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Radiotherapy cancer treatment modeling with fractional or ordinary derivative

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Abstract

This short communication presents two versions of the cancer treatment model, the ordinary derivative version and the fractional derivative version. The two models were used to simulate a cancer treatment process of a cancer patient with an initial tumor volume of 28.4 cm³. The simulated final volumes produced by the fractional derivative version were 28.17 cm³ and 5.68 cm³ the normal cells and tumor respectively, while those of the ordinary derivative version were 16.97 cm³ and 0.0 cm³. In addition, the fractional derivative version was used to simulate a no-treatment process with an initial tumor volume of 5 cm³, and the final volumes were 4.91 cm³ and 17.41 cm³ for the normal cells and tumor respectively. It was concluded that the radiotherapy treatment process was better simulated with the fractional derivative model.

Keywords: *radiotherapy, caputo fractional derivative, cancer treatment*

Introduction

The cancer treatment model is important in describing and analyzing the radiotherapy treatment process. However, predicting the outcomes of treatments is more important than describing the process. Therefore, the aim of cancer treatment models is to predict the outcome of treatment plans. There are two versions of these models, the ordinary derivative version and the fractional derivative version. The earlier models were mainly ordinary derivative versions [1-3], but recently the fractional derivatives are being integrated into the model [4-7]. Despite describing the same cancer treatment process analytically, it has not been ascertained whether the two model versions will produce the same numerical solutions. Also, it is important to investigate which model version will produce solutions that agreed with clinical data.

So, in this short communication, the two versions of the model were used to simulate a cancer treatment process of a cancer patient. The two results were interpreted and compared with the clinical data. Finally, the fractional version was used to simulate a no-treatment case.

Methods

The ordinary derivative version of the model was given by equations (1) and (2), while the fractional version was given by (3) and (4). The supplementary definitions were given by equations (5) and (6), and the definition of the Caputo fractional derivative was given by (7) [8]. .

$$\frac{d}{dt}\left(u(t)\right) = \alpha\left(1-\frac{u_1}{K_1}\right) \quad -\beta \quad -\varepsilon\chi(\ \ ,\ \ ) \qquad (1)$$

$$\frac{d}{dt}\left(u(t)\right) = \alpha\left(1-\frac{u_2}{K_2}\right) \quad -\beta \quad -\chi(\ \ ,\ \ ) \qquad (2)$$

$${}_0^cD_T^{\mu}\left(u_1(t)\right) = \alpha_1\left(1-\frac{u_1}{K_1}\right)u_1 - \beta_1 u_2 u_1 - \varepsilon\chi\left(u_1, t\right) \qquad (3)$$

$${}_0^CD_T^{\mu}\left(u_2(t)\right) = \alpha_2\left(1-\frac{u_2}{K_2}\right)u_2 - \beta_2 u_1 u_2 - \chi\left(u_2, t\right) \qquad (4)$$

$$\chi(u_1,t) = \left[\quad s(t) + 2 \quad s(t)\left(\int_0^t \exp\left(- \quad (t- \quad)\right)s(\quad)d \quad \right)\right]u_1 \qquad (5)$$

$$\chi(u_2,t) = \left[\quad s(t) + 2 \quad s(t)\left(\int_0^t \exp\left(- \quad (t- \quad)\right)s(\quad)d \quad \right) - \frac{\ln 2}{T_p}\frac{(T_d - T_k)}{T_d}\right]u_2 \qquad (6)$$

$${}_0^CD_t^{\mu}\left(f(t)\right) = \frac{1}{\Gamma(1-\mu)}\int_0^t \frac{df(x)}{dx}\frac{1}{(t-x)^{\mu}}dx,\ 0<\mu<1 \qquad (7)$$

where

u_1, u_2 are the populations of normal and cancer cells respectively,

α_1, α_2 are the respective proliferation coefficients of cells,
K_1, K_2 are the respective carrying capacities of cells,
β_1, β_2 are the respective competition coefficients of cells,
χ(u1, t) normal cells' population decay due to radiation,
χ(u2, t) cancer cells' population decay due to radiation,
ϵ is the perturbation constant,
α is the yield rate for lethal lesions,
β is the yield rate for sublethal lesions,
T_d is the total time of treatment (number of days),
T_4 is the "kick-off" time for the repopulation of the cancer cells,
T_P is the effective doubling time of the cancer cells,
S(t) is the time-varying fractionated dose rate,

Λ is the repair time constant defined as ,

T is the total time for radiotherapy (sum of (t)),

$T_{1/2}$ is the half time for the repair,

$^{C}_{0}D^{\mu}_{t}$ is the Caputo fractional derivative, and

$f(t) \in H^1(0,b)$, H^1 is a Sobolev space.

The numerical simulations of the model were done by assigning numerical values to the parameters. The proliferation coefficients α_1, α_2 were chosen as 9.7041×10^{-4} and 0.3396 respectively [1]. The competition coefficients and the perturbation constant β_1,β_2 were chosen as 0.0433, 0.2385, and 0.0008 respectively [1,7]. The radiation parameters were obtained from the clinical data of a cancer patient treated with radiotherapy [9]. The radiosensitivity values α,β were chosen as 0.3 and 0.03 respectively [9]. The half time for repair $T_{1/2}$ was chosen as 15 minutes [10]. The rate of repopulation $\ln(2)/T_p$ and T_k were chosen as 0.6 and 28 days respectively [11].

The selected patient had a tumor volume of 28.4 cm^3, uterine cervical cancer of the Squamous Cell Carcinoma type, and was administered on a radiation dose of 1.8 Gy with 25 fractions [9]. Therefore, $S(t)$ and T_d were chosen as 1.8 Gy and 35 days respectively. The time for a fractionated dose is approximately 15 minutes, thus t and T was chosen as 15 minutes and 375 minutes respectively. The T value is the summation of the fractionated times and not the total number of minutes in the days of treatment. The population of cells in a tumor is directly proportional to the volume of the tumor, and a tumor with a volume of 1 cm^3 has approximately 1 billion cells [12]. As a result, the initial population of cancer cells was scaled to 0.284 and the carrying capacities K_1, K_2 were scaled to 1. A major bottleneck in using the model is in finding a correct initial population for the normal cells, however, we assumed that the normal and cancer cells had equal initial populations. The populations of the cells and the time of treatment represented the variables in the model.

After establishing numerical values for all the parameters and variables, the ordinary derivative version of the model (equations (1) and (2)), and the fractional derivative version (equations (3) and (4)) were solved in MATLAB. The fractional differential equation code (FDE12.m) [13-17] was used to solve the Caputo fractional derivative in the model. For the fractional derivative version of the model, the value of the Caputo fractional derivative was chosen as 0.1588 in the FDE12.m code. In addition, the FDE12.m code was used for the ordinary derivative version of the model by making the value of the Caputo fractional derivative 1. Once the value of the fractional derivative becomes 1, the derivative becomes an ordinary derivative. The obtained simulated solutions represented the final populations of the cells from which the final volumes of the tumor and normal cells can be obtained. After simulating the radiotherapy treatment process with the two versions of the model, the fractional version was then used to simulate a no-treatment process. The no-treatment process occurs when the cells' population decay due to radiation was zero.

Results

The results of the simulations showed that the fractional derivative model produced scaled final populations of 0.2817 and 0.0568 for normal cells and tumor respectively, while the ordinary derivative model produced final populations of 0.1697 and 0.0. The corresponding volumetric values were 28.17 cm^3, 5.68 cm^3, 16.97 cm^3, and 0.0 cm^3. The reported final volume for the tumor was 5.67 cm^3 [9]. The simulated final tumor volume produced by the fractional derivative model, 5.68 cm^3, was in close agreement with the clinical data 5.67 cm^3. However, the simulated final tumor volume produced by the ordinary derivative model, 0.0 cm^3, deviated much from the clinical data. Furthermore, for the no-treatment case, we assumed a tumor of initial volume 5 cm^3 because the 28.4 cm^3 was an advanced tumor. Also, equal populations were assumed for the cells. The simulated results produced scaled final populations of 0.0491 and 0.1741 for normal and cancer cells, corresponding to volumes of 4.91 cm^3 and 17.41 cm^3. This implied that the assumed tumor will increase in size from 5 cm^3 to 17.41 cm^3 during a no-treatment case. The results of the three simulations were presented in Figures 1-3.

Conclusion

In this short communication, the radiotherapy process of a cancer patient was simulated with two versions of the cancer treatment model. The two versions were fractional derivative and

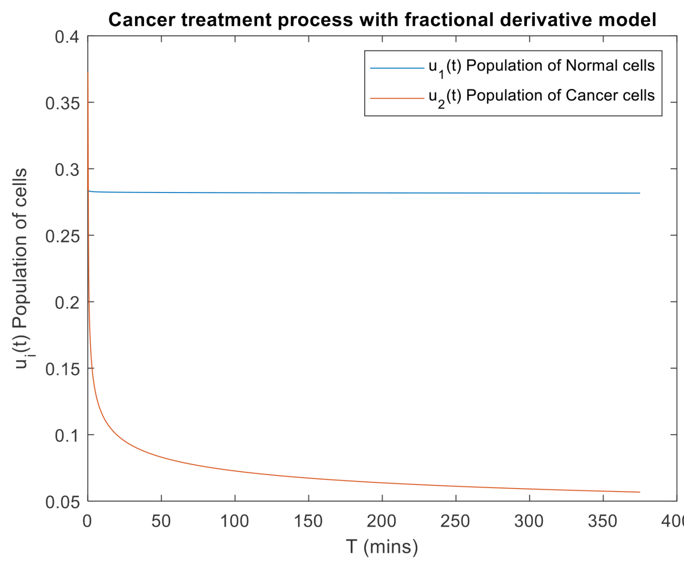

Figure 1. Population changes in the normal and cancer cells.

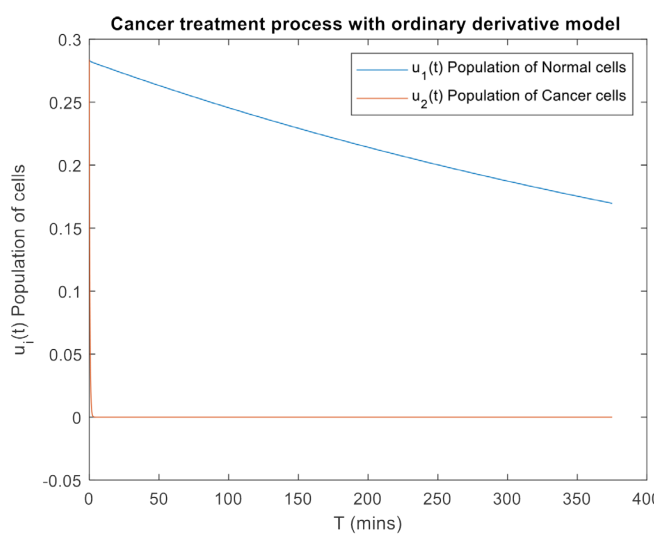

Figure 2. Population changes in the normal and cancer cells.

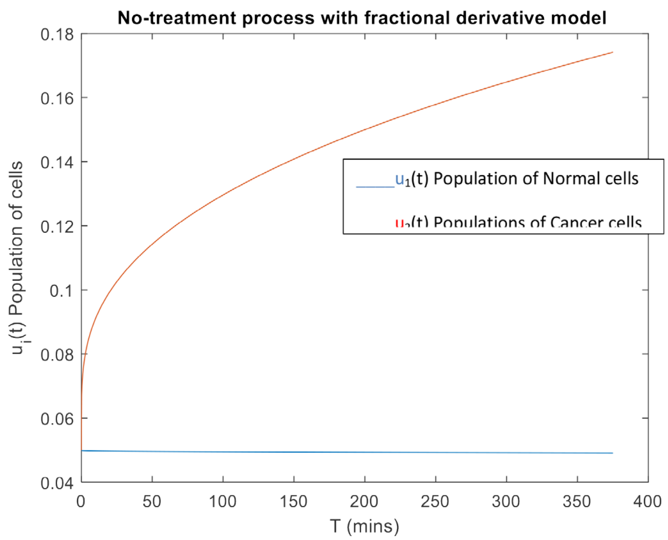

Figure 3. Population changes in the normal and cancer cells.

ordinary derivative versions. The results showed that the fractional derivative model produced better results than the ordinary derivative version. Finally, the fractional derivative model was then used to simulate the no-treatment process.

References

1. Belostotski G, Freedman H. A control theory model for cancer treatment by radiotherapy. *Int J Pure Appl Math*. 2005, 25: 447-480.
2. Freedman H, Belostotski G. Perturbed models for cancer treatment by radiotherapy. *Differen Equat Dynami Sys*. 2009; 17: 115-133.
3. Liu ZJ, Yang CX. A Mathematical Model of Cancer Treatment by Radiotherapy. *Comput Math Method Med*. 2014: 12.
4. Dokuyucu MA, Celik E, Bulut H, Baskonus HM. Cancer treatment model with the Caputo-Fabrizio fractional derivative. *Eur Phys J Plus*. 2018; 133: 92.
5. Awadalla M, Yameni Y, Abuassba K. A new Fractional Model for the Cancer Treatment by Radiotherapy Using the Hadamard Fractional Derivative. *Online Math*. 2019; 1: 14-18.
6. Farayola MF, Shafie S, Siam FM, Khan I. Numerical simulation of normal and cancer cells' populations with fractional derivative under radiotherapy. *Com Methods Prog Biomed*. 2019: 105202.
7. Farayola MF, Shafie S, Siam FM, Khan I. Mathematical modeling of radiotherapy cancer treatment using Caputo fractional derivative. *Com Methods Prog Biomed*. 2019: 105306.
8. Caputo M, Fabrizio M: A new definition of fractional derivative without singular kernel. *Progr Fract Differ Appl*. 2015. 1 :1-13.
9. Belfatto A, Riboldi M, Ciardo D, Cattani F, Cecconi A, et al.: Kinetic Models for Predicting Cervical Cancer Response to Radiation Therapy on Individual Basis Using Tumor Regression Measured In Vivo With Volumetric Imaging. *Technol Cancer Res Treat*. 2016;15: 146-158.
10. Bertuzzi A, Bruni C, Papa F, Sinisgalli C. Optimal solution for a cancer radiotherapy problem. *J Mathematical Biol*. 2013; 66: 311-349.
11. Fowler JF. Development of radiobiology for oncology-a personal view. *Phys Med Biol*. 2006; 51: R263.
12. Benzekry S, Lamont C, Beheshti A, Tracz A, Ebos JM, et al. Classical mathematical models for description and prediction of experimental tumor growth. *PLoS Computat Bilo*. 2014; 10: e1003800.
13. Diethelm K. Efficient solution of multi-term fractional differential equations using P (EC) m E methods. *Computing*. 2003; 71: 305-319.
14. Diethelm K, Ford NJ, Freed AD. Detailed error analysis for a fractional Adams method. *Numerical Algorithms*. 2004; 36: 31-52.
15. Diethelm K, Freed AD. The FracPECE subroutine for the numerical solution of differential equations of fractional order. Forschung Wissenschaftliches Rechnen. 1998; 1999: 57-71.
16. Garrappa R. On linear stability of predictor–corrector algorithms for fractional differential equations. *Int J Comp Mathem*. 2010; 87: 2281-2290.
17. Hairer E, Lubich C, Schlichte M: Fast numerical solution of nonlinear Volterra convolution equations. *SIAM J Scie Statis Comput*. 1985; 6: 532-541.

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