Faculty of Natural and Applied Sciences Journal of Scientific Innovations
Print ISSN: 2814-0877 e-ISSN: 2814-0923
www.fnasjournals.com
Volume 3; Issue 2; March 2022; Page No. 35-42

MATHEMATICAL MODELING OF THE IMPACT OF RADIATION AND OXIDATIVE STRESS ON CANCER DEVELOPMENT

***[1]Nkuturum, C., & [2]Akpan, A.U.**
[1-2]Department of Mathematics, Faculty of Natural and Applied Sciences, Ignatius Ajuru University of Education Port Harcourt, Rivers State, NIGERIA

Corresponding author (email): christienkuturum245@gmail.com;

Abstract
In this paper, the damage mechanic model of cancer caused by radiation and oxidative stress refers to the application of a mathematical model to investigate how the various state variables such as irradiation, stress-strain constitutive relationship trigger cellular damage through initiation, growth, and coalescence of tumor (cancer) with the view to providing requisite insight into the study. Three non-linear differential equations were coupled to undertake the study. The solutions to the equations indicate that the Extracellular Matrix density $\rho(x,t)$, Cell density $\rho_c(x,t)$ and Cell displacement $u(x,t)$ are the functions of time and position. Furthermore, the solutions obtained to the model equations indicate the steady-state solutions implying that the secretion surface is activating the growth or proliferation rate of cancer cells in the body of the organisms in this instance we refer to the solid tumor (cancer). The stable solutions indicated the presence of cancer cells which in a steady state grows exponentially and if unchecked defile all medication or treatment protocol employed due to the actions of radiation and oxidative stress. The established results indicated the presence of radiation and oxidative stress in the injured area acting also as the enabler of the cancer cells proliferation rate indicating a compromised immune system of the organism.

Keywords: Mathematical modeling, Radiation, Oxidative stress, Cancer development

Introduction

The application of a mathematical model to investigate how the various state variables such as irradiation, and stress-strains constitutive relationship trigger cellular damage through initiation, growth, and coalescence of tumor (cancer) is studied in detail in this paper with the view to providing requisite insight into existing knowledge on the subject. Mathematical model has become a veritable tool in various fields of human endeavour particularly aiding our understanding of many real-life phenomena is known to many authors. For example, Bradly and Enderling (2019), and Chamseddine and Rejniak, (2019) provided an excellent review of mathematical models used for different treatments of cancer. Moreira and Deutsch, (2002), Araujo and McElwain, (2004), and Lowengrub et al. (2010) reviewed tumor growth models and radiation effects. Hsu (1968) investigated the effect of radiation on the spatiotemporal distribution of oxygen inside tumour. They extended the model of Greenspan, (1972) for tumor growth and hypoxia with a linear quadratic model representing cell death due to radiotherapy. Enderling, Anderson, Chaplain, Munro and Vaidya, (2006) developed a mathematical approach for surgery and radiation treatment in early breast cancer, based on a partial differential equation and a linear-quadratic model. Many mathematical models can incorporate a large volume of quantitative information that can describe the complexity of a cell's biological pathway. Even complex biological processes can be best understood by a computational and mathematical model.

The damage mechanics model involves the formulation of mathematical equations to make engineering predictions about the initiation, propagation, and fracture in a material using state variables, which represent the effects of damage caused from thermal or mechanical loading or aging on the stiffness and remaining life of the material be it measurable variables or other physical variables, Lemaitre (1934). Thus, the damage mechanics model best suits our paper and will be employed in this course of our study.

Cite this article as:
Nkuturum, C., & Akpan, A.U. (2022). Mathematical modeling of the impact of radiation and oxidative stress on cancer development. *FNAS Journal of Scientific Innovations, 3*(2), 35-42.

Globally, cancer has emerged as one of the world's most dangerous diseases of modern times responsible for the majority of deaths before the age of 70. Cancer describes a disease that occurs when cellular changes cause uncontrolled division of cells. These abnormal, uncontrolled cells are termed cancer cells or tumor cells, or malignant cells. Cancerous cells can form tumors, weaken the immune system, and causes other changes that prevent the effective functioning of the body, Humphery (2002). Various cancers exist, prominent amongst which are; breast cancer, lung cancer, prostate cancer, colon or rectal cancer, leg cancer, throat cancer, bone cancer, and a host of others. Several factors are responsible for cancer development in an organism some of which are avoidable like smoking, heavy alcohol consumption, excess body weight, physical activities, poor nutrition, and non-preventable factors like age.

Radiation is the emission of energy as electromagnetic waves or as moving subatomic particles, especially high-energy particles which cause ionization. Radiation can damage all-important cellular components, including DNA and proteins, both through direct ionization and through induction of oxidative stress. Radiogenic damage to DNA, such as double-strand breaks (DSBs) which are typically difficult to repair and contribute in no small measure to clonogenic cell death, has been extensively studied (Barendsen, 1994; Kasten-Pisula et al., 2008; Shuryak & Brenner, 2009). Radiation-induced oxidative stress, which results in the oxidation of protein, lipids, and nucleotides, can have a variety of subtle but profound biological consequences is drawing increasing attention. For instance, oxidative stress triggered by even low doses of radiation can produce an alteration of the cellular redox balance, which last for a substantial period after exposure and may contribute to bystander effects, modified gene expression, genomic instability, change in cell survival, elevated mutagenesis rates, proliferation, and differentiation.

However, some scientists have carried out works on cancer based on the damage mechanics model of cancer under the influence of oxidative stress, Oyesanya and Nkuturum, (2019) but none has been done on the actions of radiation and oxidative stress. Based on the above-mentioned related literature it is observed that the effect of radiation and stress on tumour-cancer in the body of living organisms in damage mechanics has not been modeled, analyzed and solutions proffered to the related equation.

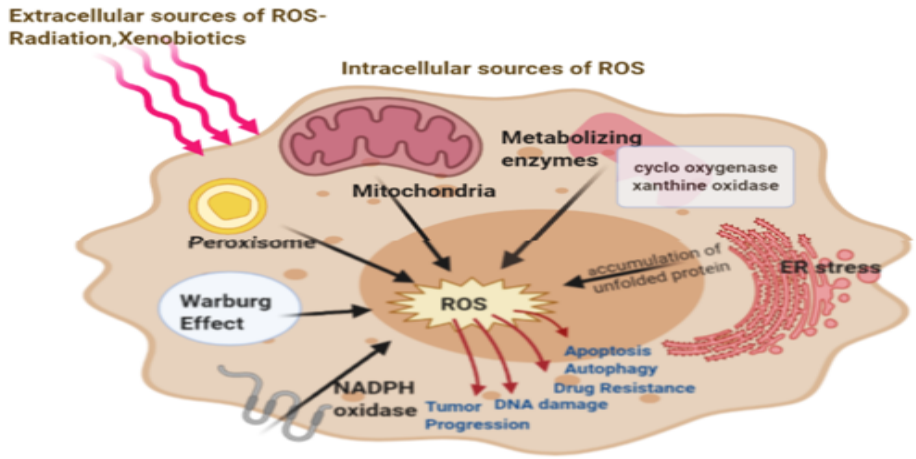

Figure 1. *Major intracellular Sources of ROS-mitochondria, peroxisome, endoplasmic reticulum (ER) stress, nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) oxidase, metabolizing enzymes, and extracellular (Radiations, Xenobiotics) sources of reactive oxygen species (ROS) generation. ROS involved in cancer resulting in the development and progression of the disease*

Cite this article as:
Nkuturum, C., & Akpan, A.U. (2022). Mathematical modeling of the impact of radiation and oxidative stress on cancer development. *FNAS Journal of Scientific Innovations, 3*(2), 35-42.

Description of parameters

N	Maximum number of cancer cell
$\sigma(x,t)$	Stress tensor
x	Position
T	Time
F	Body force
$\rho(x,t)$	Density of the (Extra-Cellular Matrix) ECM
$\rho_c(x,t)$	Cell density
ρ_{ct}	Partial differentiation of cell density w.r.t, t
∇	Laplacian operator
$n(x,t)$	Number of cells per unit volume
$u(x,t)$	Displacement vector of the matrix
D_1, D_2	Diffusion parameters
μ_1, μ_2	Shear and bulk viscosities of the ECM
α_1, α_2	Long range effect for mechanotaxis flux
Λ	Measure of cell-cell contact activation cancer cells
τ	Cell traction force
θ	Dilation
ε_t	Partial differentiation of stain tensor w.r.t. t
θ_t	Partial differentiation of dilation w.r.t t
u_t	Partial differentiation of displacement w.r.t t (velocity of deformation of matrix
n_t	Partial differentiation of cell density w.r.t t
p_t	Partial differentiation of density of the ECM w.r.t t
Φ	Growth factor
γ	Measure of the nonlocal long range cell-ECM interactions
k	Rate of destruction of cells by the cancer cell and radiation
r	Initial proliferative rate in cell growth
I	Unit tensor
S	Elastic parameter for the substrate attachments
Λ	Parameter that controls the activator of cancer cell growth
Ł	Injured area
J	The flux of cells
J_c	Convective flux contribution
J_h	Mechanotactic flux
E	Young's modulus
v	Poisson ratio
ε	Strain
ω	Frequency of radiation
A_1	Amplitude of the radiation term in the sine direction
A_2	Amplitude of the radiation term in the cosine direction

Materials and Methods

We considered a mathematical model developed for studying the effect of radiation and oxidative stress on cancer development specifically how they initiate, grow, proliferate, and coalesce using damage mechanic model in a viscoelastic and thermo elastic constitutive relationship sense noting that cancer is a soft tissue (cell) disease. The parameters to be considered are radiation damage and stress-strain relations coupled with constitutive equations and laws of elasticity coupled with damage, viscoelastic tensor equation, mechanotaxis equation with mitosis M and conservation equation for the matrix materials The model is directed by three non-linear differential equations viz; force balance equation, cell conservation equation and matrix conservation equation respectively. The model is investigated for sensitivity purposes analytically as well as numerically

Cite this article as:
Nkuturum, C., & Akpan, A.U. (2022). Mathematical modeling of the impact of radiation and oxidative stress on cancer development. *FNAS Journal of Scientific Innovations, 3*(2), 35-42.

$$\mu_1 \frac{\partial^2 \varepsilon}{\partial x_i \partial t} + \mu_2 I \frac{\partial^2 \theta}{\partial x_i \partial t} + \frac{\partial \varepsilon}{\partial x_i} + v^t I \frac{\partial \theta}{\partial x_i} + \frac{\frac{\partial \rho}{\partial x_i} + \tau I(\frac{\partial n}{\partial x_i})}{(1+\lambda n^2)} + \frac{\tau(\frac{\partial n}{\partial x_i})\gamma I \frac{\partial \rho}{\partial x_i}}{1+\lambda n^2} - A_1 \omega cos(x-kt) = s\rho u \quad (2.1)$$

$$\frac{\partial \rho_c}{\partial t} = D_1 \frac{\partial^2 n}{\partial x^2} - D_2 I \frac{\partial^4 \theta}{\partial x^4} + \alpha_1 \left(\frac{\partial n}{\partial x} + \frac{\partial^2 \rho}{\partial x^2}\right) + \alpha_2 \left(\frac{\partial n}{\partial x} + \frac{\partial^4 \rho}{\partial x^4}\right) - \nabla \bullet (nu_t) + rn(N-n) - A_2 \omega sin(x-kt) \quad (2.2)$$

$$\frac{\partial \rho}{\partial t} = u_i(\nabla \bullet \rho) + \rho.(\nabla u_t) = 1 - v\theta \quad (2.3)$$

where the dependent variables are the density fields $\rho_c(x,t)$, $\rho(x,t)$ and the displacement field $u(x,t)$ and t is the independent variable.

The parameters involved are$D_1, D_2, \alpha_{1,}\alpha_{2,}\mu_1, \mu_2, r, N, \lambda, \gamma, s, Eandv, A_1, A_2, \omega$. To solve the systems of equations above, we first non-dimensionalise the equations in a standard way for simplicity purposes to evaluate the relative importance of the various effects of the variables used in the study. Thus, rescaling distance with appropriate length scale (L) and timescale (T) and for uniform initial matrix density (ρ_0). Setting $\dot{r} = \frac{r}{L}, \dot{t} = \frac{t}{T}, \dot{n} = \frac{n}{N}, \dot{u} = \frac{u}{L}, \dot{\rho} = \frac{\rho}{\rho_0}, \dot{\nabla} = L\nabla, \dot{\theta} = \theta, \dot{\varepsilon} = \varepsilon, \dot{\gamma} = \frac{\gamma}{L^2}, \dot{r} = rNT,\ \dot{S} = \frac{s\rho_0 L^2(1+v)}{E}, \dot{\lambda} = \lambda N^2, \dot{\tau} = \frac{\tau\rho_0 N(1+v)}{E}, \dot{\alpha_1} = \frac{\alpha_1 \rho_0 T}{L^2}, \dot{\alpha_2} = \frac{\alpha_2 \rho_0 T}{L^4}, i = 1,2, \dot{N} = \frac{N(1+v)}{TE}, \dot{D} = \frac{D_1 T}{L^2}, \dot{D_2} = \frac{D_2 T}{L^4}$ (2.4)

The parameters have been reduced to 12 parameters. Now if T is the mitotic time (time of proliferation rate of cancer cells) is $\frac{1}{rN}$ then $\dot{r} = 1$ since the focus is on the proliferation rate of cancer cells on the time scale. Conversely, if T is such that $\dot{\gamma} = 1\ or \dot{\mu} = 1; i = 1\ or i = 2$ and depending on the timescale or length, a further reduction of the number of parameter groupings are considered. With this non-dimensionalisation in (2.4) depicted above and upon dropping off the asterisks parameters for simplicity equations (2.5), (2.6) and (2.7) are the obvious outcomes that can be solved by the method of traveling wave solution. A traveling wave in this study is a wave that travels without a change of shape. Thus:

$$\{(\mu_1 \varepsilon_t + \mu_2 \theta_t I) + (\varepsilon + v^t \theta I)\frac{\tau n}{1+\lambda n}(\rho + \gamma \nabla^2 \rho)I\} - A_1 \omega cos(x-kt) = s\rho u \quad (2.5)$$

$$\rho_{c,t} = D_1 \nabla^2 n - D_2 \nabla^4 n - \nabla \bullet [\alpha_1 n \nabla \rho - \alpha_2 n \nabla(\nabla^2 \rho)] - \nabla \bullet (nu_t) + rn(N-n) - A_2 \omega sin(x-kt) \quad (2.6)$$

$$\rho_t + \nabla \bullet (\rho u_t) = 1 - v\theta \quad (2.7)$$

Where $A_1, A_2, D_1, D_2, \alpha_{1,}\alpha_{2,} r, \tau, \lambda,$ are associated with cell properties and $\mu_1, \mu_2, v^t, \gamma, \omega, s$ are related to the matrix properties. All dimensionless parameters are positive.

Now let the tumor cells spread in a manner that supports the movement of the cancer cell in a steady state. In this instance, the tumor initiation is positional with time and displacement is from one point to another. Assume a boundary condition set as $u = 1, \rho_c = 1, \rho = 1$ and that the position (x) changes with time which is considered to be constant. Since all cancer initiations are positional which could be any positive real number (or constant) like 1,2,3... then putting $\frac{\partial u}{\partial t} = 1$ as equation (2.7) indicates how densely packed cancer cells are in the matrix. The dense nature illustrates the presence of temperature in the system. Similarly, when displacement u with time t starts with 1 as a constant, then the number of cancer cells n growth changes position in the functional space making n a vector of a function (x,t) in three-dimensional space, where x is the position with components x_1, x_2, x_3 and time t. i.e. $n(x,t)$. This steady movement of cancer cells conforms with the method of travelling wave solution which will is used to solve the model systems of equations in this study. Considering the variables x, a vector with componentsx_1, x_2, x_3 while t is the time variable. The resultant study model is a three-dimensional functional space. Hence from equation (2.7), applying vector calculus and considering the steady-state of soft tissues cells with growing cancer cells, u changing with time, t . By setting $u_t = \frac{\partial u}{\partial t} = 1$, the traveling wave method of solution is employed to solve the systems of equations due to its suitability in describing the cancer cell movement as well as the viscous property. Since there is no convective flux or motion then the quantity $\nabla \bullet (\rho u_t) = 0$ in equation (2.7), this implies that (2.7) reduces to

$$\rho_t = 1 - \theta v \quad (2.8)$$

Integrating (2.8) w.r.t. time using the boundary of integration from 0 to t gives

Cite this article as:
Nkuturum, C., & Akpan, A.U. (2022). Mathematical modeling of the impact of radiation and oxidative stress on cancer development. *FNAS Journal of Scientific Innovations, 3*(2), 35-42.

$$\rho = t - 3vx_i\mathrm{t} + \frac{3}{2}vkt^2 \quad (2.9)$$

Similarly, solving for $\rho_c(x,t)$ in equation (2.6) and upon integration yield

$$\rho_c = 3D_1 t\left(x_i - \frac{kt^2}{2}\right) - 3D_2 t\left(x_i - \frac{kt^2}{2}\right) - 3\alpha_1 v\left(\frac{x_i^2t^2}{2} - \frac{3x_ikt^3}{2.3} + \frac{k^2t^4}{2.4}\right) - 3\alpha_2 v\left(\frac{x_i^2t^2}{2} - \frac{3x_ikt^3}{2.3} + \frac{k^2t^4}{2.4}\right) - 3k\left(\frac{x_i^2t^2}{2} - x_ikt^2 + \frac{kt^3}{3}\right) - 3kt\left(x_i - \frac{kt}{2}\right) + rNt\left(x_i - \frac{kt}{2}\right) - r\left(\frac{x_i^2t^2}{2} - x_ikt^2 + \frac{kt^3}{2}\right) + \frac{\mathrm{A_2\omega}}{\mathrm{k}}\cos(\mathrm{x_i - kt}) \quad (2.10)$$

In the same vein, solving for $u(x,t)$. in equation (2.7)

$$u(x,t) = \frac{-3k\left(x_i^2 - 2x_ikt + k^2t^2\right)(\mu_1+\mu_2 I) + 3(x_i - kt)(I + vI) - \frac{27\tau vtI\left(x_i - \frac{3x_ikt}{2} + \frac{k^2t^2}{2}\right)}{1+\lambda\left(x_i - 2x_ikt + k^2t^2\right)}(1+\gamma) - kA_1\omega\cos(x_i - kt)}{s\left(t - 3x_ivt - \frac{3vkt^2}{2}\right)} \quad (2.11)$$

Hence, the solutions to the mathematical model of Damage Mechanics of Cancer are as obtained in equations (2.9), (2.10) and (2.11) indicate that the Extracellular Matrix density $\rho(x,t)$,Cell density$\rho_c(x,t)$ and Cell displacement $u(x,t)$ are the functions of time and position. The solutions obtained to the model equations indicate a steady-state solution implying that the cancer cells are growing exponentially with time, a testament to the fact of cancerous cells' boundless proliferations defiling all medications or the treatment strategy employed.

Model Analysis

Here the three systems of non-linear equations are analyzed qualitatively to obtain the equilibrium point and the dynamical behaviour of the equilibria

3.1 Existence of equilibrium

We obtain the steady states of the system by equating the partial derivatives on the left-hand sides to zero and solving the resulting algebraic equations. To achieve this we must admit the spread in equations (2.9), (2.10) and (2.11) solutions since cancer cells reproduction and spread is a complex process based on the experience garnered from the study. Thus we find the analytical solution to the model equations by setting ρ_e, ρ_{ce} and u_e to be the equilibrium solutions respectively for matrix density (2.1), cell density (2.2) and displacement (2.3) and if $\pi = \rho_{ce}$ in equation (2.2). The equilibrium point is a trivial solution with a non-existent density field (cell density and matrix density and displacement. i.e.

$$(\rho_e, \rho_{ce}, u_e) = (0,0,0) \quad (3.1)$$

The other equilibrium point shows the existence of cell density and displacement without matrix density which implies

$$(\rho_e, \rho_{ce}, u_{e)} = \geq \left[N, \frac{\nabla \bullet \varepsilon + vI\nabla \bullet \theta}{s}, 0\right] \quad (3.2)$$

3.2 Stability Analysis

To solve for the stability of the system of equations, a linearization approach is adopted. Linearization refers to an analytical method established in checking whether a dynamical system is stable or unstable. Some steps are involved in determining the linearization of the equilibrium solution. They are:

a) The interacting functions must be continuous and partially differentiable.

b) The interacting functions are determined with respect to the growth rate ϕ of the cancer cell in the body of the organism, traction factor L, stress factor O, diffusion factor P, haptotaxis or mechanical factor Q (movement of cancer cells) and the secretion factor R.

c) The partial derivatives are evaluated at equilibria solutions

d) The Jacobian matrix is constructed and

e) Finally, the stability of the equilibrium solution is tested

Now, considering the complex nature of cancer cells reproduction and proliferation with the experience garnered from the model solutions of this study and solutions to the non-linear systems of equations are sought as highlighted in step (b). It should be noted here that all functions are functions of the destructive rate of cells by cancer cells (wave vector) and radiation, k. We performed the linearization at this stage in order to find the growth rate ϕ of the cancer cells in the body of the organisms, the traction factor L, stress factor O, diffusion factor P, haptotaxis or mechanical factor Q

Cite this article as:
Nkuturum, C., & Akpan, A.U. (2022). Mathematical modeling of the impact of radiation and oxidative stress on cancer development. *FNAS Journal of Scientific Innovations, 3*(2), 35-42.

(movement of cancer cells) and the secretion factor R. In seeking solutions to the linearized equations (2.1), (2.2) and (2.3), the linear stability is established. Thus, we write the corresponding variables as shown below:

$$\{(\tfrac{\tau\rho\nabla\bullet n}{1+\lambda n^2}) - A_1\mathrm{co}\,(x-kt)\}\rho_c + \left(\tfrac{\tau n\nabla\bullet\rho I}{1+\lambda n^2} + \tfrac{\tau n\gamma\nabla^3\bullet\rho I}{1+\lambda n^2}\right)\rho + (\mu_1\nabla\bullet\varepsilon_1 + \mu_2\nabla\bullet\theta_t I + \nabla\cdot\varepsilon + v^t\nabla\bullet\theta I - spu)u=0 \quad (3.3)$$

$$(\rho_{ct} - D_1\nabla^2 + D_2\nabla^4 n + rNn - rn^2)\rho_c + ((\alpha_1 n\nabla^2\rho + \alpha_2 n\nabla^4\rho) - A_2\sin(x-kt)\rho + (\nabla\bullet(nu_t)))u = 0 \quad (3.4)$$

$$(v\theta - 1)\rho_c + (\rho_t)\rho + (\nabla\bullet(\rho u_t))u = 0 \quad (3.5)$$

Setting $\frac{\partial}{\partial t} = \phi, \nabla = ik, \rho_c = \rho = u = I = 1$ (3.6)

Where $\rho_{c,t}, \theta_t, u_t, \rho_t, \varepsilon_t$ are respectively the partial derivatives form and is equal to ϕ,

$$\tau_1 = \frac{\tau}{1+\lambda}, \tau_2 = \frac{\tau}{1+\lambda n^2}, \mu_1 + \mu_1 = \mu, x - kt = \xi \quad (3.7)$$

In the three-dimensional space, as this study has revealed, the analysis is limited to xi direction only owing to the growth rate ϕ and k- the cell destruction rate by cancer cells and radiation. Thus if $\rho_c - 1, \rho - 1$ and u is considerably small and upon substituting into the non-linear system of equations and keeping the linear terms in $\rho_c - 1, \rho - 1$ and u, and their derivatives, a linear system of equations as depicted in (3.3 – 3.7) will result thus:

$$(\rho_{ct} - D_1\nabla^2 n + D_2\nabla^4 n - rNn + rn^2)\rho_c + (\alpha_1 n\nabla^2\rho - \alpha_2 n\nabla^4\rho) - A_2\sin(\xi)\rho + \left(\nabla\bullet(nu_t)\right)u = 0 \quad (3.8)$$

$$\{(\tau_2\rho\nabla\bullet n) - A_1\cos(\xi)\}\rho_c + (\tau_1\nabla\bullet\rho I + \gamma I\tau_1\nabla^2\rho)\rho + (\mu_1\nabla\bullet\varepsilon_1 + \mu_2\nabla\bullet\theta_t I + \nabla\bullet\varepsilon + v^t\nabla\cdot\theta I - spu)u=0 \quad (3.9)$$

$$(v\theta - 1)\rho_c + (\rho_t)\rho + (\nabla\bullet(\rho u_t))u = 0 \quad (3.10)$$

Now, $\lambda < 1, \tau_1 > 0,$ and λ is a measure of the cell-cell contact activation of cancer cells and is nonnegative. Hence the Jacobian matrix of the damage mechanics model of cancer becomes:

$$J(\rho_{c,t}, \rho, u) = \begin{pmatrix} \emptyset - D_1\mathrm{k}^2 n + D_2\mathrm{k}^4 n - rNn + rn^2\alpha_1\mathrm{n}\mathrm{k}^2\rho - \alpha_2 n\mathrm{k}^4\rho - A_2\sin\left(\xi\right)\nabla.nu_t \\ \tau_2\nabla.nI - \mathrm{A}_1\cos\left(\xi\right)\tau_1\nabla.\rho I + \gamma\tau_1\nabla^3.\rho I\mu_1\nabla\varepsilon_1 + \mu_2\nabla.\theta_t I + \nabla.\varepsilon + v^t\nabla.\theta - su \\ v\theta - 1 \qquad\qquad \rho_c\nabla.(\rho u_t) \end{pmatrix} \begin{pmatrix} \rho_c \\ \rho \\ u \end{pmatrix} \quad (3.11)$$

The determinant in equations (4.31) has the following dependent variables: column one represents the cell densityρ_c, the second column represents the matrix density ρ and the third column represents the displacement, u. Thus, the solutions in the growth rate $\emptyset$ as the rate of destruction of normal cells by the cancer cells and radiationk^2, traction force L, the stress factor O, the diffusion factor P, the haptotaxis or mechanical factor Q (cells movement) and the secretion factor R in the model equations. Setting $L = \tau_1 - \gamma\tau_1 k^2, \mathrm{O} = (1 + \mathrm{v}^{\mathrm{t}}), \mathrm{P} = (\mathrm{D}_2\mathrm{k}^2 - \mathrm{D}_1), \mathrm{Q} = (\alpha_1 - \alpha_2)\mathrm{k}^2$ and $\mathrm{R} = (\mathrm{v}\theta - 1)$ implies that equation (3.11) yields the discussions below

The equations with ϕ gives the steady-state solutions implying that the secretion surface is activating the growth or proliferation rate of cancer cells in the body of the organisms in this instance we refer to a solid tumor (cancer) as elucidated in our introduction. The stable solutions indicated that the presence of cancer cells which is a steady-state grows exponentially if unchecked defiling all medication or treatment protocols employed due to the actions of radiation and oxidative stress. The established results indicated the presence of radiation and oxidative stress in the injured area acting also as the enabler of the cancer cells proliferation rate and an indication of a weakened immune system of the organism.

Cite this article as:
Nkuturum, C., & Akpan, A.U. (2022). Mathematical modeling of the impact of radiation and oxidative stress on cancer development. *FNAS Journal of Scientific Innovations, 3*(2), 35-42.

Simulation and Discussion of findings

We note that changes in tumor growth as a result of radiation and oxidative stress as depicted by the mathematical model solutions given in equations (2.9), (2.10) and (2.11) indicate the initiation, growth and proliferation of cancer cells in a diffusive state. The three model equations showcased the presence of cancer in the matrix and their solutions confirm progression and proliferation. These solutions prove that the process of reproduction of new cancer cells is very fast dispersing to the various part of the organism's body though two or more cells may appear close to each other thereby having enough time to grow and double their local concentration position as they compete for nutrients with normal cells due to temperature, traction force, radiation and oxidative stress which weaken the immune system. In the process of time as illustrated by the three equations cancer initiation, progression and proliferation obviously crystallized in the body of the organism.

Here the cancer growth rate in a uniform steady state is stable to small perturbation for $\phi(k^2)$ in equation (3.11) which has $\mathrm{Re}\,\phi(k^2) < 0$. We note here that the cancer cells grow with $\mathrm{Re}\,\phi(k^2) > 0$. If the cancer cell disturbance has k^2 large enough with a small wavelength of disturbances, then the steady-state solutions are linearly stable. The dispersion relation gives the initial growth rate of cancer cells of varied sizes. The model has two fixed points namely; one of the equilibria solutions is a trivial solution with no density field referring to the cell and matrix densities respectively and the displacement. That is $(\rho_{ce}, \rho_e, u_e) = (0,0,0)$. The other equilibrium solution illustrates the existence of both cell density and displacement sans matrix density which satisfies $(\rho_{ce}, \rho_e, u_e) = \left(N, \frac{\nabla\varepsilon + v\nabla\theta}{s}, 0 \right)$ showing a stable growing cancer cell in the system. The trivial equilibrium from the stability analysis reveals a stable system indicative of tumor state whereas the second equilibrium solution illustrates the presence of cancer cells in the matrix wall with displacement.

By using arbitrary values for $L = \tau_1 - \gamma\tau_1 k^2, \mathrm{O} = (1 + \mathrm{v}^{\mathrm{t}}), \mathrm{P} = (\mathrm{D}_2\mathrm{k}^2 - \mathrm{D}_1), \mathrm{Q} = (\alpha_1 - \alpha_2)\mathrm{k}^2$ and $\mathrm{R} = (\mathrm{v}\theta - 1)$ with

$$\gamma = 0.5, \tau_1 = 0.7, \phi = 0.7, s = 0.8, \mu = 7\times10^7, \theta = 0:5:100, N = 1, r = 0.8, v = 0.2, D_1 = 0.4, D_2 = 0.6$$

$$\tau = 0.7, \rho = 1.2\times10^{-2}, \lambda = 30, I = 0.3, x_1 = 2.0, x_2 = 2.5, x_3 = 3.0, k = 0.5, t: 0:5:100, A_1 = 0.2, A_2 = 0.4$$

If the above parameter is used to illustrate graphically the solutions, then the actions of radiation and oxidative stress will be seen to be on the increase showing that the cancer cells have packed up densely in the matrix and numerously in the extra-cellular matrix which begins at some point after the initial stage showing loss of bonding and at point (0,0,0) showing that there is no cancer cell and coalescence shows it is in a solid tumor state.

Conclusion

The formation of tumor-cancer cells by any morphogenetic model primarily is a non-linear phenomenon. However, cancer cells reproduction in a three-dimensional terrain can be obtained from a simple linear analysis. The model equations in this paper noted some general properties of the dispersion relation and have been used to promote cancer whose evolution, spread and propagation are aided by the surrounding tissues. Several experimental studies have shown that the neighbouring host cells tend to suppress cancer cells' reproduction by stimulating certain biochemical substances boosted by the organism's strong immune system but where the immune system is compromised the production of these biochemical substances is inhibited and hence cancer is the obvious result. Thus, a strong immune system will guarantee the secretion of these self-defense biochemical mechanisms to ward off the initiation, growth and proliferation of cancer cells but the lower the concentration of these substances the more the cancer cells are packed up. We note here that the local concentration of cancer cells amongst host tissues with radiation and oxidative stress, traction factor, dilation factor, secretion factor, diffusion factor, etc were critical to this study.

References

Araujo, R.P. & McElwain, D.L.S. (2004). A history of the study of solid tumor growth: the contribution of mathematical modeling. *Bulletin of Mathematical Biology 66* (5): 1039–91 https:10.1016/j.bulm.2003.11.002

Cite this article as:
Nkuturum, C., & Akpan, A.U. (2022). Mathematical modeling of the impact of radiation and oxidative stress on cancer development. *FNAS Journal of Scientific Innovations, 3*(2), 35-42.

Barendsen, G.W. (1994). The relationship between RBT and LET for different types of lethal damage in any mammalian cells: biophysical and molecular mechanism. *Journal of Radiation Research 3* (139) ; 257-270.

Bradly, R. & Enderling, H. (2019). Mathematical model of cancer: When to predict novel therapies and when not to. *Bulletin of Mathematical Biology 81;* 3722-3721. https://link.springer.com/article/10.1007/s11538-019-00640-x

Chamseddine, B.M. & Rejniak,K.A. (2019).Hybrid modeling framework of tumor development and treatment. *Weiley Interdisciplinary Review System Biology and Medicine 12(*3) https://doi.10.1002/wsbm.1461

Enderling, H. Anderson, A.R.A, Chaplain, M.A.J., Munro, A. J. & Vaidya, J.S. (2006). Mathematical modelling of radiotherapy strategies for early breast cancer. *Journal of Theoretical Biology 241*(1);158-171. https://doi.org/10.1016/l.ktbi.2005.11.015

Greenspan, H. (1972). Models for the growth of a solid tumor by diffusion. *Study in Applied Mathematics51(*317-340). https://doi.org/10.1002/sapm192514317

Hsu, F. (1968). The Influence of Mechanical Loads on the form of a growing Elastic Body. *Journal of Biomechanics 1303-1311.*

Humprey, J.D. (2002): Continuum Biomechanics of Soft Biological Tissues. *The Royal Society Journal*, USA.

Kasten-Pisula, U., Saker, J., Eicheler, W., Krase, M., & Dikkomey, E. (2008). Cellular and tumor radiosensitivity is correlated to epidermal growth factor receptor protein expression level in tumor without EGFR amplification. *Journal of Theoretical Biology* 2(264); 305-317. https://doi.org/10.1016/j.jtbi.2009.08.003

Lemaitre, J. (1934). *A Course on Damage Mechanics*: with a forward by Lippmann, H. Springer: New York. 2nd rev, ed.

Lowengrub, J.S, Frieboes,H.B., Jin, F., Chuang, Y.L., Li, X.,Macklin,P. Wise, S.M.& Cristini, V.(2010), Nonlinear modelling of cancer: bridging the gap between cells and tumours . *Nonlinearity. (23)* R1-R91. https://doi.10.1088/0951-7715/23/RO1

Moreira, J. & Deutsch, I. (2002). Cellular automaton model of tumour development: A critical review. *Advances in Complex Systems 5 (2-3)*; 247-267. https://doi.org/10.1142/S0219525902000572

Oyesanya, M.O. & Nkuturum, C. (2019). Graphical analysis of damage mechanics model of cancer. *Journal of the Nigerian Society for Mathematical Biology. (2);*80-104

Shuryak, I. & Brenner, D.J. (2009). A new view of radiation-induced cancer: integrating short-and long-term processesPart1: Approach. *Radiation and Environmental Biophysics 48*(3);263-274.https://doi.org/10.1007/s00411-009-0230-3