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RESEARCH ARTICLE

A New Fractional Model for the Cancer Treatment by Radiotherapy Using the Hadamard Fractional Derivative

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Abstract

In this article, a mathematical model for cancer treatment by radiotherapy is examined. The model is integrated into the Hadamard fractional derivative. First, we examine the existence of the solution. Then, the uniqueness of the solution is investigated.

Keywords: Hadamard fractional derivative, Existence and uniqueness, fixed point theory, nonlinear fractional differential equation

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1 Introduction

As is well acknowledged, cancer is one of the fatal diseases of the last century. A therapy has been carried out in the last century for this disease with manifold varieties. Four different types of conventional cancer treatments are commonly predictable today. Those treatment methods include surgery, chemotherapy, radiotherapy and immunotherapy.

Fractional calculus was introduced more than three centuries ago. The existence and uniqueness theory of the solution were studied in the earliest days. Such theory can be found in studies done by authors of [28-31].

Over years several researchers have proven that the classical approach of differential equations may fail in the modeling of some complex phenomena. However, applications of fraction differential equation in such cases are often proven efficient. The efficiency of fractional differential in sciences branches such as epidemiology, Chemistry, finance, physics, a few just to mention can be found in studies referred in [21-27].

In this study, we concern with the radiation therapy solely [1]. Radiotherapy is one of the most important treatment types to fight cancer. The goal is to kill the cancer cells radiation. With this method, hurriedly.

Proliferating cancer cells are targeted. However, the reproduction of the surrounding normal cells is adversely affected as well when the cancer cells are exterminate. Therefore, more than one model have been settled previously providing concentrations of the normal and cancerous cells [2]. Mathematical modeling is quite important to analyze real-world problems to find superior ways of understanding [3–10]. Furthermore, the modeling process offers essential information on the addressed process [11–13]. Some mathematical models have been developed previously for cancer treatment [14–16]. Belostotski [2], provided a model representing the interaction between normal and cancerous cells. Radiation's entering into the body is of great importance and occurs in 4 different ways. Motivated especially by the aforementioned work, we are concerned in this paper with the existence of solutions for the Hadamard-type fractional derivative, we investigate the following system of fractional differential equations then the cancer treatment model is given by

$$\begin{aligned} &\frac{d\rho(t)}{dt} = \alpha_1\rho\left(1-\frac{\rho}{S_1}\right) - \beta_1\rho\alpha - \varepsilon D(t)\rho, \\ &\frac{d\alpha(t)}{dt} = \alpha_2\alpha\left(1-\frac{\alpha}{S_2}\right) - \beta_2\rho\alpha - D(t)\alpha, \\ &\rho(0) = \rho_0, \alpha(0) = \alpha_0 \end{aligned} \tag{1}$$

Where in a given tissue, $\rho(t)$ represent the concentration of healthy cells, $\alpha(t)$ be the concentration of cancer cells and $D(t)$ is the strategy of the radiotherapy. It is assumed that $D(t) \equiv \gamma > 0$, when $t \in [n\omega, n\omega + L)$ (treatment stage) and

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$D(t) \equiv 0$, when $t \in [n\omega + L, (n+1)\omega)$ (no treatment stage), $\forall n = 0, 1, 2, \ldots$, where ω is the radiation treatment time [32].

The system (1) with Hadamard derivative is given as follows:

$$\begin{aligned} &{}^{H}D^{r}\rho(t) = \alpha_1\rho\left(1 - \tfrac{\rho}{S_1}\right) - \beta_1\rho\alpha - \varepsilon D(t)\rho, \\ &{}^{H}D^{r}\alpha(t) = \alpha_2\alpha\left(1 - \tfrac{\alpha}{S_2}\right) - \beta_2\rho\alpha - D(t)\alpha, \\ &\rho(0) = \rho_0, \alpha(0) = \alpha_0 \end{aligned} \tag{2}$$

2 Preliminaries

In this section we introduce some definitions, lemmas and notations of fractional calculus.

Definition 2.1 (see [28]). *The Hadamard fractional integral of order rfor a continuous function g is defined as*

$${}^{H}I^{r}g(t) = \frac{1}{\Gamma(q)}\int_a^t \left(\ln\frac{t}{s}\right)^{r-1}\frac{g(s)}{s}ds, \quad r > 0,$$

Provided that the integral exist,Γ*is the gamma function* $\Gamma(\upsilon) = \int_0^\infty e^{-t}t^{\upsilon-1}dt, \forall \upsilon > 0$.

Definition 2.2 (see [28]). *The Hadamard fractional derivative of order* $r > 0$ *for a continuous functiong* $: [a, \infty) \to \mathbb{R}$ *is defined as*

$$\begin{aligned} &{}^{H}D^{r}g(t) = \delta^{n}\left({}^{H}I^{r}g\right)(t) = \left(t\tfrac{d}{dt}\right)^{n}\tfrac{1}{\Gamma(n-r)}\int_a^t\left(\ln\tfrac{t}{s}\right)^{n-r-1}\tfrac{g(s)}{s}ds, \\ &n-1 < r < n,\ \ n = [r]+1, \text{where } \delta = t\left(\tfrac{d}{dt}\right), [r] \text{ denotes the integer part of the real number } r \end{aligned}$$

Lemma 2.1 (see [28]). *Let* $u, x \in C_\delta^n([a,T],\mathbb{R})$, where $C_\delta^n[a,T] = \left\{u,x : [a,T] \to \mathbb{R} : \delta^{(n-1)}u \in C[a,T]\right\}$. *Then*

$${}^{H}I^{r}\left({}^{H}D^{r}u\right)(t) = u(t) - \sum_{j=1}^{n} c_j\left(\ln\frac{t}{a}\right)^{r-j}.$$

3 Existence of solutions

In this section, we will prove the existence of the solution for the fractional cancer treatment model by radiotherapy.

Now applying the operator${}^{H}I^{r}$in eq (2), we obtain the following.

$$\begin{aligned} \rho(t) - c_1\left(\ln\tfrac{t}{a}\right)^{r-1} &= {}^{H}I^{r}\left(\alpha_1\rho\left(1-\tfrac{\rho}{S_1}\right) - \beta_1\rho\alpha - \varepsilon D(t)\rho\right), \\ \alpha(t) - d_1\left(\ln\tfrac{t}{a}\right)^{r-1} &= {}^{H}I^{r}\left(\alpha_2\alpha\left(1-\tfrac{\alpha}{S_2}\right) - \beta_2\rho\alpha - D(t)\alpha\right), \end{aligned} \tag{3}$$

For simplicity we define the kernels as

$$\begin{aligned} Q(t,\rho(t)) &= \alpha_1\rho\left(1-\tfrac{\rho}{S_1}\right) - \beta_1\rho\alpha - \varepsilon D(t)\rho, \\ Q(t,\alpha(t)) &= \alpha_2\alpha\left(1-\tfrac{\alpha}{S_2}\right) - \beta_2\rho\alpha - D(t)\alpha. \end{aligned}$$

Now we Identify an operator E so that $E : H \to H$.

Then we get

$$\begin{aligned} E\rho(t) &= c_1\left(\ln\tfrac{t}{a}\right)^{r-1} + \tfrac{1}{\Gamma(r)}\int_a^t\left(\ln\tfrac{t}{s}\right)^{r-1}\tfrac{Q(s,\rho(s))}{s}ds, \\ E\alpha(t) &= d_1\left(\ln\tfrac{t}{a}\right)^{r-1} + \tfrac{1}{\Gamma(r)}\int_a^t\left(\ln\tfrac{t}{s}\right)^{r-1}\tfrac{Q(s,\alpha(s))}{s}ds. \end{aligned} \tag{4}$$

We will then show that this operator is compact.

Lemma 3.1. *The mapping* $E : H \to H$ *is completely continuous.*

Proof. Let $S \subset H$ be bounded, $\exists l_1, l_2 > 0$, such that $\|\rho\| < l_1$ and $\|\alpha\| < l_2$.Let $M_1 = \max_{\substack{a \le t \le T \\ a \le \rho \le l_1}} |Q(t,\rho(t))|$ and $M_2 = \max_{\substack{a \le t \le T \\ a \le \alpha \le l_2}} |Q(t,\alpha(t))|$, $\forall \rho, \alpha \in S \subset H$, we have

$$\begin{aligned}|E\rho(t)| &\le \left|c_1\left(\ln\tfrac{t}{a}\right)^{r-1}\right| + \left|\tfrac{1}{\Gamma(r)}\int_a^t \left(\ln\tfrac{t}{s}\right)^{r-1}\tfrac{Q(s,\rho(s))}{s}ds\right| \\ &\le |c_1|\left(\ln\tfrac{t}{a}\right)^{r-1} + \tfrac{1}{\Gamma(r)}\int_a^t \left(\ln\tfrac{t}{s}\right)^{r-1}|Q(s,\rho(s))|\tfrac{ds}{s} \\ &\le |c_1|\left(\ln\tfrac{t}{a}\right)^{r-1} + \left(\tfrac{1}{\Gamma(r)}\int_a^t \left(\ln\tfrac{t}{s}\right)^{r-1}\tfrac{ds}{s}\right)M_1,\end{aligned}$$

then

$$\|E\rho\| \le |c_1|\left(\ln\frac{T}{a}\right)^{r-1} + \left(\frac{1}{\Gamma(r+1)}\left(\ln\frac{T}{a}\right)^{r}\right)M_1,$$

similarly

$$\|E\alpha\| \le |d_1|\left(\ln\frac{T}{a}\right)^{r-1} + \left(\frac{1}{\Gamma(r+1)}\left(\ln\frac{T}{a}\right)^{r}\right)M_2.$$

Hence $E(S)$ is bounded, next we consider $t_1, t_2 \in [a,T]$ such that $t_1 < t_2$ and $\rho, \alpha \in S$ and then we have

$$\begin{aligned}|E\rho(t_2) - E\rho(t_1)| &\le \left|c_1\left(\left(\ln\tfrac{t_2}{a}\right)^{r-1} - \left(\ln\tfrac{t_1}{a}\right)^{r-1}\right)\right| \\ &+ \tfrac{1}{\Gamma(r)}\int_a^{t_1}\left(\left(\ln\tfrac{t_2}{s}\right)^{r-1} - \left(\ln\tfrac{t_1}{s}\right)^{r-1}\right)|Q(s,\rho(s))|\tfrac{ds}{s} \\ &+ \tfrac{1}{\Gamma(r)}\int_{t_1}^{t_2}\left(\ln\tfrac{t_2}{s}\right)^{r-1}|Q(s,\rho(s))|\tfrac{ds}{s} \\ &\to 0, \text{ as } t_1 \to t_2,\end{aligned} \tag{5}$$

and

$$\begin{aligned}|E\alpha(t_2) - E\alpha(t_1)| &\le \left|c_1\left(\left(\ln\tfrac{t_2}{a}\right)^{r-1} - \left(\ln\tfrac{t_1}{a}\right)^{r-1}\right)\right| \\ &+ \tfrac{1}{\Gamma(r)}\int_a^{t_1}\left(\left(\ln\tfrac{t_2}{s}\right)^{r-1} - \left(\ln\tfrac{t_1}{s}\right)^{r-1}\right)|Q(s,\alpha(s))|\tfrac{ds}{s} \\ &+ \tfrac{1}{\Gamma(r)}\int_{t_1}^{t_2}\left(\ln\tfrac{t_2}{s}\right)^{r-1}|Q(s,\alpha(s))|\tfrac{ds}{s} \\ &\to 0, \text{ as } t_1 \to t_2.\end{aligned} \tag{6}$$

Note that the right hand side of the above inequalities (5),(6) are independent of $\rho, \alpha \in S$ respectively. Therefore, $E(S)$ is equicontinuous, so that $\overline{E(S)}$ is compact via the Arzela-Ascoli theorem. □

Theorem 3.1. *Let $D : [\rho_1, \rho_2] \times [0,\infty) \to [0,\infty)$, then $D(t,\cdot)$ is non-decreasing for each $t \in [\rho_1, \rho_2]$.There exist positive constants u_1, u_2, so that $B(n)u_1 \le Q(t,u_1)$, $B(n)u_2 \ge D(t,u_2)$, $0 \le u_1(t) \le u_2(t)$, $\rho_1 \le t \le \rho_2$.Thus the equation has a positive solution.*

Proof. Proof. We only need to consider the fixed point for the operator E,we consider $E : H \to H$ is completely continuous. Let $\rho_1 \le \rho_2$, $\alpha_1 \le \alpha_2$. Then

$$\begin{aligned}E\rho_1(t) &= c_1\left(\ln\tfrac{t}{a}\right)^{r-1} + \tfrac{1}{\Gamma(r)}\int_a^t\left(\ln\tfrac{t}{s}\right)^{r-1}\tfrac{Q(s,\rho_1(s))}{s}ds \\ &\le c_1\left(\ln\tfrac{t}{a}\right)^{r-1} + \tfrac{1}{\Gamma(r)}\int_a^t\left(\ln\tfrac{t}{s}\right)^{r-1}\tfrac{Q(s,\rho_2(s))}{s}ds \\ &\le E\rho_1(x,t)\end{aligned}$$

and

$$\begin{aligned}E\alpha_1(t) &= d_1\left(\ln\tfrac{t}{a}\right)^{r-1} + \tfrac{1}{\Gamma(r)}\int_a^t\left(\ln\tfrac{t}{s}\right)^{r-1}\tfrac{Q(s,\alpha_1(s))}{s}ds \\ &\le d_1\left(\ln\tfrac{t}{a}\right)^{r-1} + \tfrac{1}{\Gamma(r)}\int_a^t\left(\ln\tfrac{t}{s}\right)^{r-1}\tfrac{Q(s,\alpha_2(s))}{s}ds \\ &\le E\alpha_1(x,t).\end{aligned}$$

Hence E is a non-decreasing operator, so that the operator $E : \langle u_1, u_2\rangle \to \langle u_1, u_2\rangle$ is compact and continuous via lemma 1. That is H is a normal cone of E. □

4 Uniqueness solutions

Based on the fixed point theory, in the previous section we proved that the coupled cancer treatment fractional model involving Hadamard fractional derivative has an existing solution. The purpose of this section is to show the uniqueness of solutions to the model (2). For this let us assume that there is two special coupled solutions (ρ_1, ρ_2) and (α_1, α_2), where the following conditions holds true

$(A_1)\, \exists N_\rho > 0$, such that $|Q(t,\rho_1(t)) - Q(t,\rho_2(t))| \le N_\rho\, |\rho_1 - \rho_2|\,, \forall t \in [a,T]\,, \forall \rho_1, \rho_2 \in \mathbb{R}$,

$(A_2)\, \exists N_\alpha > 0$, such that $|Q(t,\alpha_1(t)) - Q(t,\alpha_2(t))| \le N_\alpha\, |\alpha_1 - \alpha_2|\,, \forall t \in [a,T]\,, \forall \alpha_1, \alpha_2 \in \mathbb{R}$.

Theorem 4.1. *Given the conditions$(A_1)$and (A_2). In addition, if $\frac{N_\rho}{\Gamma(r+1)}\left(\ln\frac{T}{a}\right)^r < 1$ and $\frac{N_\alpha}{\Gamma(r+1)}\left(\ln\frac{T}{a}\right)^r < 1$, then the system (2) has a unique positive solution.*

Proof. In the previous section we proved that the operator E is bounded, next we show that the operator is a contraction, then

$$\begin{aligned} |E\rho_1(t) - E\rho_2(t)| &\le \frac{1}{\Gamma(r)} \int_a^t \left(\ln\frac{t}{s}\right)^{r-1} |Q(s,\rho_1(s)) - Q(s,\rho_2(s))| \frac{ds}{s} \\ &\le \frac{N_\rho}{\Gamma(r)} |\rho_1 - \rho_2| \int_a^t \left(\ln\frac{t}{s}\right)^{r-1} \frac{ds}{s}, \end{aligned}$$

implies

$$\begin{aligned} \|E\rho_1 - E\rho_2\| &\le \frac{N_\rho}{\Gamma(r+1)}\left(\ln\frac{T}{a}\right)^r \|\rho_1 - \rho_2\| \\ &\le \|\rho_1 - \rho_2\|, \end{aligned}$$

similarly

$$\begin{aligned} \|E\alpha_1 - E\alpha_2\| &\le \frac{N_\alpha}{\Gamma(r+1)}\left(\ln\frac{T}{a}\right)^r \|\alpha_1 - \alpha_2\| \\ &\le \|\alpha_1 - \alpha_2\|. \end{aligned}$$

Implying that the operator E is a contraction, then by Banach contraction mapping theorem we can say that the cancer treatment fractional model (2) has a unique positive solution. □

5 Conclusion

We first integrated a cancer treatment model with the Hadamard fractional derivative. After that, we investigated the existence of the solution of the cancer treatment model. Finally, we analyzed how the model has a unique positive solution and under which conditions. Hopefully, this work will help the researchers working on cancer education and treatment.

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