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## Tumor growth mathematical modeling and application of chemo-immunotherapy and radiotherapy treatments

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### Abstract

This research involves three propositions. First, we proposed a model that represents tumor growth caused by carcinogenic substances from an initially diagnosed level; secondly, we proposed several therapeutic models for chemotherapy, immunotherapy, and radiotherapy, respectively, with a steady supply of dosage, with the aim of solving the cell proliferation issue. Thirdly, we modified the tumor growth model where we considered the therapeutic effect on the tumor cell with several interactive terms. The proposed models were solved analytically where tumor cell functions with and without therapeutic effects were obtained. On the other hand, we obtained independent solutions of chemotherapy, immunotherapy, and radiotherapy functions were also obtained, with some pertinent parameters. We developed numerical simulation codes using Wolfram Mathematica software, version 12 to simulate the various functions by varying the pertinent parameters to study their effect on tumor growth and to study each significant level. Numerical simulation was carried out, and it was observed that continuous exposure to radiation could cause pain and normal cell death, thereby supporting the tumor cell proliferation, but the chemotherapeutic and immunotherapeutic drugs help in shrinking the tumor and reducing cell proliferation. The simulated results for the mixed treatment application for all therapies indicate that there is a successful and faster decrease in tumor size by combining the treatment regimes. In conclusion, we have successively proposed and solved mathematical models that represent tumor growth without treatment and with the application of treatment. The models in this article can be used by scientists and oncologists in studying tumor cell proliferation.

**Keywords:** Modeling, carcinogenic, treatment, cancer, tumor, proliferation, radiotherapy, chemotherapy, immunotherapy, growth

### 1. Introduction

Cancer is defined as any disease in which normal cells are damaged and do not die as quickly as they divide via mitosis. Carcinogens may increase the risk of cancer by altering cellular metabolism or directly damaging DNA in cells, interfering with biological processes and inducing uncontrolled, malignant division, eventually leading to tumor formation. Severe DNA damage usually results in programmed cell death; however, if the programmed cell death pathway is damaged, the cell cannot prevent itself from becoming a cancer cell. There are numerous naturally occurring carcinogens. Aflatoxin B<sub>1</sub>, a potent, naturally occurring microbial carcinogen produced by the fungus *Aspergillus flavus* growing on stored grains, nuts, and peanut butter, is an example of a potent, naturally occurring microbial carcinogen. Some viruses, such as hepatitis B and human papilloma virus have been found to cause cancer in humans <sup>[1]</sup>.

According to <sup>[2]</sup> and <sup>[3]</sup>, cancer is a complex disease that grows locally and has the ability to spread to other organs in the body. Furthermore, cancer management is a growing concern in an aging population and is becoming increasingly important in developing countries, according to <sup>[4]</sup>. According to the International Agency for Research on Cancer (IARC), by 2030, there will be approximately 26 million new cancer cases and 17 million cancer deaths worldwide <sup>[5]</sup>.

Any substance, radionuclide, or radiation that promotes carcinogenesis, or the formation of cancer, is referred to as a carcinogen.

This could be because of their ability to damage the genome or disrupt cellular metabolic processes. Several radioactive substances are carcinogens, but their carcinogenic activity is attributed to the radiation they emit, such as gamma rays and alpha particles. Non-radioactive carcinogens include inhaled asbestos, certain dioxins, and tobacco smoke. Although the general public associates carcinogenicity with synthetic chemicals [6] argued that it can occur in both natural and synthetic substances.

Radiation therapy (also known as radiotherapy) is a type of cancer treatment in which high doses of radiation are used to kill cancer cells and shrink tumors. Radiation not only kills or slows the growth of cancer cells, but it can also harm healthy cells nearby. Damage to healthy cells can have unintended consequences, such as a breakdown in immune defenses. Radiation is used in low doses in x-rays to see inside your body, as in x-rays of your teeth or broken bones. Radiation therapy, in high doses, kills cancer cells or slows their growth by damaging their DNA. Cancer cells that have had their DNA damaged beyond repair either stop dividing or die [7].

When damaged cells die, the body breaks them down and removes them. Radiation therapy does not immediately kill cancer cells. It can take days or weeks of treatment to damage DNA enough for cancer cells to die.

The cancer cells then continue to die for weeks or months after the radiation therapy is finished.

In some cases, radiation therapy may be the only option. However, radiation is frequently combined with other cancer treatments such as surgery, chemotherapy, and immunotherapy. Radiation therapy may be administered before, during, or after these other treatments to increase the likelihood that the treatment will be effective [8].

When radiation therapy is administered, it depends on the type of cancer being treated as well as whether the goal of radiation therapy is to treat the cancer or relieve symptoms [9].

Immunotherapy is a type of cancer treatment that stimulates the immune system to fight the disease. The immune system aids the human body in its fight against infections and other diseases. It is made up of white blood cells as well as lymphatic organs and tissues. Immunotherapy falls under the category of biological therapy. Biological therapy is a type of cancer treatment that employs substances derived from living organisms, [10].

Chemotherapy is the application of any drug to the treatment of any disease. Most people, however, associate chemotherapy (or "chemo") with cancer-treatment drugs. It's critical to understand that not all cancer medications and drugs work the same way. Traditional or standard chemo used to be the only type of drug that could treat cancer, but now there are many different types of drugs used to treat cancer, [11]. Chemotherapy is a systemic treatment because the drug travels throughout the body and can kill cancer cells that have spread (metastasized) to areas of the body far from the original (primary) tumor. This distinguishes it from treatments such as surgery and radiation.

Radiation therapy targets a specific area of the body in order to kill or damage cancer cells. These types of treatments are known as "local treatments" because they only affect one part of the body [12].

Chemotherapy is commonly administered at regular intervals known as "cycles." A cycle is defined as the administration of one or more drugs on one or more days, followed by a period of several days or weeks without treatment. This allows normal cells to recover from the effects of the drug.

Doses may be given a certain number of days in a row, or every other day for a number of days, followed by a period of rest. Some medications work best when administered continuously over a set number of days. Because the entire process involves several stages, mathematical modeling is an essential tool for understanding tumor growth and response to chemotherapy.

To systematically relate the initiation of tumor growth, mathematical models are required.

Its progression and invasion are responsible for the tumor tissue's and the surrounding environment's heterogeneity.

The dependence of the tumor size on time is expressed mathematically in tumor growth modeling. The Malthusian Law: this model is concerned with the tumor's population rather than individual cells.

The population growth rate as a function of time is taken into account. When there is no treatment for the tumor, the population grows in an erratic manner. Individual increases, however, are negligible when compared to the total population when the population is very large.

In other words, population growth is roughly continuous and, in fact, a differentiable function of time. Given the tumor population, and assuming that the population's rate of change is proportional to the number of individuals in it at any given time, we have a differential equation [13]. The use of mathematical modeling of biological processes to improve quantitative understanding of bio-medical phenomena is common. This quantitative understanding is applicable in both clinical and experimental settings. One important application of modeling exercises is in cancer biology, according to Watanabe 2016 [14]. Many mathematical models have been developed to represent some aspects of cancer [15] and [16], but to the best of our knowledge, this research is the first to consider a mixed therapeutic treatment involving radiotherapy.

### 1.1 Objectives of the research

The objectives of this research is to propose novelty models that represent tumor growth and cell proliferation caused by carcinogenic agent (substance) and the application of radiotherapy and other therapeutic treatments in reducing or controlling the size of the tumor. Secondly, solve the proposed models analytically with the consideration of the initial concentration of tumor and the application of initial dosage of the therapeutic drugs. Lastly, perform a numerical computation using Wolfram Mathematica software, where the effect of the various therapeutic drugs is to be investigated as singular basis and on mixed combinations.

## 2. Mathematical Formulation

We consider the fact that cancerous tumor is triggered by a carcinogenic substance and proliferate and metastasized with a growth rate. The exponential model is the simplest model used to describe tumor [17]. Proposed that tumors grow exponentially with one cell given rise to two cells, these two cells to four cells, and so on. This growth scheme leads to an uncontrolled growth of the tumor cells. In view of Collins work, we propose a mathematical model that represents tumor growth caused by carcinogens, secondly, propose several treatment models for chemotherapy, immunotherapy and radiotherapy respectively and introduce the treatments on the tumor growth model with the aim of reducing the tumor size and controlling cell proliferation. In view of the

forementioned considerations, we divide the propositions into two sections; first the section that deals with tumor growth without treatment and the aspect that deals with the application of the treatments on the tumor growth.

**2.1 Tumor Growth without Treatment**

$$\frac{dy}{dt} = \gamma_1 e^{\alpha_1 t} y \tag{1}$$

$$y(t = 0) = y_0$$

**2.2 Tumor Growth with Application of treatment**

Here, we formulate mathematical models for the various therapeutic treatments such as chemotherapy, immunotherapy and radiotherapy, and how these treatments help in reducing the cell proliferation, thereby reducing the tumor size. The treatment models and the modified tumor cells models as follows:

$$\frac{dy}{dt} = \gamma_1 e^{\alpha_1 t} y - \alpha_2 M y - \alpha_3 I y - \alpha_4 R_d y \tag{2}$$

$$\frac{dM}{dt} = v_M - d_4 M \tag{3}$$

$$\frac{dI}{dt} = v_I - d_5 I \tag{4}$$

$$\frac{dR_d}{dt} = h_m - d_6 R_d \tag{5}$$

$$y(t = 0) = y_0, M(t = 0) = M_0 \text{ and } R_d(t = 0) = R_{0d}, I(t = 0) = I_0$$

**3. Method of Solution**

The method of solution is direct separation of variable for the tumor cells proliferation equation (1) without treatment and with therapeutic treatment equations (2-5). In order to study the tumor cell proliferation caused by carcinogenic substance without specific treatment administered, we have to solve equation (1), which is:

$$\int \frac{dy}{y} = \gamma_1 \int e^{\alpha_1 t} dt \tag{6}$$

$$\log_e y = \frac{\gamma_1}{\alpha_1} e^{\alpha_1 t} + C_1 \tag{7}$$

$$y = e^{\frac{\gamma_1}{\alpha_1} e^{\alpha_1 t} + C_1} \tag{8}$$

$$y = e^{C_1} e^{\frac{\gamma_1}{\alpha_1} e^{\alpha_1 t}} \tag{9}$$

Applying the initial conditiony  $(t = t_0) = y_0$  on equation (9), we have:

$$y = y_0 e^{-\frac{\gamma_1}{\alpha_1} \frac{\gamma_1}{\alpha_1} e^{\alpha_1 t}} = y_0 e^{\left(-\frac{\gamma_1}{\alpha_1} + \frac{\gamma_1}{\alpha_1} e^{\alpha_1 t}\right)} \tag{10}$$

Having solved equation (1) analytically with the case of without the treatments, we shall now solve the treatment models before introducing it into the subsequent modified tumor cell proliferation. The chemo-immunotherapeutic and radiotherapy treatment models are recalled as:

$$\frac{dM}{dt} + d_4 M = v_M \tag{11}$$

$$\frac{dI}{dt} = v_I - d_5 I \tag{12}$$

$$\frac{dR_d}{dt} = h_m - d_6 R_d \tag{13}$$

Where,  $R_d(t)$ ,  $M(t)$  and  $I(t)$  denote the radiotherapy, chemotherapy and immunotherapy drugs concentrations over time respectively. To investigate chemotherapeutic treatment on the tumor cell proliferation, we solve equation (11), where we have:

$$M = M_c + M_p \quad M = Ae^{-d_4t} + \frac{v_M}{d_4} \tag{14}$$

We apply the initial tumor cell condition  $M(0) = M_0$  in equation (14), which reduces to

$$M = \left(M_0 - \frac{v_M}{d_4}\right)e^{-d_4t} + \frac{v_M}{d_4} \tag{15}$$

$$M(t) = M_0e^{-d_4t} + \frac{v_M}{d_4}(1 - e^{-d_4t}) \tag{16}$$

In a similar vein, to study the impact of immunotherapeutic drugs on the tumor cell proliferation, we solve equation (12) as follows:

$$I = I_c + I_p \quad I = Ae^{-d_5t} + \frac{v_I}{d_5} \tag{17}$$

We apply the initial tumor cell condition  $I(0) = I_0$  in equation (17), which reduces to

$$I = \left(I_0 - \frac{v_I}{d_5}\right)e^{-d_5t} + \frac{v_I}{d_5} \tag{18}$$

$$I = I_0e^{-d_5t} + \frac{v_I}{d_5}(1 - e^{-d_5t}) \tag{19}$$

Finally, to investigate the effect of radiotherapy on tumor cells proliferation, we solve equation (13) as follows:

$$R_d = R_{dc} + R_{dp} \tag{20}$$

$$R_d(t) = A_3e^{-d_6t} + \frac{h_m}{d_6}$$

We apply the initial tumor cell condition  $R_d(0) = R_{d0}$  in equation (20), which reduces to

$$R_d = \left(R_{d0} - \frac{h_m}{d_6}\right)e^{-d_6t} + \frac{h_m}{d_6} \tag{21}$$

$$R_d = R_{d0}e^{-d_6t} + \frac{h_m}{d_6}(1 - e^{-d_6t}) \tag{22}$$

Now, we have to substitute the therapeutic treatment solutions (16), (19) and (22), with their initial dosage into the modified tumor cell proliferation equation (2), we have the following:

$$\frac{dy}{y} = \left( \gamma_1 e^{\alpha_1 t} - \alpha_2 \left( M_0 e^{-d_4 t} + \frac{v_M}{d_4} (1 - e^{-d_4 t}) \right) - \alpha_3 \left( I_0 e^{-d_5 t} + \frac{v_I}{d_5} (1 - e^{-d_5 t}) \right) - \alpha_4 \left( R_{d0} e^{-d_6 t} + \frac{h_m}{d_6} (1 - e^{-d_6 t}) \right) \right) dt \tag{23}$$

Integrating both sides of equation (23), we have:

$$\int \frac{dy}{y} = \left( \frac{\gamma_1 e^{\alpha_1 t} - \alpha_2 \left( -\frac{M_0}{d_4} e^{-d_4 t} + \frac{v_M}{d_4} \left( t + \frac{e^{-d_4 t}}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} e^{-d_5 t} + \frac{v_I}{d_5} \left( t + \frac{e^{-d_5 t}}{d_5} \right) \right)}{-\alpha_4 \left( -\frac{R_{d0}}{d_6} e^{-d_6 t} + \frac{h_m}{d_6} \left( t + \frac{e^{-d_6 t}}{d_6} \right) \right)} \right) \tag{24}$$

Solving the LHS of equation (24), we have:

$$\log_e y = \left( \frac{\gamma_1 e^{\alpha_1 t} - \alpha_2 \left( -\frac{M_0}{d_4} e^{-d_4 t} + \frac{v_M}{d_4} \left( t + \frac{e^{-d_4 t}}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} e^{-d_5 t} + \frac{v_I}{d_5} \left( t + \frac{e^{-d_5 t}}{d_5} \right) \right)}{-\alpha_4 \left( -\frac{R_{d0}}{d_6} e^{-d_6 t} + \frac{h_m}{d_6} \left( t + \frac{e^{-d_6 t}}{d_6} \right) \right)} \right) + C_2 \tag{25}$$

Taking the exponentials of equation (25), we obtained:

$$y = e^{\left( \left( \frac{\gamma_1}{\alpha_1} e^{\alpha_1 t} - \alpha_2 \left( -\frac{M_0}{d_4} e^{-d_4 t} + \frac{v_M}{d_4} \left( t + \frac{e^{-d_4 t}}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} e^{-d_5 t} + \frac{v_I}{d_5} \left( t + \frac{e^{-d_5 t}}{d_5} \right) \right) - \alpha_4 \left( -\frac{R_{d0}}{d_6} e^{-d_6 t} + \frac{h_m}{d_6} \left( t + \frac{e^{-d_6 t}}{d_6} \right) \right) \right) \right) + C_2} \tag{26}$$

Simplifying equation (26), we have:

$$y = e^{C_2} e^{\left( \frac{\gamma_1}{\alpha_1} e^{\alpha_1 t} - \alpha_2 \left( -\frac{M_0}{d_4} e^{-d_4 t} + \frac{v_M}{d_4} \left( t + \frac{e^{-d_4 t}}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} e^{-d_5 t} + \frac{v_I}{d_5} \left( t + \frac{e^{-d_5 t}}{d_5} \right) \right) - \alpha_4 \left( -\frac{R_{d0}}{d_6} e^{-d_6 t} + \frac{h_m}{d_6} \left( t + \frac{e^{-d_6 t}}{d_6} \right) \right) \right)} \tag{27}$$

Upon further simplification of equation (27), we obtained:

$$y(t) = B e^{\left( \frac{\gamma_1}{\alpha_1} e^{\alpha_1 t} - \alpha_2 \left( -\frac{M_0}{d_4} e^{-d_4 t} + \frac{v_M}{d_4} \left( t + \frac{e^{-d_4 t}}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} e^{-d_5 t} + \frac{v_I}{d_5} \left( t + \frac{e^{-d_5 t}}{d_5} \right) \right) - \alpha_4 \left( -\frac{R_{d0}}{d_6} e^{-d_6 t} + \frac{h_m}{d_6} \left( t + \frac{e^{-d_6 t}}{d_6} \right) \right) \right)} \tag{28}$$

Applying the initial condition  $y(t = 0) = y_0$  in equation (28), we have:

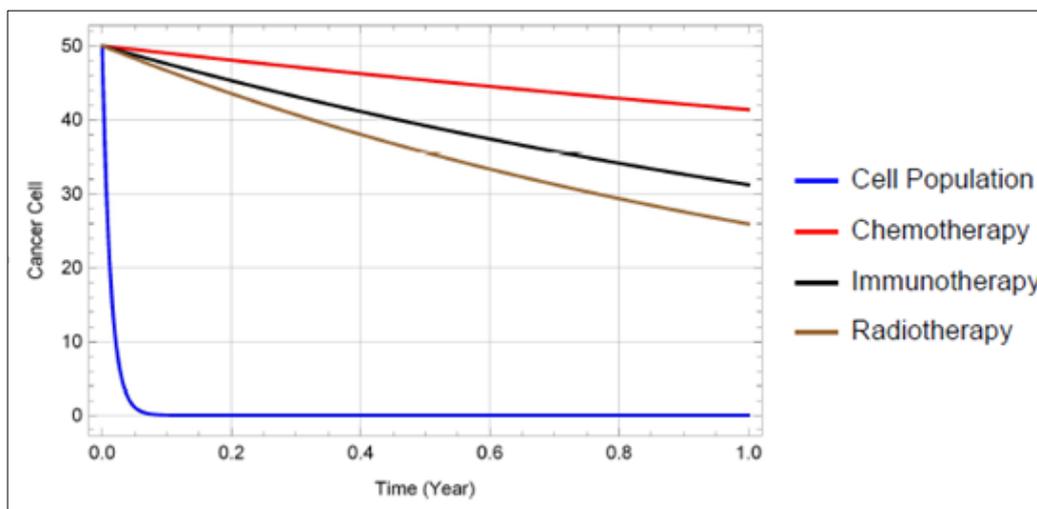
$$y(t) = \left( y_0 e^{-\left( \frac{\gamma_1}{\alpha_1} - \alpha_2 \left( -\frac{M_0}{d_4} + \frac{v_M}{d_4} \left( \frac{1}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} + \frac{v_I}{d_5} \left( \frac{1}{d_5} \right) \right) - \alpha_4 \left( -\frac{R_{d0}}{d_6} + \frac{h_m}{d_6} \left( \frac{1}{d_6} \right) \right) \right)} \right) e^{\left( \frac{\gamma_1}{\alpha_1} e^{\alpha_1 t} - \alpha_2 \left( -\frac{M_0}{d_4} e^{-d_4 t} + \frac{v_M}{d_4} \left( t + \frac{e^{-d_4 t}}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} e^{-d_5 t} + \frac{v_I}{d_5} \left( t + \frac{e^{-d_5 t}}{d_5} \right) \right) - \alpha_4 \left( -\frac{R_{d0}}{d_6} e^{-d_6 t} + \frac{h_m}{d_6} \left( t + \frac{e^{-d_6 t}}{d_6} \right) \right) \right)} \tag{29}$$

#### 4. Results

The analytical and simulated results are presented in this section. The simulation was done using Wolfram Mathematica software, version 12, to study the effects of the treatments, on the tumor cell proliferation. Let us recall the models analytical solutions obtained in section 3 above as:

$$y(t) = y_0 e^{\frac{\gamma_1}{\alpha_1} t} e^{\frac{\gamma_1}{\alpha_1} e^{\alpha_1 t}} \tag{30}$$

$$y(t) = \left( y_0 e^{-\left( \frac{\gamma_1}{\alpha_1} - \alpha_2 \left( -\frac{M_0}{d_4} + \frac{v_M}{d_4} \left( \frac{1}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} + \frac{v_I}{d_5} \left( \frac{1}{d_5} \right) \right) - \alpha_4 \left( -\frac{R_{d0}}{d_6} + \frac{h_m}{d_6} \left( \frac{1}{d_6} \right) \right) \right)} \right) e^{\left( \frac{\gamma_1}{\alpha_1} e^{\alpha_1 t} - \alpha_2 \left( -\frac{M_0}{d_4} e^{-d_4 t} + \frac{v_M}{d_4} \left( t + \frac{e^{-d_4 t}}{d_4} \right) \right) - \alpha_3 \left( -\frac{I_0}{d_5} e^{-d_5 t} + \frac{v_I}{d_5} \left( t + \frac{e^{-d_5 t}}{d_5} \right) \right) - \alpha_4 \left( -\frac{R_{d0}}{d_6} e^{-d_6 t} + \frac{h_m}{d_6} \left( t + \frac{e^{-d_6 t}}{d_6} \right) \right) \right)} \tag{31}$$



**Fig 1:** Effect of Chemotherapeutic Treatment on Tumor Growth with other parameters values

$$\gamma_1 = 20, \alpha_1 = 0.35, \alpha_2 = 0.54, \alpha_3 = 0.65, \alpha_4 = 0.75, v_I = 5, h_m = 5, d_4 = 0.3, d_5 = 0.6, d_6 = 0.8$$

**Table 1:** Effect of Chemotherapeutic Treatment on Tumor Growth

Time	$y(v_m = 5)$	$y(v_m = 10)$	$y(v_m = 15)$	$y(v_m = 20)$
0.0	50	50	50	50
0.1	0.0296479	0.0299539	0.0302653	0.0305819
0.2	0.0000295829	0.000030859	0.0000322064	0.0000336332
0.3	4.83719E-8	5.33277E-8	5.89085E-8	6.5206E-8
0.4	1.26486E-10	1.5115E-10	1.81508E-10	2.19064E-10

0.5	5.17155E-13	6.88373E-13	9.2537E-13	1.25679E-12
0.6	3.23863E-15	4.94471E-15	7.68402E-15	1.21637E-14
0.7	3.04813E-17	5.50922E-17	1.02506E-16	1.96655E-16
0.8	4.23739E-19	9.37899E-19	2.17113E-18	5.27125E-18
0.9	8.56383E-21	2.40731E-20	7.22923E-20	2.33022E-19
1.0	2.48005E-22	9.20625E-22	3.75363E-21	1.69364E-20

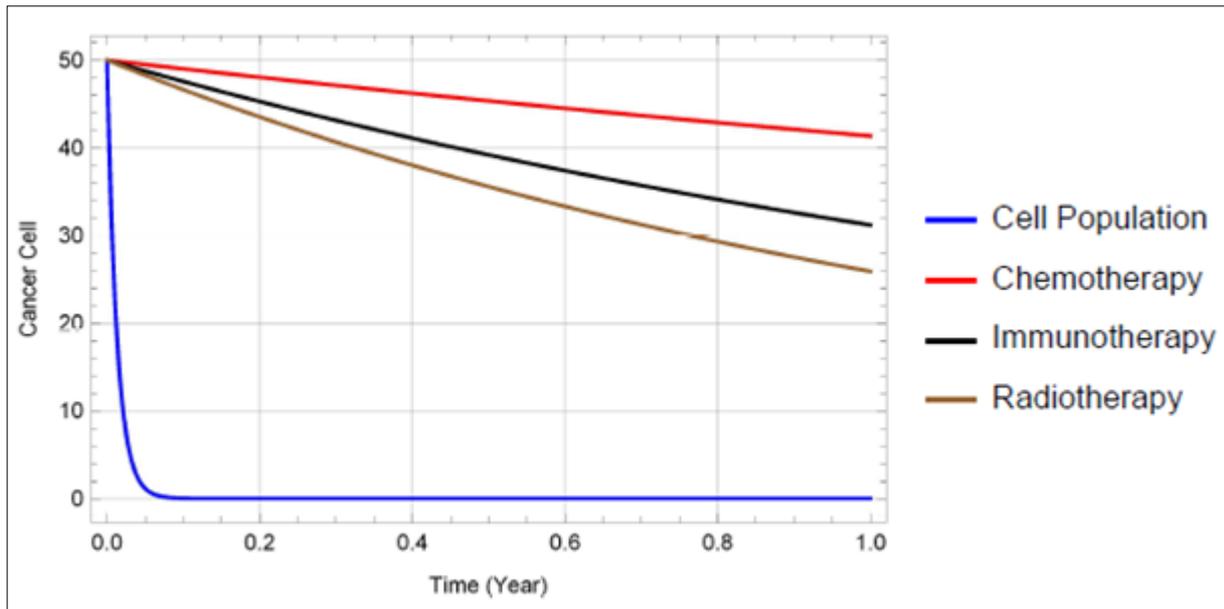


Fig 2: Effect of Radiotherapy on Tumor Growth with other parameters values

$$\gamma_1 = 20, \alpha_1 = 0.35, \alpha_2 = 0.54, \alpha_3 = 0.65, \alpha_4 = 0.75, v_l = 5, v_m = 5, d_4 = 0.3, d_5 = 0.6, d_6 = 0.8$$

Table 2: Effect of Carcinogen on Tumor Cell Proliferation with Therapeutic Treatment

Time	$y(h_m = 5)$	$y(h_m = 10)$	$y(h_m = 15)$	$y(h_m = 20)$
0.0	50	50	50	50
0.1	0.0296479	0.0299539	0.0302653	0.0305819
0.2	0.0000295825	0.000030858	0.0000322064	0.0000336332
0.3	4.83719E-8	5.33277E-8	5.89085E-8	6.5206E-8
0.4	1.26486E-10	1.5115E-10	1.81508E-10	2.19064E-10
0.5	5.17155E-13	6.88373E-13	9.2537E-13	1.25679E-12
0.6	3.23863E-15	4.94471E-15	7.68402E-15	1.21637E-14
0.7	3.04813E-17	5.50922E-17	1.02506E-16	1.96655E-16
0.8	4.23739E-19	9.37899E-19	2.17113E-18	5.27125E-18
0.9	8.56383E-21	2.40731E-20	7.22923E-20	2.33022E-19
1.0	2.48005E-22	9.20625E-22	3.75363E-21	1.69364E-20

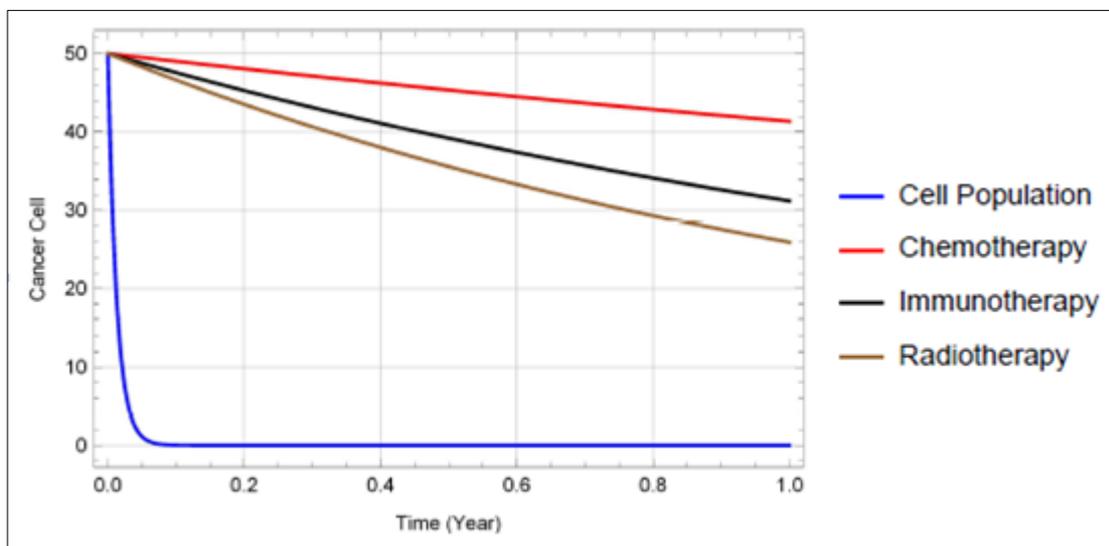
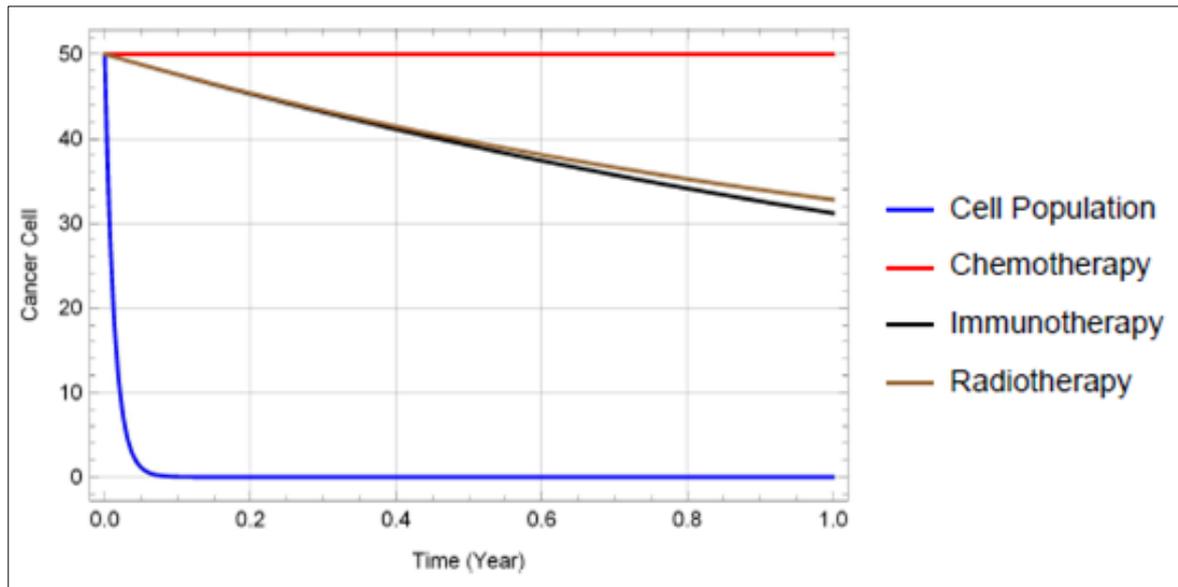


Fig 3: Effect of Immunotherapeutic Treatment on Tumor Growth, with other parameters values

$$\gamma_1 = 20, \alpha_1 = 0.35, \alpha_2 = 0.54, \alpha_3 = 0.65, \alpha_4 = 0.75, v_m = 5, h_m = 5, d_4 = 0.3, d_5 = 0.6, d_6 = 0.8$$

**Table 3:** Effect of Immunotherapeutic Treatment on Tumor Growth

Time	$y(v_l = 5)$	$y(v_l = 10)$	$y(v_l = 15)$	$y(v_l = 20)$
0.0	50	50	50	50
0.1	0.0296479	0.0291793	0.0287182	0.0282643
0.2	0.0000295829	0.0000277912	0.0000261081	0.0000245268
0.3	4.83719E-8	4.21428E-8	3.67158E-8	3.19877E-8
0.4	1.26486E-10	9.94582E-11	7.82061E-11	6.14951E-11
0.5	5.17155E-13	3.57754E-13	2.47484E-13	1.71203E-13
0.6	3.23863E-15	1.92411E-15	1.14313E-15	6.79149E-16
0.7	3.04813E-17	1.52039E-17	7.58362E-18	3.78267E-18
0.8	4.23739E-19	1.73699E-19	7.12026E-20	2.91873E-20
0.9	8.56383E-21	2.82753E-21	9.33569E-22	3.08238E-22
1.0	2.48005E-22	6.47163E-23	1.68875E-23	4.40674E-24

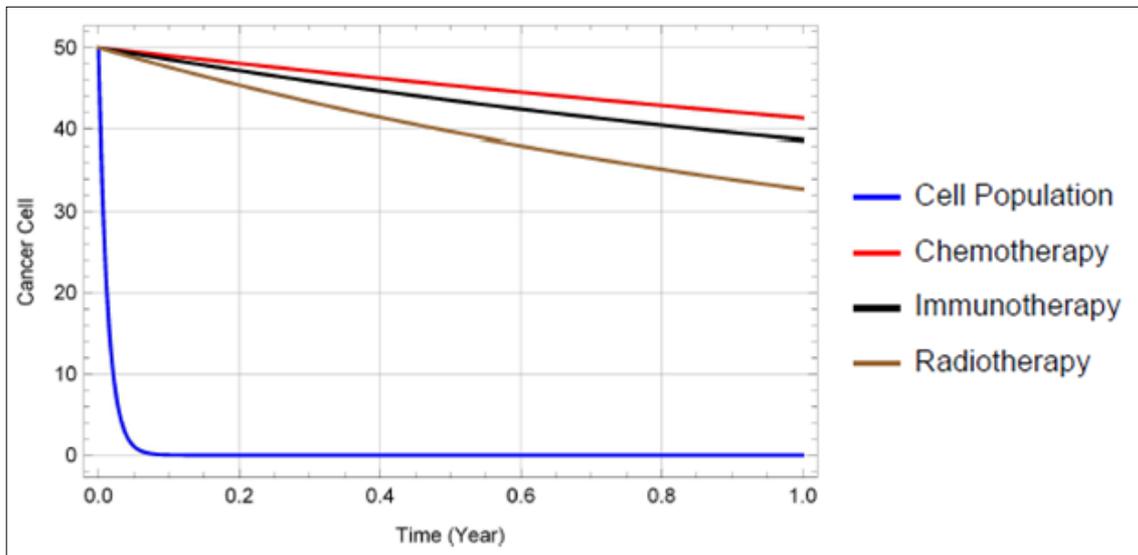


**Fig 4:** Effect of Radio-chemotherapeutic Treatment on Tumor Growth with other parameters

$$\gamma_1 = 20, \alpha_1 = 0.35, \alpha_2 = 0.54, \alpha_3 = 0.65, \alpha_4 = 0.75, v_l = 5, d_4 = 0.3, d_5 = 0.6, d_6 = 0.8$$

**Table 4:** Effect of Radio-chemotherapeutic Treatment on Tumor Growth

Time	$y(v_m = 5, h_m = 5)$	$y(v_m = 10, h_m = 10)$	$y(v_m = 15, h_m = 15)$	$y(v_m = 20, h_m = 20)$
0.0	50	50	50	50
0.1	0.0296479	0.0287249	0.0278307	0.0269643
0.2	0.0000295429	0.0000261305	0.0000230811	0.0000203875
0.3	4.83719E-8	3.67803E-8	2.79664E-8	2.12646E-8
0.4	1.26486E-10	7.84225E-11	4.86228E-11	3.01467E-11
0.5	5.17155E-13	2.48408E-13	1.19319E-13	5.73132E-14
0.6	3.23863E-15	1.14825E-15	4.07107E-16	1.44339E-16
0.7	3.04813E-17	7.62006E-18	1.90494E-18	4.76219E-19
0.8	4.23739E-19	7.15254E-20	1.20732E-20	2.03791E-21
0.9	8.56383E-21	9.36808E-22	1.02479E-22	1.12103E-23
1.0	2.48005E-22	1.69115E-23	1.15319E-24	7.86361E-26

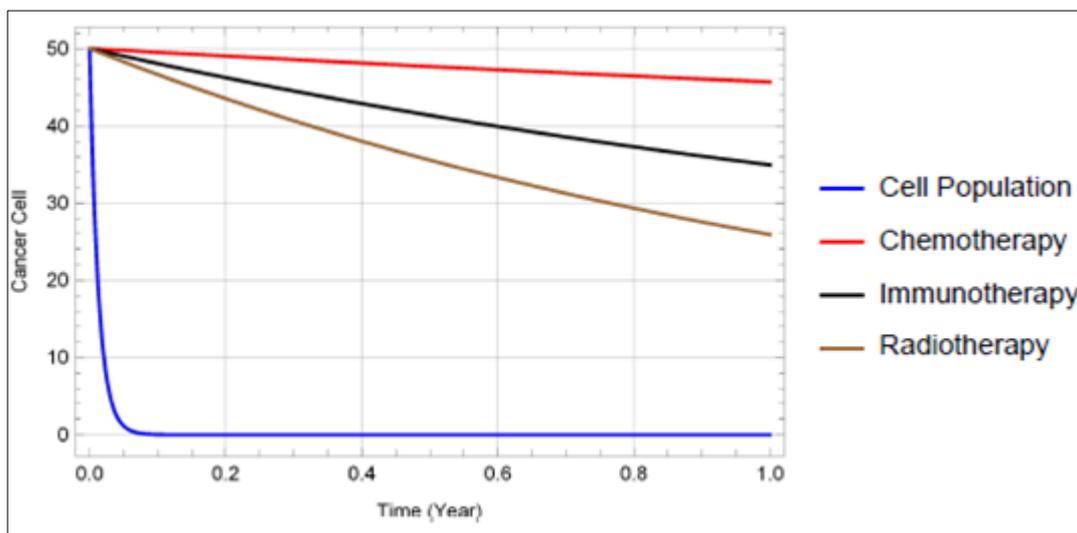


**Fig 5:** Effect of Radio-Immunotherapeutic Treatment on Tumor Growth with other parameters

$$\gamma_1 = 20, \alpha_1 = 0.35, \alpha_2 = 0.54, \alpha_3 = 0.65, \alpha_4 = 0.75, v_m = 5, d_4 = 0.3, d_5 = 0.6, d_6 = 0.8$$

**Table 5:** Effect of Radio-Immunotherapeutic Treatment on Tumor Growth

Time	$y(v_I = 5, h_m = 5)$	$y(v_I = 10, h_m = 10)$	$y(v_I = 15, h_m = 15)$	$y(v_I = 20, h_m = 20)$
0.0	50	50	50	50
0.1	0.0296479	0.0286513	0.0276883	0.0267577
0.2	0.0000295829	0.0000258824	0.0000226449	0.0000198123
0.3	4.83719E-8	3.60548E-8	2.68741E-8	2.0031E-8
0.4	1.26486E-10	7.58937E-11	4.55376E-11	2.73234E-11
0.5	5.17155E-13	2.36942E-13	1.08558E-13	4.97373E-14
0.6	3.23863E-15	1.07859E-15	3.59211E-16	1.19631E-16
0.7	3.04813E-17	7.04804E-18	1.62968E-18	3.76823E-19
0.8	4.23739E-19	6.51762E-20	1.00249E-20	1.54195E-21
0.9	8.56383E-21	8.41949E-22	8.27759E-23	8.13808E-24
1.0	2.48005E-22	1.50158E-23	9.09146E-25	5.50452E-26



**Fig 6:** Effect of Chemo-immunotherapeutic Treatment on Tumor Growth with other parameters values

$$\gamma_1 = 20, \alpha_1 = 0.35, \alpha_2 = 0.54, \alpha_3 = 0.65, \alpha_4 = 0.75, h_m = 5, d_4 = 0.3, d_5 = 0.6, d_6 = 0.8$$

**Table 6:** Effect of Chemo-immunotherapeutic Treatment of Tumor Growth

Time	$y(v_m = 5, v_l = 5)$	$y(v_m = 10, v_l = 10)$	$y(v_m = 15, v_l = 15)$	$y(v_m = 20, v_l = 20)$
0.0	50	50	50	50
0.1	0.0296479	0.0287919	0.0279607	0.0271534
0.2	0.0000295829	0.0000263583	0.0000234852	0.0000209253
0.3	4.83719E-8	3.74545E-8	2.90012E-8	2.24557E-8
0.4	1.26486E-10	8.08119E-11	5.16309E-11	3.29871E-11
0.5	5.17155E-13	2.59461E-13	1.30174E-13	6.53091E-14
0.6	3.23863E-15	1.21696E-15	4.57289E-16	1.71833E-16
0.7	3.04813E-17	8.19911E-18	2.20546E-18	5.93242E-19
0.8	4.23739E-19	7.81389E-20	1.44091E-20	2.65708E-21
0.9	8.56383E-21	1.03875E-21	1.25995E-22	1.52826E-23
1.0	2.48005E-22	1.90195E-23	1.45861E-24	1.1186E-25

**6. Discussion of Results**

Having solved the proposed models and presented the results analytically, in tabular form and graphically, we shall discuss each of the results as follows:

In view of the simulation results presented in section 5, it is noticed that chemotherapeutic dosage increase decreases the tumor size thereby reducing the cells proliferation as seen in Fig 1. But we Table I illustrated that the size of the tumor increases as we increases the dosage of the chemotherapeutic drug. The result is of the view that such drug must have been due to malfunctioning or blood-drug reaction. However, in a tumor size tends to decrease for every dosage of the chemotherapeutic drug dose before decreasing as clearly seen in Table I.

Fig 2 showed the effect of radiotherapy dosage in treating the tumor growth, it can be seen that there is a decrease in tumor/cells death for the radiotherapy dose of 5 gray (Gy). However, we noticed a slight increase in tumor growth which is the result of the effect of radiotherapy effect on the normal cells from 0.0296479 to 0.0305819 for the radiotherapy dosage from 5 to 20 grays as depicted in Table II. Fig 3 showed a decrease in tumor size for every increase in the immunotherapeutic drug dose. It is seen in Table 3 that there is a sharp drop in tumor side from the initial size of 50 units to 0.0000295829 for the dose of 5. However, it is seen that there is an increase in size of the tumor, for a decrease in the immunotherapeutic drug is increased as depicted in Fig 3.

Fig 4 depicts the combined effect of chemotherapeutic drug and radiotherapy dose, which showed that the tumor size decreases for an increase in chemotherapeutic and immunotherapeutic drugs of 5. The resulting decrease in tumor size was confirmed in Table IV, the table show that the tumor size decreases from 0.0296479 to 0.0269643 after the stable initial sizes. Fig 5 also indicates a decrease in tumor size for an increase in steady supply of immunotherapeutic drug and radiotherapy from 5 to 20 gray (Gy). The study also investigates the chemo-immunotherapeutic drug effect on tumor size as indicted using Fig 6 and Table VI. The Table 6 indicates a decrease on the vertical for every dose and decrease in tumor size for an increase in chemo-immunotherapeutic drug.

**7. Conclusion**

In this study, we have been able to formulate a mathematical model representing tumor growth as well as the application of therapeutic treatment in treating and to cure the tumor size. We shall conclude as:

- a) Increase in chemotherapeutic drug could result to a slight increase in tumor size, and this is an indication that there is high level of tumor cell proliferation.
- b) Application of radiotherapy in gray (Gy) increase could cause an increase in tumor size and which showed a case of drug reaction and hence such drug has to stop forthwith.
- c) Immunotherapeutic drug results to a decrease in tumor size, that is a clear indication that immunotherapeutic drug is effectiveness in killing tumor cell and reducing the tumor size.
- d) The combined therapeutic treatment is more effective because it helps in reducing the tumor size, thereby inhibiting cell proliferation.

**Definition of Parameters**

- $\gamma_1$  Tumor causing agent or substance in the body
- $\alpha_1$  Tumor Growth rate and Proliferation
- $d_4$  Fading rate of chemotherapy drug from the body
- $d_5$  Fading rate of immunotherapy drug from the body
- $\alpha_2$  Elimination rate of tumor cells by interacting with chemotherapeutic drugs
- $\alpha_3$  Elimination rate of tumor cells by interacting with immunotherapeutic drugs
- $\alpha_4$  Elimination rate of tumor cells by coming in contact with radiation treatment
- $v_M$  Steady supply of chemotherapeutic drugs into the body
- $v_l$  Steady supply of immunotherapeutic drugs into the body
- $h_m$  Steady exposure to radiotherapy treatment
- $R_d$  Radiotherapy
- $y$  Proliferating tumor cell
- $M$  Chemotherapeutic drug
- $I$  Immunotherapeutic drug
- $I$  Immunotherapeutic drug
- $y_0 = 50$  Initial concentration of proliferating cells at  $t = 0$

$M_0 = 50$  Initial concentration of chemotherapeutic drug at  $t = 0$

$I_0 = 50$  Initial concentration of immunotherapeutic drug at  $t = 0$

$R_{d_0} = 50$  Initial Dosage of Radiation exposure at  $t = 0$

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