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Mathematical models of tumor growth

Sara Medojević
University of Donja Gorica, Podgorica, Montenegro
sara.medojevic@udg.edu.me

***Abstract* —Cancer is one of the deadliest diseases, therefore it is necessary to develop tools that will be useful in the decision-making process. One of those are mathematical models that are used to predict the growth of tumors and the changes that occur as a result of radiation. The determination of the most suitable model is based on the type of tumor. The models presented in this paper are based on ordinary differential equations. Gompertz model is presented as a model that originated from the generalized two-parameter model. Although the Gompertz model is used for determining tumor volume, in this paper it is shown how it can be used to determine the maximum volume of a tumor. The second model presented in this paper is the kinetic model. Kinetic model is used for showing changes in cancer volume before, during and after the active radiation effect. In addition, it can be used for comparing the affect of different radiation doses. The Gompertz model is applied to a benign tumor (meningioma), while the kinetic model is applied to a malignant tumor (hepatocellular carcinoma). As observing the volume at a certain time span implies solving a system of ordinary differential equations, proposed models are written in the form of codes in MATLAB.**

***Keywords*:** mathematical models, Gompertz model, kinetic model, tumor growth, radiation

1 INTRODUCTION

Cancer is one of the most common causes of death in the world, which makes it one of the deadliest diseases. Statistics from the World Cancer Research Fund from 2020 show that 18.1 million people have cancer [9]. Which method of treatment is the most effective and how mathematical modeling can be helpful, it is necessary to understand what tumors are and how they develop.

A neoplasm is any abnormal growth of cells. The term tumor is usually used as a synonym for neoplasm. Tumors can be benign or malignant, which is one of the key factors that determine the way to fight the disease.

A stems tumor from a single cell that begins to abnormally expand (proliferation process). What characterizes a benign tumor is that it remains confined to its original location. It is usually enclosed in a fibrous capsule and does not spread to other tissues and organs in the body. As benign tumors remain localized at the place of origin, they can usually be removed by surgery and are not life-threatening. The fact that tumors originate from a single cell does not mean that they will remain benign. Normal cells mutate into cancerous cells through a series of changes that lead to abnormal cell growth, culminating in malignancy. Only malignant tumors are considered cancers and their ability to invade normal tissues and spread throughout the body (metastasize) is what makes them so dangerous [4].

When making a decision on how to treat cancer, it is necessary to consider the type and stage of the cancer, location, volume and the rate of cell proliferation. While most benign tumors are usually removed by surgery, the removal of malignant tumors usually involves a combination of chemotherapy and radiotherapy. Radiation works by making small breaks in the DNA inside the cell. These interruptions prevent cancer cells from growing and dividing further [1]. Cancer cells then either lose the ability to proliferate or die. Although radiation is an effective method of cancer treatment, in addition to affecting cancer cells, it significantly endangers healthy cells and the immune system. Weakening of the immune system reduces the body's ability to defend itself. Also, the immune system has a role to identify and remove dead cells by breaking them down and eliminating them from the body. It is extremely important to see the impact of cancer on the surrounding tissues, the speed of growth as early as possible and accordingly make a decision on the method of treatment that kills the cancer the fastest and with the least severe consequences to the body. This problem can be solved by mathematical modeling.

Mathematical tumor modeling refers to the use of mathematical equations (most often differential and logarithmic), probability theory and computer simulations to understand tumor growth and spread. Due to its complexity and the individuality of each case, there are different models that monitor tumor growth. Thus, in the case of benign tumors, the rate of tumor growth and its dependence in relation to the developed new blood vessels (tumor vasculature) are most often monitored, while in the case of malignant tumors, the ratio of the volume of the tumor in relation to the amount of radiation, the number of proliferating, dead, removed cells, etc. is additionally monitored.

In the Section 2, Gompertz and kinetic models are presented. Kinetic model observes the tumor volume in relation to one dose of Gy (Gray) radiation.

In Section 3, the implementation of the proposed models in MATLAB will be presented, as well as their application to a benign tumor (meningioma) and a malignant tumor (hepatocellular carcinoma).

2 MATHEMATICAL MODELS

Mathematical models can be divided into two groups: two-parameter and multi-parameter. Two-parameter

models are usually applied on benign tumors, while multi-parameter models are usually applied on malignant tumors. In the following, the models derived from the generalized two-parameter model will be presented [6].

2.1 Gompertz model

One of the simplest model for modeling tumor growth is the logistic model. Tumor growth can be represented by a sigmoid curve, i.e. growing curve with one inflection point that converges asymptotically towards the maximum volume of the tumor K. What makes this model suitable for representing tumor growth is its characteristic that the growth coefficient (as the function approaches an asymptote) decreases, which is consistent with the general growth patterns of organs and organisms. Tumors whose volume is less than $1mm^3$ can grow without developing vascular structures. All tumors larger than $1mm^3$ develop new blood vessels so that nutrients can reach the tumor, allowing it to continue growing.

The tumor is usually not detected in the stages when its volume is less than $1mm^3$ (if we exclude controlled and experimental conditions), therefore $V_0 = 1$ can be taken for the volume at the initial moment $t = 0$.

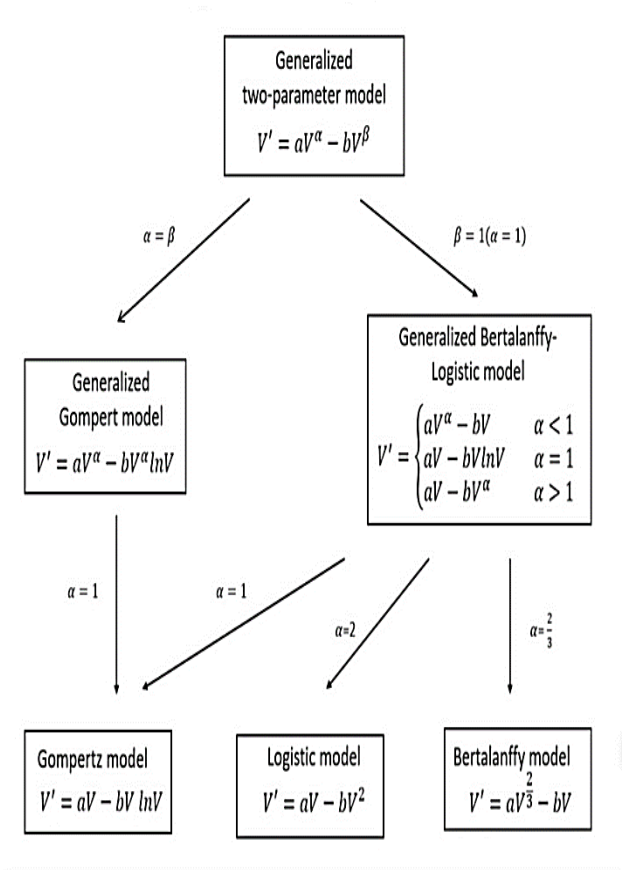

Figure 1: Mathematical models originated from the generalized two-parameter model

As stated in [3], the logistic model describes tumor volume as

$$\frac{dV}{dt} = aV\left(1 - \frac{V}{k}\right) \qquad (1)$$
$$V(t=0) = V_0$$

where a is the coefficient that depends on cell proliferation and V_0 is the initial volume. It is noticed that the expression $1 - \frac{V}{k}$ describes the probability that a cell will divide at a specific time (V depends on t).

Model (1) can be expanded to generalized logistic model where a is a coefficient that depends on cell proliferation.

$$\frac{dV}{dt} = aV\left(1 - \left(\frac{V}{k}\right)^{V}\right) \qquad (2)$$

In order to solve problem (2), Cauchy's problem needs to be solved. Cauchy's problem has an explicit solution

$$V(t) = \frac{V_0 K}{(V_0^{v} + (K^{v} + V_0^{v})e^{-avt})^{\frac{1}{v}}} \qquad (3)$$

It can be noticed that the solution of equation (2) is gotten when $v = 1$ is inserted in equation (3).

By transforming the generalized logical model, the Gompertz model is obtained.

$$\frac{dV}{dt} = ae^{-\beta t}V \qquad (4)$$
$$V(t=0) = V_0$$

where a represents the initial cell proliferation and β is the decreased proliferation cell rate [7].

An essential characteristic of the Gompertz model is that it shows an exponential decline in the relative growth rate. The solution to the previous problem (4) is

$$V(t) = V_0 e^{\frac{a}{\beta}(1 - e^{-\beta t})}$$

indicating that maximum volume of the tumor is

$$K = V_0 e^{\frac{a}{\beta}}$$

2.2 Kinetic model

The kinetic model of tumor volume is applied to malignant tumors. This model shows what effect radiation has on malignant cells and how it affects the total volume of the cancer. Since a large dose of radiation cannot be given at once, it must be divided into lumps of smaller doses. This is why radiation treatments can last from a few days to 7 weeks, depending on the type and stage of the cancer. As stated in [8], this model observes the behavior of tumors after a single treatment with a lower dose of radiation. Cancer consists of dividing and non-dividing cells.

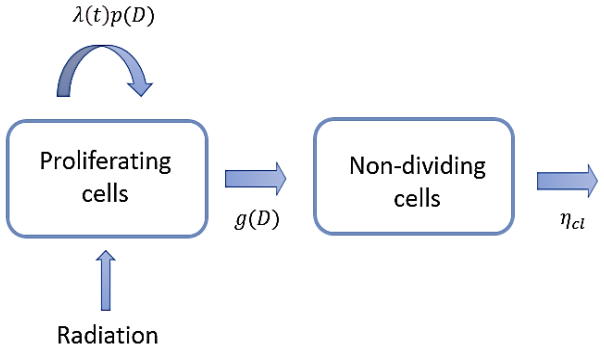

Figure 2: The effect of radiation on dividing cells

Figure 2 illustrates the effect of radiation on dividing cells. When dividing cells are exposed to radiation D, a certain number of cells continue to divide at a tumor growth rate $\lambda(t)$ per time t with a cell proliferation probability $p(D)$, while others stop dividing with probability$g(D)$.

Cells that do not divide are later removed from the organism at the cell removal rate η_{cl}. Cancer consists of dividing and non-dividing cells, therefore the total volume of cancer is obtained as the sum of the volume of the part of the dividing tumor cells $V_T(t)$ and the volume of the part of the non- dividing tumor cells $V_{ND}(t)$.

$$V = V_T(t) + V_{ND}(t)$$

This model belongs to the group of models based on ordinary differential equations (ODE). Then the volume of proliferating cells, as well as the tumor growth rate at time t can be obtained as

$$\frac{dV_T}{dt} = \lambda(t)V_T$$

$$\frac{d\lambda}{dt} = -\theta\lambda(0)\lambda$$

where θ is the retardation factor of the vascular structure, and λ(0) is the initial tumor growth rate.

Tumor behavior can be observed during and after the active effect of radiation. Let t_R be the initial moment of radiation and t_{rad} be the time period of active radiation effect.

Let $t_R \le t \le t_R + t_{rad}$, then

$$\frac{dV_T}{dt} = \lambda(t)p(D)V_T - g(D)V_T$$

represents the volume of proliferating cells,

$$\frac{dV_{ND}}{dt} = g(D)V_T - \eta_{cl}V_{ND}$$

represents the volume of non-dividing cells,

$$\frac{d\lambda}{dt} = -\theta\lambda(0)\lambda$$

tumor growth rate.

Let $t > t_R + t_{rad}$, then

$$\frac{dV_T}{dt} = \lambda(t)V_T$$

represents the volume of proliferating cells,

$$\frac{dV_{ND}}{dt} = -\eta_{cl}V_{ND}$$

represents the volume of non-dividing cells,

$$\frac{d\lambda}{dt} = -\theta\lambda(0)\lambda$$

tumor growth rate.

There is constant χ(D) that depends on the radiation dose D with parameters α, β chosen so that the function best fits the data obtained

$$\chi(\mathrm{D}) = \alpha D\left(1 + \frac{D}{\alpha/\beta}\right)$$

or

$$\chi(\mathrm{D}) = \alpha D + \beta D^2$$

When radiation affects tumor cells, the cells either die or survive. The rate of surviving cells is defined as

$$S(D) = e^{-\chi(\mathrm{D})} = e^{-(\alpha D + \beta D^2)}$$

Then the tumor volume of dividing cells and non-dividing cells can be observed in the time before radiation t_- and in the time after radiation t_+

$$V_T(t_+) = S(D)V_T(t_-)$$

$$V_{ND}(t_+) = (1 - S(D))V_T(t_-)$$

Each individual cell will continue to divide with probability p or will not divide with probability $q = 1 - p$. Then the number of dividing cells N_D and the number of non-dividing cells N_{ND} at time T^* is obtained as

$$\frac{dN_D}{dt} = \frac{2p-q}{T^*}N_D \qquad (5)$$

$$\frac{dN_{ND}}{dt} = \frac{q}{T^*}N_D \qquad (6)$$

where initial condition values are $N_D(0)=N_0$ and $N_{Nd}(0)=0$.

The solutions of equations (5,6) is found as

$$N_D(t) = N_0 \exp\left(\frac{2p-q}{T^*}t\right)$$

$$N_{ND}(t) = \frac{q}{2p-q} N_0 \exp\left(\frac{2p-q}{T^*} t - 1\right)$$

Also, connection can be made between the number of dividing cells at time T_m before radiation and time T^* after radiation as

$$\exp\left(\frac{2p-q}{T^*} T_m\right) \exp\left(-\frac{2}{T^*} T_m\right) = S(D) = e^{-\chi(D)} \quad (7)$$

The solutions of equations (7) is found as

$$p(D) = 1 - \frac{T^*}{3T_m} \chi(D) \quad (8)$$

$$g(D) = \frac{\chi(D)}{3T_m} \quad (9)$$

As the period of cancer death cells lasts t_{rad} time, the number of proliferating cells that will die in t_{rad} time can be approximated to the survival fraction by $S(D)$

$$\int_{t_-}^{t_-+t_{rad}} g(D) N_D(t) dt \approx (1 - S(D)) N_D(t_-)$$

3 DESCRIPTION OF THE MODEL IN THE MATLAB ENVIRONMENT

The following mathematical models will be presented in MATLAB.

3.1 Gompertz model

The Gompertz model of tumor growth begins by defining the initial parameters: V_0 which represents the initial volume of the tumor in mm^3, a which represents the initial cell proliferation rate in mm^3/day and b which represents the decrease proliferation cell rate in mm^3/day.

```
% Gompertz model

% Parameters are defined
V0 = 2162; % Initial tumor volume
a = 0.0005; % Initial cell proliferation rate
b = 0.001; % Decrease proliferation cell rate

% Time span is defined
tspan = [0,3650];

% ODE function is defined
dVdt = @(t,V) a * V * exp(-b * t);

% The system of ODEs is solved
[t,V] = ode45(dVdt, tspan, V0);

% Tumor volume is ploted
plot(t,V);
xlabel('Time (day)');
ylabel('Tumor volume (mm^3)');
title('Gompertz model of tumor growth')
```

Figure 3: Code for the Gompretz model in MATLAB

Then, the time period for which the growth of the tumor is monitored is defined, as well as the ODE (equation (4)). By solving equation (4), the volume of the tumor is determined. As the tumor volume is observed in a certain time interval, it is necessary to solve the system of ODE equations. It is best to use the $ode45$ function, since it is a first-order ODE system. Finally, the obtained results are presented in a coordinate system in which the x-axis represents the time moments in which the tumor volume is observed and the y-axis represents the volume of the tumor.

3.2 Implementation on the benign tumor

The growth of a benign tumor (type of meningioma) located in the middle cranial fossa will be shown in the following section.

The MRI image shows that the initial volume is $V_0 = 2162$, $a = 0.0005$ is the initial rate of tumor proliferation and $b = 0.001$ is decrease proliferation cell rate[1].

In the Figure 5 tumor growth for $t = [0,3650]$ is shown. The model shows that the volume has logarithmic growth and that volume of the tumor after 10 years will be $V = 3518.51\ mm^3$.

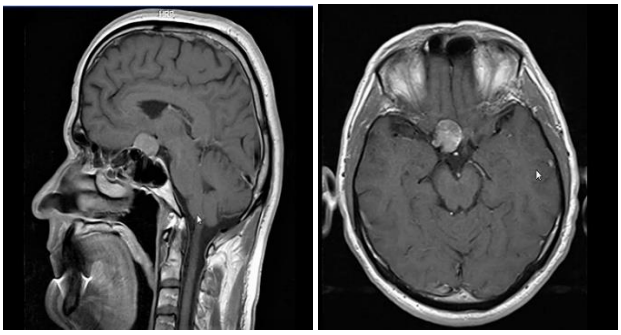

Figure 4: MRI image of a benign tumor

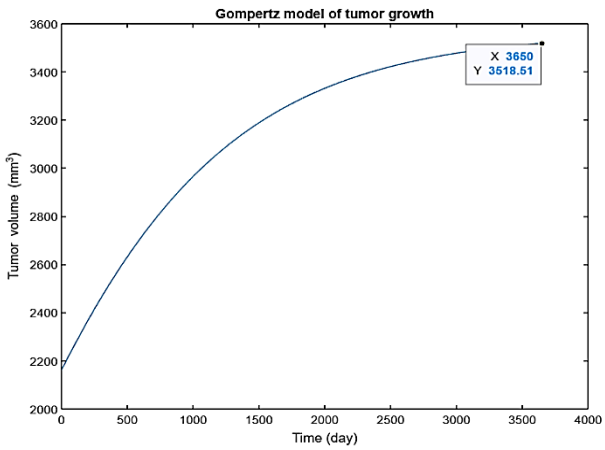

Figure 5: Graphic representation of tumor growth for $t = 3650$

[1] The parameters a and b were not obtained from the MRI scaning. Based on the history of the disease and research on meningioma type tumors, it is assumed that the parameters and a and b have the given values.

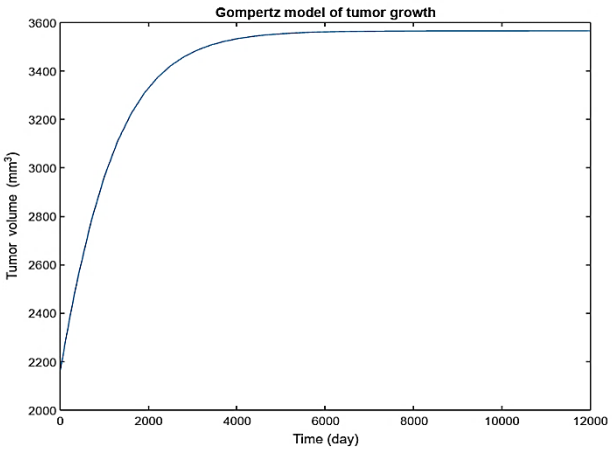

Figure 6: Graphic representation of tumor growth when $t \to \infty$

The tumor grows to its maximum size K which is determined by the growth rate, the location of the tumor and the tumor vasculature.

As the capacity K is on the asymptote of the function, from the graph in the Figure 6 it can be seen that $V \to 3564\, mm^3$, which if compared with the value obtained using the formula

$$K = V_0 e^{\frac{a}{\beta}} = 2162 * e^{\frac{0.0005}{0.001}} = 3564.54\, mm^3$$

is a good approximation of the proposed tumor growth over time.

In observing the growth of a tumor, we have to pay attention to the time it takes for the tumor to reach its double volume compared to the initial observation. This information can be important when making a decision about the method of treatment. The time it takes for a tumor to double its volume can indicate how fast the tumor is growing. As the observed tumor is located in the middle cranial fossa, due to its location and the insufficient amount of nutrients available to the tumor, regardless of the passage of time, the tumor will not reach its double volume, which can be concluded from the graph presented in the Figure 6.

3.3 Kinetic model

Kinetic model for monitoring tumor growth begins by setting the initial parameters: D which represents the radiation dose, $theta$ which represents the vascular growth retardation factor, $lambda0$ which represents the cancer growth rate at the initial moment, TR which represents radiation start time, $trad$ representing the radiation time, $Tstar$ representing the time instant after radiation, Tm represents the time instant before radiation.

The proposed mathematical models can make predictions whether the predictions are made on a smaller or larger sample of data. A large sample would imply that the parameters at moments $t_{i_1}, t_{i_2}, t_{i_3}, \dots, t_{i_k}$ are known where $0 \le i_1 < i_2 < \dots < i_k < \infty$. Due to the uniqueness of each individual sample, what can happen is that the predictions of the proposed model do not match the input data. In order to reduce the approximation error, the parameters $alpha$ and $beta$ are introduced. The parameters $alpha$ and $beta$ represent the parameters taken to fit the model to the data obtained from the MRI scans.

```
% Parameters are defined
D = 6; % Radiation dose
theta = 0.2; % Vascular growth retardation factor
lambda_0 = 0.1; % Initial tumor growth rate
TR = 2; % Time of radiation
trad = 1; % Active radiation-effect time
Tstar = 5; % Time instant after trad
Tm = 1; % Time instant before TR
alpha = 0.01; % Parameter alpha
beta = 0.01; % Parameter beta

% Functions for p(D) and g(D) are defined
chi = alpha*D + beta*D^2;
p = @(D) 1 - (Tstar/(3*Tm))*chi;
g = @(D) chi/(3*Tm);

% ODEs are defined
ode_fun = @(t, y) tumor_volume_ode(t, y, D, ...
    lambda_0, theta, p, g, TR, trad);

% Initial conditions are set
VT0 = 67759.26; % Initial volume of proliferating
                % tumor
VND0 = 0; % Initial volume of non-dividing cells
lambda0 = lambda_0;

% ODEs are solved
tspan = [0 TR+trad+5]; % Time interval
y0 = [VT0; VND0; lambda0]; % Initial conditions
[t, y] = ode45(ode_fun, tspan, y0);
% The results are ploted
figure;
subplot(2,2,1);
plot(t, y(:,1));
xlabel('Time (days)');
ylabel('VT(t)');
title('Proliferating tumor volume');

subplot(2,2,2);
plot(t, y(:,2));
xlabel('Time (days)');
ylabel('VND(t)');
title('Non-dividing tumor volume');

subplot(2,2,3);
plot(t, y(:,3));
xlabel('Time (days)');
ylabel('lambda(t)');
title('Tumor growth rate');

subplot(2,2,4);
plot(t, p(D)*y(:,1));
hold on;
plot(t, g(D)*y(:,1));
xlabel('Time (days)');
ylabel('Cell transition rate');
legend('Dividing cells', 'Non-dividing cells');
```

Figure 7: The first part of the kinetic model code in MATLAB

```
function dydt = tumor_volume_ode(t, y, D, ...
    lambda0, theta, p, g, TR, trad)
    VT = y(1); % Proliferating tumor volume
    VND = y(2); % Non-dividing tumor volume
    lambda = y(3); % tumor growth rate

    if t >= TR && t < TR + trad
        dp = p(D);
        dg = g(D);
    else
        dp = 0;
        dg = 0;
    end

    dVTdt = lambda*p(D)*VT - g(D)*VT;
    dVNDdt = g(D)*VT - theta*VND;
    dlambda_dt = -theta*lambda0*lambda;

    dydt = [dVTdt; dVNDdt; dlambda_dt];
end
```

Figure 8: The second part of the kinetic model code in MATLAB

Then, the functions $p(D)$ and $g(D)$ (equations (8) and (9)) are defined and the initial conditions are set.

$VT0$ represents the total initial volume of dividing cells, and $VND0$ represents the total initial volume of non-dividing cells. After setting the time interval on which the cancer behavior is observed, the ODE system is solved using the $ode45$ function.

As shown in Section 2.2, two cases are considered: when $t_R \leq t \leq t_R + t_{rad}$ and when $t > t_R + t_{rad}$. It can be noticed that when $t > t_R + t_{rad}$ probability is $p(D) = 0$ and $g(D) = 0$. Therefore, it is necessary to create a function that takes one value of the functions for $p(D)$ and $g(D)$ when $t > t_R + t_{rad}$ and the other in other cases .

Making a decision on what amount of radiation is the most suitable for a patient is extremely important. In order to make the best possible decision, it is necessary to create a model that compares the effects of different amounts of radiation on cancer. Having this information available allows doctors to make a decision at what time and for what amount to irradiate patient. These models are the most suitable when working with a large database, but they can also be used on a smaller database. In order for the model to make better predictions, what needs to be done is to monitor changes in tumor volume and enter new data. This would reduce the error made by the model.

The code presented in Figure 7 and 8 calculates the influence of one dose of irradiation on tumor volume, while the following code compares different doses of radiation on tumor volume.

As these codes are built on the same mathematical model, values of parameters $theta, lambda, TR, trad, Tstar, Tm, alpha, beta, VT0, VND0, lambda0$ as well as the definition of functions $p(D), g(D), VT, VND$ the only difference is that for the value of D is taken a list of values.

The code starts by setting the initial conditions. As the tumor volume must be calculated for each radiation dose D at each time instant t, a function must be created that will solve those systems of equations. A for loop is used so that the function can take each value from list D. Then the functions p(D) and g(D) are defined and solved so that the function takes one value when $t_R \leq t \leq t_R + t_{rad}$ and another when $t > t_R + t_{rad}$. Then the obtained data are presented on the same graph. Time t is represented on the x-axis and tumor volume is represented on the y-axis.

```
% Parameters are defined
Tm = 1; % Time instant before TR
TR = 2; % Time of radiation
trad = 1; % Active radiation-effect time
Tstar = 5; % Time instant after trad
theta = 0.2; % Vascular growth retardation factor
alpha = 0.01; % Parameter alpha
beta = 0.01; % Parameter beta
eta_cl = 0.1; % Cell removal rate
VT0 = 67759.26; % Initial volume of non-dividing cells
D_values = [5, 5.5, 6, 6.5]; % Radiation doses

% Time interval and initial conditions are set
tspan = [0 ,20];
VT_init = VT0;
VND_init = 0;
lambda_init = 0.1;

% ODEs are solved for each radiation dose
for i = 1:length(D_values)
    D = D_values(i);

    % Functions for p(D) and g(D) are defined
    chi = @(D) alpha*D + beta*D^2;
    p = @(D) 1 - (Tstar/(3*Tm))*chi(D);
    g = @(D) chi(D)/(3*Tm);

    % ODEs for TR <= t < TR + trad are defined
    ode1 = @(t, y) [y(1)*lambda_init*p(D) -
        g(D)*y(1); g(D)*y(1) - eta_cl*y(2);
        -theta*lambda_init*y(3)];

   % ODEs for TR <= t < TR + trad are solved
   [t1, y1] = ode45(ode1, [TR, TR+trad], ...
       [VT_init, VND_init, lambda_init]);

   % ODEs for t > TR + trad are defined
   ode2 = @(t, y) [y(1)*y(3); -eta_cl*y(2);
       -theta*lambda_init*y(3)];

   % ODEs for t > TR + trad are solved
   [t2, y2] = ode45(ode2, [TR+trad, tspan(2)], ...
       [y1(end,1), y1(end,2), lambda_init]);

   % Solutions from both time intervals are
   % concatenated
   t = [t1; t2];
   y = [y1; y2];

   % The results are ploted
   plot(t, y(:,1));
   hold on;
end

legend('D = 5', 'D = 5.5', 'D = 6', 'D = 6.5');
xlabel('Time (days)');
ylabel('Tumor volume (mm^3)');
title(['Tumor volume in dependence of different ' ...
    'radiation doses']);
```

Figure 9: Kinetic model code for observing changes in cancer volume in relation to the amount of radiation in MATLAB

3.4 Implementation on the malignant tumor

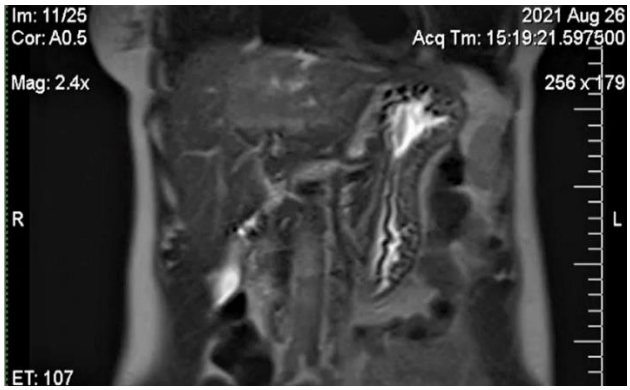

Figure 10: MRI image of a malignant tumor

The growth of a malignant tumor (type of hepatocellular carcinoma) located in the left lobe of the liver will be shown in the following section.

The MRI scan shows that the cancer volume is $V_T = 67759.26\, mm^3$, as this value is taken in initial moment $t = 0$, it is concluded that V_{ND}=0. The parameters are defined as : $D = 6Gy$[2] radiation dose, $\theta = 0.2$ the retardation factor of the vascular structure , $\lambda(0) = 0.01$ rate of cancer growth, $t_R = 2$ radiation start time, $t_{rad} = 1$ radiation time , $T^* = 5$ time instant after radiation, T_m time instant before radiation, $\alpha = 0.01$, $\beta = 0.01$, $\eta_{cl} = 0.1$[3].

At the moment $t = 0$ and $V_T = 67759.26\, mm^3$ as the cancer was not affected by radiation or chemotherapy. Due to the effect of radiation, cells that divide change into cells that do not divide, and then they die and get removed from the body. Therefore, from the Figure 11 it can be seen how the total volume of proliferating cells decreases during the period of active radiation time effect, where as seen on the Figure 12 the total volume of non-dividing cells increases.

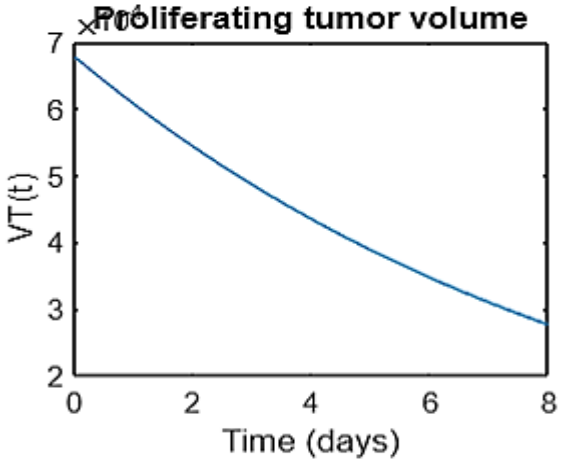

Figure 11: Graphic representation of the total volume of the proliferating cells

As radiation affects the blood vessels that bring nutrients to the cancer, disrupting those connections slows tumor growth. As can be seen from the graph (Figure 13), the tumor growth rate is decreasing.

On the graph shown in Figure 14 it can be seen how the cell transition rate is obtained. The function that describes dividing cells as well as the function that describes non-dividing cells are convex.. The number of dividing cells is decreasing, because the radiation has affected the cells. Although the number of non-dividing cells should be increasing, because dividing cells are transitioning into non-dividing cells, the number of cells that died is greater than the number of non-dividing cells , therefore our function decreases. If it's kept up with the radiations and the graph is plotted as $t \to \infty$, the number of non-dividing cells and the number of dividing cells would approach the x-axis.

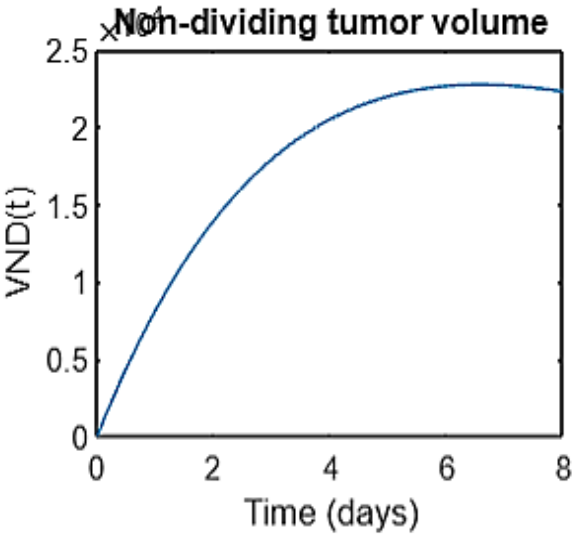

Figure 12: Graphic representation of the total volume of the non-dividing cells

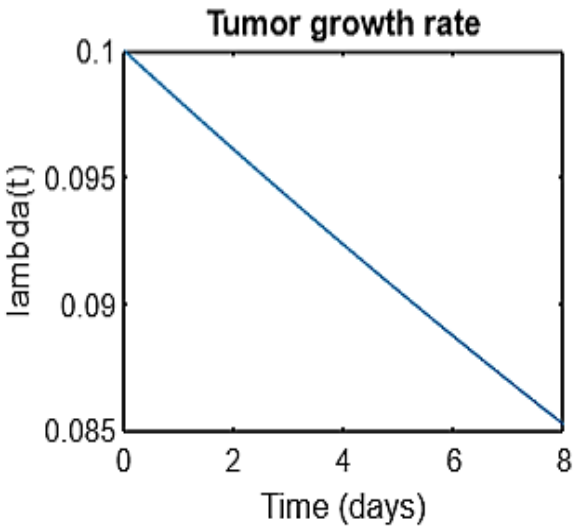

Figure 13: Graphic representation of the growth rate

[2] Gray (Gy) is the SI unit of the absorbed dose of ionizing radiation by the body (the amount of energy absorbed by the body under the influence of radiation) [5].

[3] Note: The parameters are not obtained from the MRI scan. Based on the medical history and research on hepatocellular carcinoma, it is assumed that the parameters have given values [2].

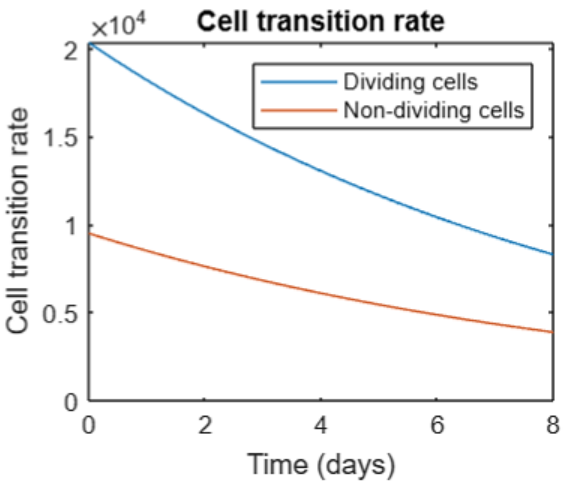

Figure 14: Graphical representation of cell transition rates from dividing to non-dividing cells

The dose of radiation to which a patient is exposed to depends on the type, stage and location of the cancer, the patient's age, previous medical history, etc.

There are two approaches: exposure to lower doses of radiation more times or exposure to higher doses of radiation fewer times.

On the graphic shown in Figure 15 it can be seen that the dose of 6.5 Gy has the greatest impact. For all 4 values, it can be seen that they have the greatest decrease during the active radiation effect, after which the volume is on the rise again. This happens because the cancer was treated with only 1 dose of radiation. For the graph to continue decreasing, multiple exposure to radiation would be necessary as well as chemotherapy.

Of course, higher dose of radiation does not mean a better outcome for the patient. Since radiation affects healthy cells in addition to malignant cells, it must be taken into account not to damage too many healthy structures. If the immune system is damaged, regardless of how much of the tumor is killed, body will not be able to fight the disease.

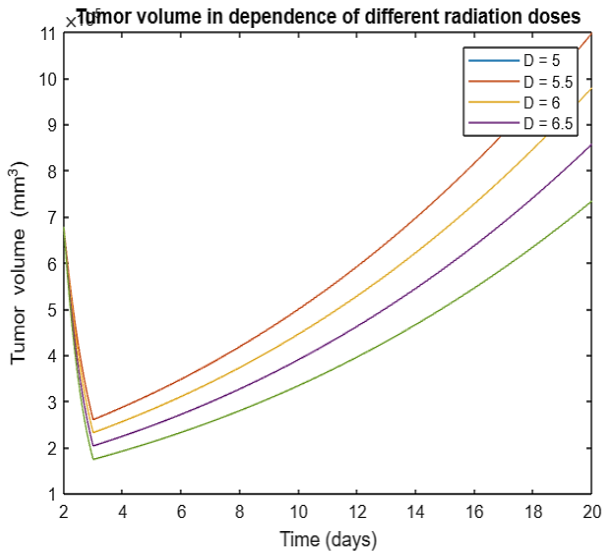

Figure 15: Graphical representation of the tumor volume in dependence of different radiation doses

4 Conclusion

This paper presents mathematical models that help to monitor the growth of benign and malignant tumors. It is shown that the proposed mathematical models can be used to monitor tumor growth, as well as how much influence the initial parameters have on the final outcome. The model can be adapted to follow avascular and vascular growth. Mathematical models of tumor growth are most often used during experimental studies of tumor growth (on animals) and the effect of radiation on them. A larger database improves the accuracy of the obtained data. This paper showed that the proposed models can be used to monitor tumor growth in humans as well. As the models were applied to a smaller sample, the reliability of the obtained results is debatable. In order to ensure the highest possible reliability of the obtained results, it is necessary to increase the sample size and observe tumor growth at shorter time intervals. Also, it would be desirable to introduce a confidence interval estimation that would describe the reliability of each obtained data.

5 Summary

As cancer is one of the deadliest diseases, models have been developed that are used to predict tumor growth. Those are mathematical models which connect mathematical equations, probability and computer science. In this paper Gomperz and kinetic models are presented. Although these models are usually used in animal experiments and with larger database, in the paper it is shown that it can be used on humans and with smaller database. The Gomperz model was implemented on a benign tumor. It is shown how it will grow throughout time and its maximum volume. Two codes were written for a kinetic model that were implemented on a malignant tumor. It was shown what affect one dose of irradiation has on the tumor as well as how different doses of radiation affect the tumor. In order to improve the reliability of the data, it is necessary to work on a larger data base, shorter observation intervals and it would be desirable to introduce a confidence interval estimation that would describe the reliability of each obtained data.

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