$$

The dimensionless parameters listed below are introduced.

$$y = \frac{y^*}{a},\ t = \frac{t^*}{a^2},\ \vartheta = \frac{(\theta - \theta_0)}{(\theta_b - \theta_0)} \tag{8}$$

To obtain the result, substitute the dimensionless quantities (8) in Equations (3) and (7).

$$\frac{\partial \vartheta}{\partial t} = \alpha \left(1 + \frac{4}{3} R\right) \frac{\partial^2 \vartheta}{\partial y^2} - (\gamma - \lambda)\vartheta + (\beta + \gamma) \tag{9}$$

As a result, the subject to the boundary conditions modify.

$$\vartheta(y,0) = 37,\ \vartheta(0,t) = 37,\ \vartheta(1,0) = 45 \tag{10}$$

where

$$\alpha_1 = \frac{k_b}{\rho_b C p_b},\ \beta = \frac{a^2 \varepsilon}{k_b \rho_b C p_b (\theta_b - \theta_0)},\ \gamma = \frac{a^2 Q_m}{\rho_b C p_b} \text{ and } R = \frac{-4\sigma\theta_b^4}{k_b \delta}$$

To make our system more general, as compared to the classical model, by using the time-fractional Caputo derivative definition, Equation (9) becomes

$${}^C D_t^\alpha \vartheta(y,t) = \alpha \left(1 + \frac{4}{3} R\right) \frac{\partial^2 \vartheta}{\partial y^2} - (\gamma - \lambda)\vartheta + (\beta + \gamma) \tag{11}$$

Taking Laplace transform, we get

$$q^{\alpha}\overline{\vartheta}(y,q) - q^{\alpha-1}\vartheta(y,0) = \alpha\left(1+\frac{4}{3}R\right)\frac{\partial^2\overline{\vartheta}}{\partial y^2} - (\gamma-\lambda)\overline{\vartheta} + (\beta+\gamma)\frac{1}{q} \tag{12}$$

$$\overline{\vartheta}(y,0) = \frac{37}{q},\ \overline{\vartheta}(0,q) = \frac{37}{q},\ \overline{\vartheta}(1,0) = \frac{45}{q} \tag{13}$$

By using Equation (13) in (12), we get

$$\overline{\vartheta}(y,q) = A\cosh\left(y\sqrt{\frac{q^{\alpha}+a_2}{a_1}}\right) + B\sinh\left(y\sqrt{\frac{q^{\alpha}+a_2}{a_1}}\right) + \frac{37q^{\alpha}+a_3}{q(q^{\alpha}+a_2)} \tag{14}$$

$$A = \frac{37}{q} - \frac{37q^{\alpha}+a_3}{q(q^{\alpha}+a_2)}$$

$$B = \frac{45}{q\sinh\left(\sqrt{\frac{q^{\alpha}+a_2}{a_1}}\right)} - \frac{37q^{\alpha}+a_3}{q(q^{\alpha}+a_2)}\left(\frac{\cosh\left(\sqrt{\frac{q^{\alpha}+a_2}{a_1}}\right)-1}{\sinh\left(\sqrt{\frac{q^{\alpha}+a_2}{a_1}}\right)}\right) - \frac{37}{q}\frac{\cosh\left(\sqrt{\frac{q^{\alpha}+a_2}{a_1}}\right)}{\sinh\left(\sqrt{\frac{q^{\alpha}+a_2}{a_1}}\right)}$$

where

$$a_1 = \alpha_1\left(1+\frac{4}{3}R\right),\ \ a_2 = \gamma-\lambda,\ \ a_3 = \beta+\gamma$$

In the Laplace transform domain, the solution of Equation (14) is found. This equation's inverse Laplace transform is highly intricate and difficult to handle, especially in practical applications. As a result, adopting numerical inversion is a more stable and convergent method for the inverse Laplace transform, since the truncated error for five multiple terms is small. Table 1 validates the numerical results for Durbin's and Zakian's algorithms. In the real-time realm, Saqib et al. [32] use the Durbin and Zakian inversion algorithms.

Table 1. Compression of temperature profile for Durbin's and Zakian's Algorithm.

y	Durbin's Algorithm	Zakian's Algorithm
0	37	37
0.1	36.76483	36.76488
0.2	36.68123	36.68129
0.3	36.74372	36.74376
0.4	36.96405	36.96411
0.5	37.37310	37.37315
0.6	38.02321	38.02327
0.7	38.99283	38.99284
0.8	40.39212	40.39214
0.9	42.36186	42.36189
1	45	45

3. Results and Discussion

The current research examines a fractional approach of one-dimensional multilayer time-dependent bioheat for determining temperatures in living biological tissue, such as breast tissue, during microwave heating. The results of the computational research were shown in figures using Mathcad-15 software. The standard thermophysical parameters for heat transport in biological tissue need a diversity of investigation. Due to metabolic heat creation in the tissue, boundary conditions and heat sources are present. Figure 1 depicts the effect of the radiation parameter R on the temperature gradient. The temperature gradient rises as the value of R increases, due to increases in the efficiency at which heat infiltrates the cancerous cells as a result of radiotherapy. Figure 2 depicts the variation in

the temperature profile in proportion to the blood perfusion parameter. Figure 2 is linear in nature, and, as the value of γ is increased, the maximum temperature is attained. However, it nearly indicates that a rise in biological tissue temperature is caused by an increase in blood perfusion. Figure 3 shows the temperature distribution after a variational increase in the metabolic heat source. Metabolic heat generated in the tissue is required for the efficient transport of energy required for chemical processes such as muscular effort, membrane pumps, glucose generation from glucose, and protein building from amino acids. Almost all of the metallic energy consumed in these reactions is converted into heat by living tissue. The temperature profiles climb as the value of λ increases, leading to the deaths of cancerous cells. The behavior of the porosity parameter β on a temperature profile is shown in Figure 4. It is evident that temperature is proportional to porosity, that is, the temperature profile rises when the porosity parameter is increased. The theory behind this action is that the porosity term increases blood flow via porous tissue, forcing the blood cells to travel faster. Figure 5 shows the effect of changing the thermal conductivity values on temperature. During hypothermia therapy, this graph depicts the relationship between blood temperature and thermal conductivity. It has been noticed that increasing the values of thermal conductivity raises the temperature. The variation of the fractional parameter is summarized in Figure 6. All the other physical parameters are fixed, and the variation of the fractional parameter gives us verities of the solution, which means that the fractional phenomena are used to generalize the solution and find the best data fitting for experimental study. This diagram depicts the problem's memory effect. In Table 1, the inverse Laplace transforms through Zakian's and Durbin's algorithms are numerically compared. It is obvious that they share the same profile.

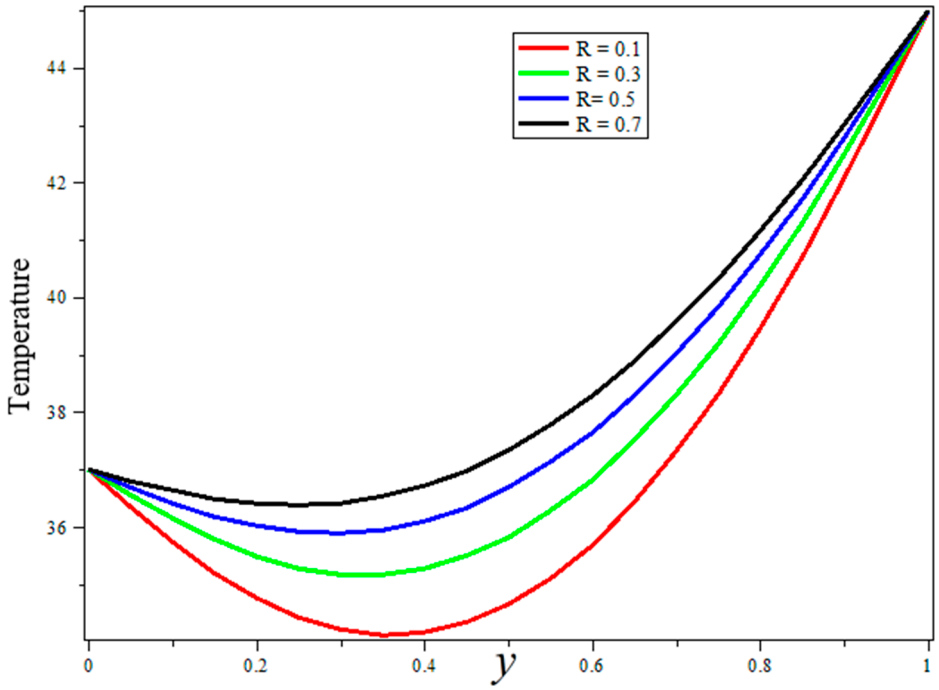

Figure 1. The influence of radiation parameters on the temperature field during tumor hyperthermia therapy.

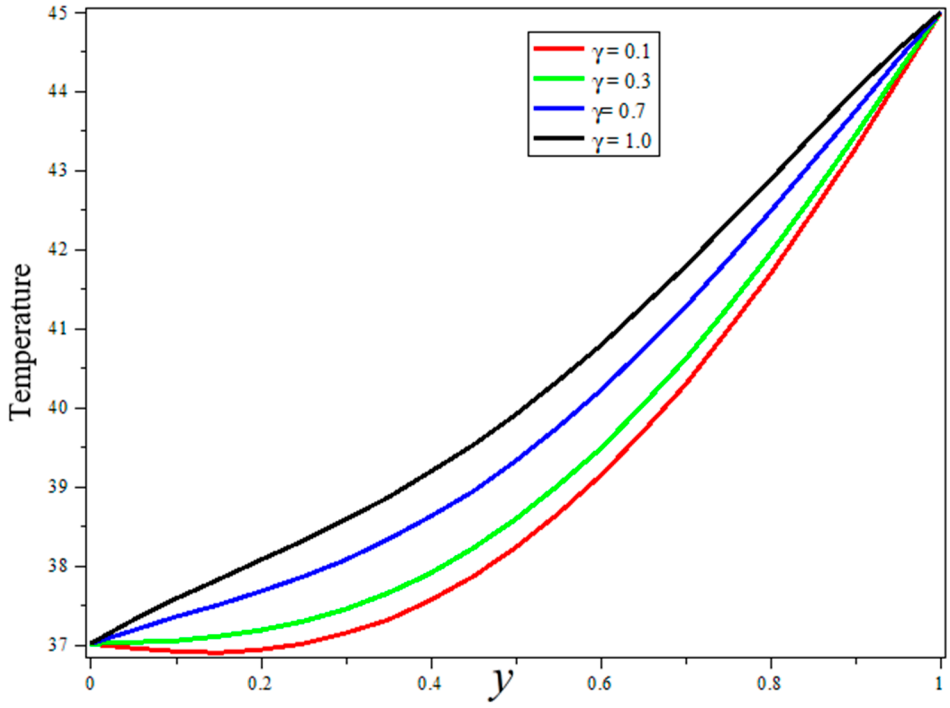

Figure 2. The impact of vascularization on the temperature field during hyperthermia tumor treatment.

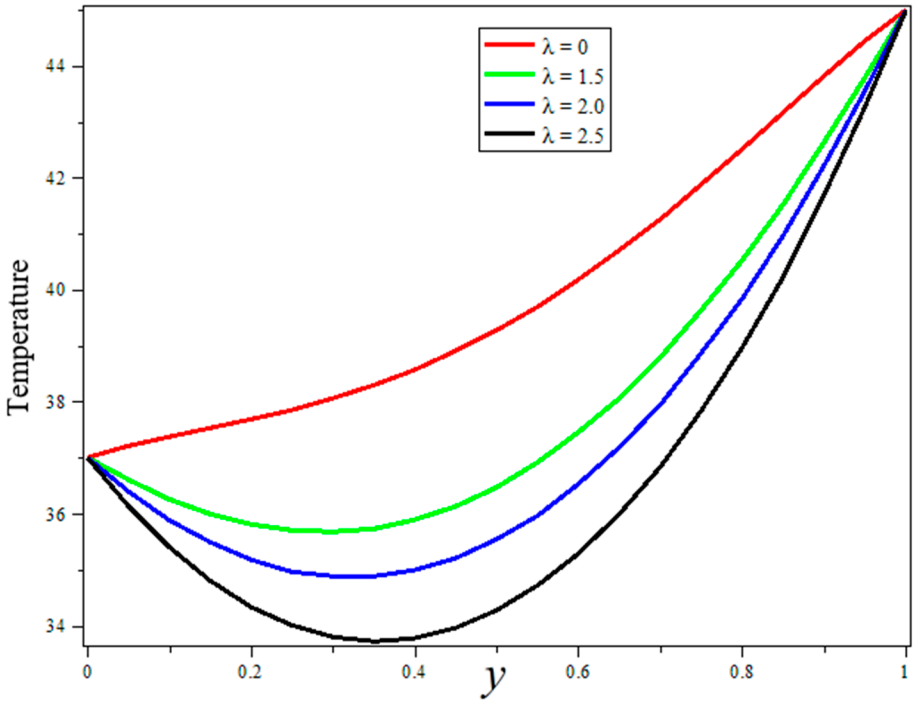

Figure 3. The impact of the source of heat on the temperature field throughout hyperthermia tumor treatment.

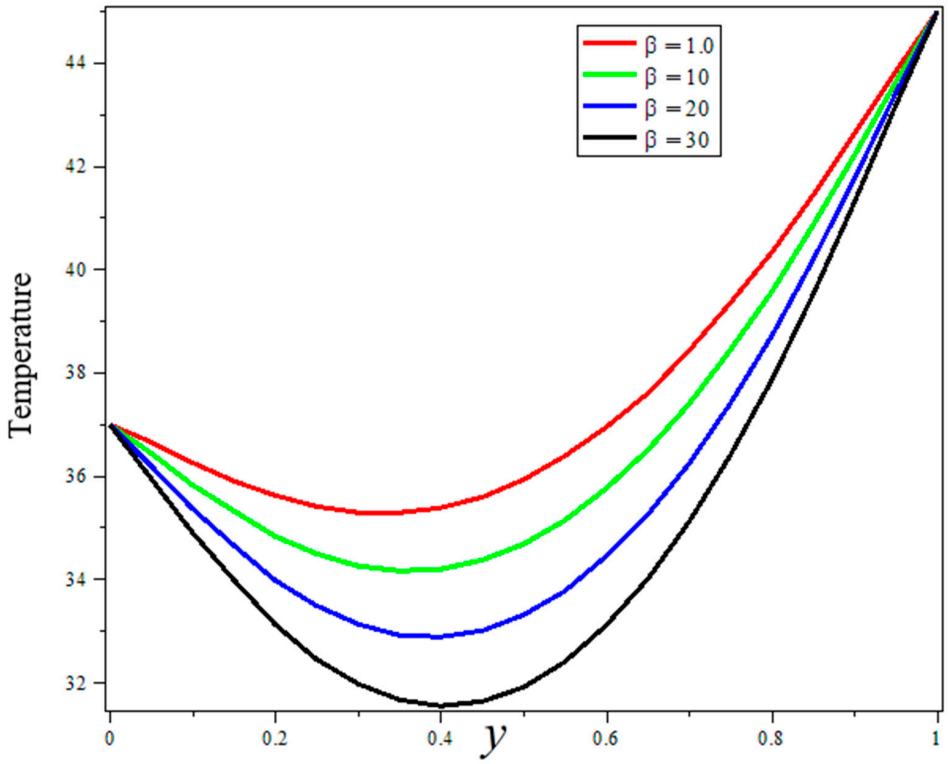

Figure 4. The influence of porous structure on the temperature field under tumor hyperthermia.

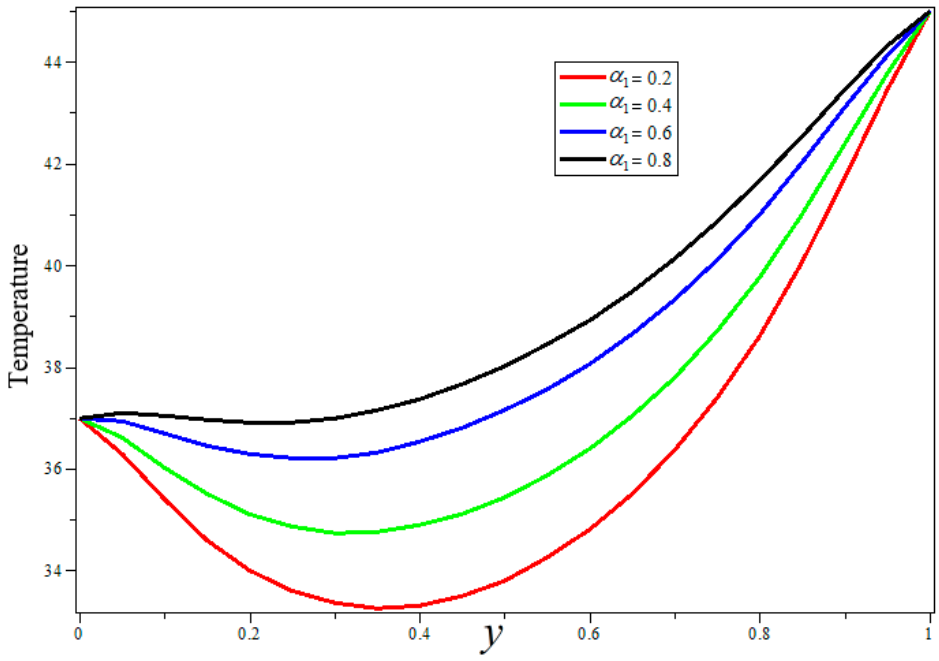

Figure 5. The influence of blood thermal conductivity on the temperature field during tumor hyperthermia.

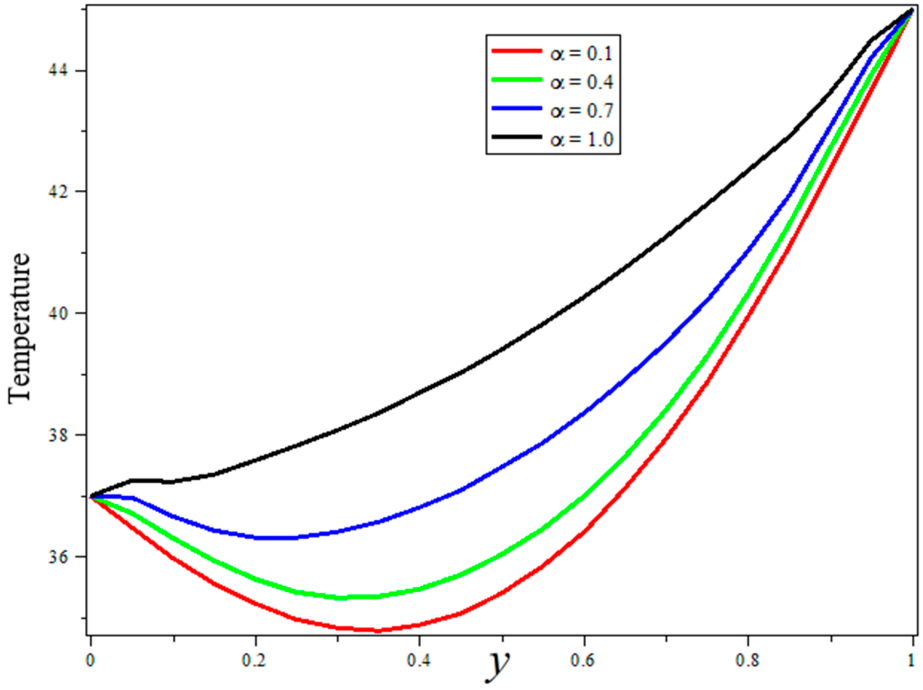

Figure 6. The impact of a fractional parameter on the temperature field under tumor hyperthermia.

4. Conclusions

This research explores microwave radiation heating for breast-cancer hyperthermia treatment in a porous medium with fractional derivative access. The governing equation is formulated via a partial differential equation, and after that the fractional derivative is used to make our equation more generalized. The solution is found by the joint Laplace transform and Durbin's and Zakian's numerical algorithms. The main outcomes are as follows.

- The fractional model is more suitable for data fitting and memory effect.
- The solution obtained by using Durbin's and Zakian's numerical techniques coincides perfectly.
- Blood thermal conductivity, blood perfusion, and radiation parameters are shown to have good agreements for a temperature boost during treatment.
- Porosity and heat sources can be used for better temperature control during treatment.

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Nomenclature

ρ_b	Density of blood	σ	Stefan Boltzmann
Cp_b	Blood-specific heat at a constant pressure	ε	Porosity of the tissue
$\theta(y,t)$	Temperature profile	k	Permeability of the porous medium
k_b	Blood thermal conductivity	$R = \frac{-4\sigma\theta_b^4}{k_b\delta}$	Radiation parameters
ω_b	Blood volumetric perfusion rate	α	Fractional derivative parameter
C_b	Specific heat of tissue	$\gamma = \frac{a^2 Q_m}{\rho_b C p_b}$	Vascularization parameter
$Q(\theta)$	Body-heating coefficient	λ	Source-of-heat parameter
E	Electric field	$\alpha_1 = \frac{k_b}{\rho_b C p_b}$	Thermal conductivity parameter
$\beta = \frac{a^2\varepsilon}{k_b\rho_b C p_b(\theta_b-\theta_0)}$	Porosity parameter	δ	Mean absorption coefficient

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