ANDROGEN DRIVEN EVOLUTIONARY POPULATION
DYNAMICS IN PROSTATE CANCER GROWTH

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Abstract. Prostate cancer worldwide is regarded the second most frequent
diagnosed cancer in men with (899,000 new cases) while in common cancer
it is the fifth. Regarding the treatment of progressive prostate cancer the
most common and effective is the intermittent androgen deprivation therapy.
Usually this treatment is effective initially at regressing tumorigenesis, mostly
a resistance to treatment can been seen from patients and is known as the
castration-resistant prostate cancer (CRPC), so there is no any treatment and
becomes fatal. Therefore, we proposed a new mathematical model for the
prostate cancer growth with fractional derivative. Initially, we present the
model formulation in detail and then apply the fractional operator Atangana-
Baleanu to the model. The fractional model will be studied further to analyze
and show its existence of solution. Then, we provide a new iterative scheme
for the numerical solution of the prostate cancer growth model. The analytical
results are validated by considering various values assigned to the fractional
order parameter α.

1. Introduction. The healthy prostate and most prostate carcinomas depend on
androgen hormones such as 5a-dihydrotestosterone (DHT) and testosterone for
growth, survival and proliferation [9]. The androgen receptor (AR) binds both DHT
and testosterone but it is five times greater affinity for DHT than testosterone. Once
an androgen is bound to the AR, the androgen-AR complex subsequently under-
goes phosphorylation and dimerization. The resulting homo-dimer translocates to
the nucleus where it binds to specific sequences in DNA called androgen-response
elements in gene promoter regions and positively regulate the genes expression in
growth, survival and proliferation [11]. AR signaling inhibition therefore regresses

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tumor progression [10, 1]. For progressive prostate cancer, androgen deprivation therapy is widely used and initially effective [18]. Side effects of androgen deprivation therapy include erectile dysfunction, loss of libido, loss of muscle mass, fatigue, anemia, osteoporosis and bone fractures, obesity and insulin resistance [21]. To monitor cancer progression and treatment efficacy, serum prostate-specific antigen (PSA) levels are measured. Prostate cancer diagnosis is typically associated with high levels of PSA while a reduction in PSA levels indicates effective treatment. Although androgen deprivation is often initially effective, all the patients show their resistance to treatment and advance to a fatal hormone-refractory state [18]. In order to reduce the cost of treatment, side effects, and potentially delay the development of castration-resistance, therapy can be applied intermittently [21]. This so-called intermittent androgen deprivation (IAD) therapy is typically given until the patients PSA level falls below some threshold value [1]. Once the PSA level falls below the threshold, the treatment of the patient becomes off and it is still remain when the level of the PSA arose to the some specified threshold, and the process is repeated [1]. In an effort to predict the time of treatment resistance, Portz, Kuang and Nagy [20] mechanistically formulated and data validated a mathematical prostate cancer growth model. Here, we propose to perform a systematic analysis of the rich nonlinear properties of the solutions of their mathematical model. Such findings may generate practical insights helpful for predicting the major mechanism of a castration resistance developing in individual prostate cancer patients after a period of IAD. Prostate cancer growth models received intensive interest in the last few years [9, 7]. Our model generalizes the model in [20] where castration-sensitive (CS) and castration-resistant (CR) populations are modeled by the following equations:

\[
\begin{align*}
\frac{dX_1}{dt} &= \mu_m \left(1 - \frac{q_1}{Q_1}\right)X_1 - D_1(Q_1)X_1 - \lambda_1(Q_1)X_1 + \lambda_2(Q_2)X_2, \\
\frac{dX_2}{dt} &= \mu_m \left(1 - \frac{q_2}{Q_2}\right)X_2 - D_2(Q_2)X_2 - \lambda_2(Q_2)X_2 + \lambda_1(Q_1)X_1.
\end{align*}
\]

The dynamics of the cell population is given by the intracellular androgen concentration, or cell quota, represented by the variable $Q_i$, where $i$ represents the $i$th population. The cellquota dependent proliferation rate $\mu_m \left(1 - \frac{q_i}{Q_i}\right)$ originates in mathematical ecology and captures the dynamics of nutrient dependent growth. $\mu_m$ represents the maximum proliferation rate and $q_i$ is the minimum cell quota. We assume $q_2 < q_1$, on the basis that the CR cells dependency on androgen are low and can proliferate at apparently low levels of serum androgen [21, 6]. The functions $\lambda_1(Q_1) = c_1 \frac{K_1^n}{Q_1^n + K_1^n}$ and $\lambda_2(Q_2) = c_2 \frac{Q_2^n}{Q_2^n + K_2^n}$ are the rates of the cell-phenotype accommodative switch from $X_1$ to $X_2$ and vice versa, respectively. The cell-death rates (CDRs), $D_i(Q_i) = d_i \frac{R_i^n}{Q_i^n + R_i^n} + \delta_i$, for $i = 1, 2$, consist of androgen-dependent rate $d_i \frac{R_i^n}{Q_i^n + R_i^n}$ and androgen-independent rate $\delta_i$ for $i = 1, 2$. The cell quota $Q_i$ is modeled by:

\[
\frac{dQ_i}{dt} = \nu_m \frac{q_m - Q_i}{q_m - q_i} \frac{A}{A + \nu_h} - \mu_m(Q_i - q_i) - bQ_i, \quad i = 1, 2.
\]

Cellular uptake of serum androgen $A(t)$ is governed by the intracellular concentration $Q_i$, the maximum cell quota $q_m$, and maximum and half-saturation constants $\nu_m$ and $\nu_h$. The parameter $b$ measures the decrease in intracellular androgen
whereas the expression $\mu_M(Q_i - q_i)$ measures the growth. We propose to perform a systematic analysis of the rich nonlinear properties of the solutions of the mathematical model consisting of equations (1-2). Specifically, we will first perform comprehensive numerical simulation of the model system and sensitivity analysis on key parameters of this model and use the results to guide our mathematical analysis on the global rich dynamics of the model system (1-2). System (1-2) models the evolutionary dynamics of prostate cancer growth subject to the limitation of androgen (A) which can be regulated by many treatments, especially IAD. These castration-sensitive (CS) and castration-resistant (CR) populations interact in a very interesting way: if there is no conversion from CR cells back to CS cells, then the model system is in fact describes a predator-prey type of interaction with CR cells acting as predator species and CS cells as prey species. This is an interesting special case warrant our close scrutiny. Another special but realistic case of great interest is the situation that cell quota dynamics is much faster than population growth and death dynamics. In such case, we can apply the routine quasi-steady-state argument and set

$$0 = \nu_m \frac{q_m - Q_i - A}{q_m - q_i} A + \nu_n (Q_i - q_i) - bQ_i.$$ 

These algebraic equations allow us to express cell quotas in terms of parameters, including androgen level A.

Some recent work regarding the prostate and other related cancer types are investigated in [13, 16, 22]. In [13], Jain et al. studied prostate cancer growth model related to human to investigate the implication of cell kinetic changes. In [16], Lorenzo et al. formulated a mathematical model for the prostate cancer growth and presented the mathematical results. Modeling and analysis of the prostate cancer growth model to androgen ablation therapy is studied in [22]. All these results are the current investigations, which show the advancement in the subject of prostate cancer growth. The researchers are still looking to have models that are realistically fit to the original phenomenon of the prostate cancer growth and their application to the community. In the following paragraphs, we give some details literature on the use of the fractional calculus related to practical phenomenon of infectious diseases.

Fractional calculus is widely used nowadays to formulate model of real life problems. One of the advantage of the fractional calculus is the generalization of the model where one can able to study the dynamics of the model at any arbitrary derivative. The fractional derivative includes the Caputo, Caputo-Fabrizio and the Atangana-Baleanu derivatives which are successfully applied to many problems [17, 8, 14, 15, 24, 25] and the references therein. In these mentioned papers, the authors used the fractional calculus and applied to the problems in science engineering. For example in [17], the author used the Caputo fractional derivative and obtained analytical results to the oxygen diffusion equation from capillary to tissue. An analysis of the projective synchronization with in the scope of fractional operators are investigated in [8]. A pine trees dynamics with in the scope of fractional calculus is considered in [14]. The newly very famous derivative known as Atangana-Baleanu derivative is applied to tuberculosis model with relapse in [15]. The dynamics of tuberculosis in fractional derivative is considered in [24]. The authors in [25] used the Caputo-Fabrizio derivative and obtain analytical as well as
numerical results for a new fractional Hepatitis B model. All the above references are presented to model the dynamics of a real life problems very successfully by using the fractional derivative. Thus, we consider a new prostate cancer growth model in Atangana-Baleanu derivative in non-local and non-singular kernel. The other two derivatives have the singularity and the local issue, which is not more powerful than that of the Atangana-Baleanu derivative. Due to the non-local and non-singular kernel, the Atangana-Baleanu derivative is more useful to study the dynamics of such prostate cancer growth model effectively.

The purpose of this work is to formulate a mathematical model for the prostate cancer growth model in order to describe well their dynamics. For this purpose, we give a brief details of the mathematical formulation with the terms related to the prostate cancer growth. In order to have rich dynamics of the prostate cancer growth model, we apply the non-local and non-singular that well addressed effectively the dynamics of the model. We presented a detailed literature about the prostate cancer growth model and some recent literature on fractional calculus and its advantages to the epidemiological models in Section 1. Further, in Section 2, we provide the basic definitions involved in the Atangana-Baleanu derivative. The Atangana-Baleanu derivative and its application to the prostate cancer growth model is considered in Section 3. Some mathematical results for the prostate cancer growth model is discussed in Section 4. The numerical solution of the fractional prostate cancer growth model through a new reliable numerical scheme is presented in Section 5. Further in Section 5, the prostate cancer growth model in fractional derivative is used to obtain their graphical results using the proposed numerical scheme with various values of the fractional order parameter. The results presented in this paper are summarized in Section 6.

2. Basic concepts of Atangana-Baleanu derivative. Before we study the prostate cancer growth model in Atangana-Baleanu derivative first we give some background of the Atangana-Baleanu derivative. The following definitions are presented:

Definition 1. [19]. A Caputo derivative of order \( \alpha \) for a given function \( f : [a, b] \to \mathbb{R} \), is defined as follows:

\[
\frac{C^\alpha}{a} D_t^\alpha (f(t)) = \frac{1}{\Gamma(n-\alpha)} \int_a^t h^n(\zeta)(t-\zeta)^{n-\alpha-1} d\zeta,
\]

where \( n-1 < \alpha < n \).

Definition 2. Consider \( f \in H^1(a, b) \), where \( b \) greater than \( a \), and \( 0 \leq \alpha \leq 1 \), then we define the Atangana-Baleanu derivative in the following:

\[
a^{ABC} D_t^\alpha f(t) = \frac{B(\alpha)}{1-\alpha} \int_a^t f'(\zeta)E_{\alpha} \left[ \frac{\alpha(t-\zeta)-\alpha}{1-\alpha} \right] d\zeta.
\]

Definition 3. The fractional integral for the Atangana-Baleanu derivative is expressed as follows:

\[
a^{ABC} I_t^\alpha f(t) = \frac{1-\alpha}{B(\alpha)} f(t) + \frac{\alpha}{B(\alpha)\Gamma(\alpha)} \int_a^t f(\zeta)(t-\zeta)^{\alpha-1} d\zeta.
\]

One can restore the original function for the case when \( \alpha = 0 \).

Some results regarding the Atangana-Baleanu derivative are presented in the following:
Figure 1. The dynamics of the prostate cancer growth model with $\alpha = 1$.

Theorem 1. [2]. The following is hold for a function $f \in C[a,b]$:

$$\|a^ABC_t^\alpha f(t)\| < \frac{B(\alpha)}{1-\alpha} \|f(t)\|, \text{ where } \|f(t)\| = \max_{a \leq t \leq b} |f(t)|.$$  \hfill (6)

The Lipschitz condition is satisfied by the Atangana-Baleanu derivative,

$$\|a^ABC_t^\alpha f_1(t) - a^ABC_t^\alpha f_2(t)\| < \varpi \|f_1(t) - f_2(t)\|.$$  \hfill (7)
Figure 2. The dynamics of the prostate cancer growth model with $\alpha = 0.98$.

Theorem 2. [2]. A fractional differential is given by the following equation,

$$\begin{align*}
\frac{ABC}{A} D_t^\alpha f(t) &= F(t), \\
\end{align*}$$

possess a unique solution given by

$$
f(t) = \frac{1 - \alpha}{B(\alpha)} F(t) + \frac{\alpha}{B(\alpha)\Gamma(\alpha)} \int_a^t F(\zeta)(t - \zeta)^{\alpha - 1} d\zeta.
$$

(9)
3. Basic model in Atangana-Baleanu form. The model equations considered in (1-2) are given and presented in the following:

\[
\begin{align*}
\frac{dX_1}{dt} &= \mu_m \left(1 - \frac{q_1}{Q_1}\right)X_1 - D_1(Q_1)X_1 - \lambda_1(Q_1)X_1 + \lambda_2(Q_2)X_2, \\
\frac{dX_2}{dt} &= \mu_m \left(1 - \frac{q_2}{Q_2}\right)X_2 - D_2(Q_2)X_2 - \lambda_2(Q_2)X_2 + \lambda_1(Q_1)X_1, \\
\frac{dQ_1}{dt} &= \nu_m \frac{q_m - Q_1}{q_m - q_i} A - \mu_m(Q_i - q_i) - bQ_1, \quad i = 1, 2, \\
\frac{dQ_2}{dt} &= \nu_m \frac{q_m - Q_2}{q_m - q_i} A + \nu_h - \mu_m(Q_1 - q_1) - bQ_1,
\end{align*}
\]

where

\[
\begin{align*}
\lambda_1(Q_1) &= c_1 \frac{K^n_1}{Q^n_1 + K^n_1}, \quad \lambda_2(Q_2) = c_2 \frac{Q^n_2}{Q^n_2 + K^n_2}, \\
D_1(Q_1) &= d_1 \frac{R^n_1}{Q^n_1 + R^n_1} + \delta_1, \quad D_2(Q_2) = d_2 \frac{R^n_2}{Q^n_2 + R^n_2} + \delta_2.
\end{align*}
\]

We further write the model equations given by (10-11) as follows,

\[
\begin{align*}
\frac{dX_1}{dt} &= \mu_m \left(1 - \frac{q_1}{Q_1}\right)X_1 - D_1(Q_1)X_1 - \lambda_1(Q_1)X_1 + \lambda_2(Q_2)X_2, \\
\frac{dX_2}{dt} &= \mu_m \left(1 - \frac{q_2}{Q_2}\right)X_2 - D_2(Q_2)X_2 - \lambda_2(Q_2)X_2 + \lambda_1(Q_1)X_1, \\
\frac{dQ_1}{dt} &= \nu_m \frac{q_m - Q_1}{q_m - q_1} A - \mu_m(Q_1 - q_1) - bQ_1, \\
\frac{dQ_2}{dt} &= \nu_m \frac{q_m - Q_2}{q_m - q_2} A + \nu_h - \mu_m(Q_2 - q_2) - bQ_2.
\end{align*}
\]

Finally, we present the model (12) together with androgen dynamics equation as follows,

\[
\begin{align*}
\frac{dX_1}{dt} &= \mu_m \left(1 - \frac{q_1}{Q_1}\right)X_1 - \left(d_1 \frac{R^n_1}{Q^n_1 + R^n_1} + \delta_1\right)X_1 - \left(c_1 \frac{K^n_1}{Q^n_1 + K^n_1}\right)X_1 \\
&\quad + \left(c_2 \frac{Q^n_2}{Q^n_2 + K^n_2}\right)X_2, \\
\frac{dX_2}{dt} &= \mu_m \left(1 - \frac{q_2}{Q_2}\right)X_2 - \left(d_2 \frac{R^n_2}{Q^n_2 + R^n_2} + \delta_2\right)X_2 - \left(c_2 \frac{Q^n_2}{Q^n_2 + K^n_2}\right)X_2 \\
&\quad + \left(c_1 \frac{K^n_1}{Q^n_1 + K^n_1}\right)X_1, \\
\frac{dQ_1}{dt} &= \nu_m \frac{q_m - Q_1}{q_m - q_1} A - \mu_m(Q_1 - q_1) - bQ_1, \\
\frac{dQ_2}{dt} &= \nu_m \frac{q_m - Q_2}{q_m - q_2} A + \nu_h - \mu_m(Q_2 - q_2) - bQ_2, \\
\frac{dA}{dt} &= \gamma(a_0 - A) - \gamma a_0 u(t), \\
\frac{dP}{dt} &= \sigma_o(X_1 + X_2) + \sigma_1 X_1 \frac{Q^n_1}{Q^n_1 + \omega^n_1} + \sigma_2 X_2 \frac{Q^n_2}{Q^n_2 + \omega^n_2} - \delta_3 P,
\end{align*}
\]

where \( u(t) = 1 \), when the treatment on, and \( u(t) = 0 \), when the treatment off. PSA is produced by both AD and AI cells at rate \( \sigma_o \), where \( \sigma_1 \) and \( \sigma_2 \) are used for the increase of cell quota where \( \delta_3 \) is the PSA clearance rate. The details of the parameters used in the model (13) and their values are given in Table 1.
The study investigates the existence and uniqueness results for the prostate cancer model. The model considered in (13) can be written in Atanga-Baleanu derivative in the following form:

\[
\begin{align*}
0^\text{AB} D^\alpha_t X_1 &= \mu_m \left(1 - \frac{q_1}{Q_1}\right) X_1 - \left(d_1 \frac{R_1^m}{Q_1^m + R_1^m} + \delta_1\right) X_1 - \left(c_1 \frac{K_1^n}{Q_1^m + K_1^n}\right) X_1 \\
&\quad + \left(c_2 \frac{Q_2^n}{Q_2^m + K_2^n}\right) X_2, \\
0^\text{AB} D^\alpha_t X_2 &= \mu_m \left(1 - \frac{q_2}{Q_2}\right) X_2 - \left(d_2 \frac{R_2^m}{Q_2^m + R_2^m} + \delta_2\right) X_2 - \left(c_2 \frac{Q_2^n}{Q_2^m + K_2^n}\right) X_2 \\
&\quad + \left(c_1 \frac{K_1^n}{Q_1^m + K_1^n}\right) X_1,
\end{align*}
\]

\[ (14) \]

The parameters and their values used in the model simulation are as follows:

| Parameter | Description | Value | Reference |
|-----------|-------------|-------|-----------|
| \(\mu_m\) | Maximum proliferation rate | 0.025 day^{-1} | [5] |
| \(q_1, q_2\) | Minimum AD and AI cell quota | 0.175, 0.1 day^{-1} | [6] |
| \(\delta_1, \delta_2\) | Androgen-independent rate | 0.02 day^{-1} | [12] |
| \(d_1, d_2\) | AD and AI cell apoptosis rate | 0.0015, 0.015 day^{-1} | [5] |
| \(c_1\) | Mutation rate from AD to AI | 0.00015 day^{-1} | [12] |
| \(c_2\) | Mutation rate from AI to AD | 0.0001 day^{-1} | [12] |
| \(q_m\) | Cell maximum quota | 5 day^{-1} | Assumed |
| \(\nu_m\) | Uptake rate of the maximum cell quota | 0.275 nM day^{-1} | Assumed |
| \(\nu_h\) | Uptake rate half-saturation level | 4 nM d | Assumed |
| \(b\) | Degradation rate of cell quota | 0.09 day^{-1} | [12] |
| \(K_1\) | Half-saturation level from AD to AI mutation | 0.08 nM | [12] |
| \(K_2\) | Half-saturation level from AI to AD | 1.7 nM | [12] |
| \(R_1, R_2\) | Androgen dependent rates | 1.3, 0.8 | Assumed |
| \(\gamma_1\) | Androgen clearance rate | 0.08 | [12] |
| \(a_0\) | Normal androgen concentration | 10 | [12] |
| \(\sigma_0\) | Production rate of PSA | 0.004 | [12] |
| \(\sigma_1, \sigma_2\) | AD and AI Production rate of PSA | 0.05, 0.05 | [12] |
| \(\varpi_1, \varpi_2\) | Half saturation level of AD and AI PSA | 1.3, 1.1 | [12] |
| \(\delta_3\) | PSA clearance rate | 0.08 | [12] |

In Table 1, we list the parameters and their values used in the simulation.

4. Existence and uniqueness for the prostate cancer model. The present section investigates the existence and uniqueness results for the prostate cancer...
Figure 3. The dynamics of the prostate cancer growth model with $\alpha = 0.96$. We use the application of fixed point theory to obtain the existence and uniqueness results for the prostate cancer growth model (14). To do this, we first express the model (14) in the following form:

\[
\begin{aligned}
ABC \frac{D_t g(t)}{t} &= \mathcal{H}(t, g(t)), \\
g(0) &= g_0, \quad 0 < t < T < \infty.
\end{aligned}
\] (15)
In model (15), \( g(t) = (X_1, X_2, Q_1, Q_2, A, P) \) represents the vector with the given state variables, where \( \mathcal{H} \) shows a continuous vector function and is given in the following:

$$
\mathcal{H} = \left( \begin{array}{c}
\mathcal{H}_1 \\
\mathcal{H}_2 \\
\mathcal{H}_3 \\
\mathcal{H}_4 \\
\mathcal{H}_5 \\
\mathcal{H}_6
\end{array} \right) = \left( \begin{array}{c}
\mu_m \left( 1 - \frac{q_1}{Q_1} \right) X_1 - \left( d_1 \frac{R^n}{Q_1 + R^n} + \delta_1 \right) X_1 \\
- \left( c_1 \frac{K^n}{Q_1 + K^n} \right) X_1 + \left( c_2 \frac{K^n}{Q_2 + K^n} \right) X_2 \\
\mu_m \left( 1 - \frac{q_2}{Q_2} \right) X_2 - \left( d_2 \frac{R^n}{Q_2 + R^n} + \delta_2 \right) X_2 \\
- \left( c_2 \frac{K^n}{Q_2 + K^n} \right) X_2 + \left( c_1 \frac{K^n}{Q_1 + K^n} \right) X_1 \\
\nu_m \frac{q_m - Q_1}{q_m - q_1} \frac{A}{A + r_1} - \mu_m (Q_1 - q_1) - bQ_1, \\
\nu_m \frac{q_m - Q_2}{q_m - q_2} \frac{A}{A + r_2} - \mu_m (Q_2 - q_2) - bQ_2, \\
\gamma (a_0 - A) - \gamma a_0 u(t) \\
\sigma_o (X_1 + X_2) + \sigma_1 X_1 \frac{Q_1}{Q_1 + \omega_1} + \sigma_2 X_2 \frac{Q_2}{Q_2 + \omega_2} - \delta_3 P
\end{array} \right),
$$

and the vector \( g_0(t) = \left( X_1(0), X_2(0), Q_1(0), Q_2(0), A(0), P(0) \right) \) shows the initial values of the state variables. Also, the given function \( \mathcal{H} \) satisfies the Lipschitz condition given by:

$$
\| \mathcal{H}(t, g_1(t)) - \mathcal{H}(t, g_2(t)) \| \leq \mathcal{N} \| g_1(t) - g_2(t) \|. \quad (16)
$$

We give the following result in order to prove the existence and uniqueness results associated to the prostate cancer growth model given by model (14).

**Theorem 3.** The prostate cancer growth model given by (14) has a unique solution provided the conditions given below and satisfy:

$$
\frac{(1 - \alpha)}{ABC(\alpha)} \mathcal{N} + \frac{\alpha}{ABC(\alpha) \Gamma(\alpha)} T_{\text{max}}^\alpha \mathcal{N} < 1. \quad (17)
$$

**Proof.** The Atangana-Baleanu integral given by (5) is used to apply on both sides of the system (15), and the following nonlinear Volterra integral equation is obtained,

$$
g(t) = g_0 + \frac{1 - \alpha}{ABC(\alpha)} \mathcal{H}(t, g(t)) + \frac{\alpha}{ABC(\alpha) \Gamma(\alpha)} \int_0^t (t - \xi)^{\alpha - 1} \mathcal{H}(\xi, g(\xi)) d\xi. \quad (18)
$$

Consider \( U = (0, T) \) and the operator \( \Omega : \mathcal{L}(U, R^6) \rightarrow \mathcal{L}(U, R^6) \) given by

$$
\Omega[g(t)] = g_0 + \frac{1 - \alpha}{ABC(\alpha)} \mathcal{H}(t, g(t)) + \frac{\alpha}{ABC(\alpha) \Gamma(\alpha)} \int_0^t (t - \xi)^{\alpha - 1} \mathcal{H}(\xi, g(\xi)) d\xi. \quad (19)
$$

Then, equation given by (18) becomes,

$$
g(t) = \Omega[g(t)]. \quad (20)
$$

The property of supremum norm on \( U, \| \cdot \|_U \) leads to:

$$
\| g(t) \|_U = \sup_{t \in U} \| g(t) \|, \quad g(t) \in \mathcal{L}. \quad (21)
$$
Figure 4. The dynamics of the prostate cancer growth model with $\alpha = 0.9$. Obviously, $\mathcal{L}(U, R^6)$ together with norm $\| \cdot \|_U$ give a Banach space. Moreover, we have the following inequality,

$$\left\| \int_0^t K(t, \zeta) g(\zeta) d\zeta \right\| \leq T \| K(t, \zeta) \|_U \| g(t) \|_U,$$

(22)
with $g(t) \in \mathcal{L}(U, R^6)$, $K(t, \zeta) \in \mathcal{L}(U^2, R)$ such that,
\[
\|K(t, \zeta)\|_U = \sup_{t, \zeta \in U} |K(t, \zeta)|.
\] (23)

The application of the definition described in (20), gives the following,
\[
\|\Omega[g_1(t)] - \Omega[g_2(t)]\|_U \leq \left\| \left(1 - \alpha\right) \frac{\alpha}{ABC(\alpha)} H(t, g_1(t)) + \frac{\alpha}{ABC(\alpha) \Gamma(\alpha)} \times \int_0^t (t - \zeta)^{\alpha - 1} \left(\mathcal{H}(\zeta, g_1(\zeta)) - \mathcal{H}(\zeta, g_2(\zeta))\right) d\zeta \right\|_U .
\] (24)

Using the triangular inequality together with the Lipschitz condition given by the equation (16) and the result given in (22) lead to the following result, which we obtained after some tedious computations,
\[
\|\Omega[g_1(t)] - \Omega[g_2(t)]\|_J \leq \left(\frac{(1 - \alpha)N}{ABC(\alpha)} + \frac{\alpha}{ABC(\alpha) \Gamma(\alpha)} NT_{\text{max}}^\alpha \right) \times \|g_1(t) - g_2(t)\|_U .
\] (25)

So, we have finally, the result given by
\[
\|\Omega[g_1(t)] - \Omega[g_2(t)]\|_U \leq B \|g_1(t) - g_2(t)\|_U ,
\] (26)

where
\[
B = \frac{(1 - \alpha)N}{ABC(\alpha)} + \frac{\alpha}{ABC(\alpha) \Gamma(\alpha)} NT_{\text{max}}^\alpha .
\]

If the condition given by (17) holds then the operator $\Omega$ will be a contraction. So, the above results lead to the existence of the model solution given by (15).

5. Numerical procedure for Atangana-Baleanu derivative. The present section explores a numerical procedure for the solution of a fractional prostate cancer growth model given by (14). The scheme we used for our prostate cancer growth model in fractional derivative is proposed by the authors in [23], to obtain the approximate solution of the fractional order model in the Atangana-Baleanu operator. This novel scheme is based on the two-step Lagrange polynomial together with the use of the fundamental theorem of fractional calculus. To present an iterative scheme for the fractional prostate cancer growth model (14), initially, we describe the method in detail and then its application to our proposed fractional (14) to present an iterative scheme. We mentioned that this scheme is used by many authors for their proposed problems [3, 4].

We write the system (15) in the form presented below by using the fundamental theorem described in fractional calculus:
\[
g(t) - g(0) = \frac{(1 - \alpha)}{ABC(\alpha)} \mathcal{H}(t, g(t)) + \frac{\alpha}{ABC(\alpha) \times \Gamma(\alpha)} \int_0^t \mathcal{H}(\zeta, x(\zeta))(t - \zeta)^{\alpha - 1} d\zeta .
\] (27)

We have for $t = t_{n+1}$, $n = 0, 1, 2, ...,$
\[
g(t_{n+1}) - g(0) = \frac{1 - \alpha}{ABC(\alpha)} \mathcal{H}(t_n, g(t_n)) +
\]
Figure 5. The dynamics of the prostate cancer growth model with $\alpha = 0.8$.

\[
\frac{\alpha}{\Gamma(\alpha)} \int_0^{t_{n+1}} \mathcal{H}(\zeta, g(\zeta))(t_{n+1} - \zeta)^{\alpha-1} d\zeta,
\]

\[
= \frac{1 - \alpha}{\Gamma(\alpha)} \mathcal{H}(t_n, g(t_n)) + \frac{\alpha}{\Gamma(\alpha)} \sum_{j=0}^{n} \int_{t_j}^{t_{j+1}} \mathcal{H}(\zeta, g(\zeta))(t_{n+1} - \zeta)^{\alpha-1} d\zeta, \tag{28}
\]
The function given by $H(\zeta, g(\zeta))$ is approximated over the interval $[t_j, t_{j+1}]$, by using the interpolation polynomial, we have

$$H(\zeta, g(\zeta)) \approx \frac{H(t_j, g(t_j))}{h}(t - t_{j-1}) - \frac{H(t_{j-1}, g(t_{j-1}))}{h}(t - t_j).$$

(29)
Substituting this equation into equation (28), the following is obtained,

\[
g(t_{n+1}) = g(0) + \frac{1 - \alpha}{ABC(\alpha)} \mathcal{H}(t_n, g(t_n)) + \\
\frac{\alpha}{ABC(\alpha) \Gamma(\alpha)} \sum_{j=0}^{n} \left( \frac{\mathcal{H}(t_j, g(t_j))}{h} \int_{t_j}^{t_{j+1}} (t - t_j)(t_{n+1} - t)^{\alpha-1} dt \right) \\
- \frac{\mathcal{H}(t_{j-1}, g(t_{j-1}))}{h} \int_{t_j}^{t_{j+1}} (t - t_j)(t_{n+1} - t)^{\alpha-1} dt. \tag{30}
\]

The integrals given in equation (30) are solved and after some rigorous computations, the final approximate solution is presented by:

\[
g(t_{n+1}) = g(t_0) + \frac{1 - \alpha}{ABC(\alpha)} \mathcal{H}(t_n, g(t_n)) + \\
\frac{\alpha}{ABC(\alpha) \Gamma(\alpha)} \sum_{j=0}^{n} \left( \frac{h^\alpha \mathcal{H}_j(t_j, g(t_j))}{\Gamma(\alpha + 2)} ((n+1-j)^\alpha(n-j+2+\alpha) - (n-j)^\alpha(n-j+2+2\alpha)) \\
- \frac{h^\alpha \mathcal{H}(t_{j-1}, g(t_{j-1}))}{\Gamma(\alpha + 2)} ((n+1-j)^\alpha+1 - (n-j)^\alpha(n-j+1+\alpha)) \right). \tag{31}
\]

The procedure described above can then be applied directly to our proposed model given by (14), and we have for our model equations by denoting

\[
\begin{aligned}
P_1 &= \frac{1 - \alpha}{ABC(\alpha)}, \\
P_2 &= ((n+1-j)^\alpha(n-j+2+\alpha) - (n-j)^\alpha(n-j+2+2\alpha)), \\
P_3 &= ((n+1-j)^\alpha+1 - (n-j)^\alpha(n-j+1+\alpha)), \\
P_4 &= \frac{\alpha}{ABC(\alpha)},
\end{aligned}
\]

and have,

\[
X_1(t_{n+1}) = X_1(t_0) + P_1 \mathcal{H}_1(t_n, g(t_n)) \\
+ P_4 \sum_{j=0}^{n} \left( \frac{h^\alpha \mathcal{H}_1(t_j, g(t_j))}{\Gamma(\alpha + 2)} P_2 - \frac{h^\alpha \mathcal{H}_1(t_{j-1}, g(t_{j-1}))}{\Gamma(\alpha + 2)} P_3 \right),
\]

\[
X_2(t_{n+1}) = X_2(t_0) + P_1 \mathcal{H}_2(t_n, g(t_n)) \\
+ P_4 \sum_{j=0}^{n} \left( \frac{h^\alpha \mathcal{H}_2(t_j, g(t_j))}{\Gamma(\alpha + 2)} P_2 - \frac{h^\alpha \mathcal{H}_2(t_{j-1}, g(t_{j-1}))}{\Gamma(\alpha + 2)} P_3 \right),
\]

\[
Q_1(t_{n+1}) = Q_1(t_0) + P_1 \mathcal{H}_3(t_n, g(t_n)) \\
+ P_4 \sum_{j=0}^{n} \left( \frac{h^\alpha \mathcal{H}_3(t_j, g(t_j))}{\Gamma(\alpha + 2)} P_2 - \frac{h^\alpha \mathcal{H}_3(t_{j-1}, g(t_{j-1}))}{\Gamma(\alpha + 2)} P_3 \right),
\]

\[
Q_2(t_{n+1}) = Q_2(t_0) + P_1 \mathcal{H}_4(t_n, g(t_n)) \\
+ P_4 \sum_{j=0}^{n} \left( \frac{h^\alpha \mathcal{H}_4(t_j, g(t_j))}{\Gamma(\alpha + 2)} P_2 - \frac{h^\alpha \mathcal{H}_4(t_{j-1}, g(t_{j-1}))}{\Gamma(\alpha + 2)} P_3 \right). \tag{33}
\]
\begin{align*}
A(t_{n+1}) &= A(t_0) + P_1 \mathcal{H}_5(t_n, g(t_n)) \\
&\quad + P_4 \sum_{j=0}^{n} \left( \frac{h^\alpha \mathcal{H}_5(t_j, g(t_j))}{\Gamma(\alpha + 2)} P_2 - \frac{h^\alpha \mathcal{H}_5(t_{j-1}, g(t_{j-1}))}{\Gamma(\alpha + 2)} P_3 \right), \\
P(t_{n+1}) &= P(t_0) + P_1 \mathcal{H}_5(t_n, g(t_n)) \\
&\quad + P_4 \sum_{j=0}^{n} \left( \frac{h^\alpha \mathcal{H}_5(t_j, g(t_j))}{\Gamma(\alpha + 2)} P_2 - \frac{h^\alpha \mathcal{H}_5(t_{j-1}, g(t_{j-1}))}{\Gamma(\alpha + 2)} P_3 \right).
\end{align*}

Figure 7. The dynamics of the prostate cancer growth model with \( \alpha = 0.5 \).
Numerical results given in Figures 1-7 are obtained by using the scheme presented above for the dynamics of the prostate cancer fractional model (14). In the present simulation, each Figure has sub-figures (a-f) which respectively show the dynamics of androgen dependent cells, androgen independent cells, cell quota \(Q_1\) and \(Q_2\), androgen dynamics and the serum PSA.

The bold line represents the integer case while the dashed line represents the behavior of the model variables for the non-integer case. Considering various values of \(\alpha\) and solution of the prostate cancer growth model are shown graphically. We consider the value for the fractional order parameter \(\alpha = 1, 0.98, 0.96, 0.9, 0.8, 0.7\) and 0.5 and presented the graphical results. From these graphical results, we can see that by decreasing the fractional order parameter \(\alpha\) from integer to non-integer the behavior of the androgen dependent dynamics increases while the dynamics of the androgen independent cells, the cell quota \(Q_1, Q_2\), androgen dynamics, and the serum PSA are decreasing well and the fact can be seen in Figures 1-7. Most interesting case is by choosing the value of the fractional order parameter \(\alpha = 0.5\).
The dynamics of the behavior of androgen dependent dynamics increases while the dynamics of the androgen independent cells, the cell quota $Q_1$, $Q_2$, androgen dynamics, and the serum PSA are decreasing efficiently. From these graphical results, we can suggest the fractional calculus in the sense of Atangana-Baleanu operator is more useful than the integer order derivative. Further, we obtain the graphical results given in Figures 8-11 by using various values, which are assigned to the arbitrary order parameter $\alpha = 1, 0.98, 0.96, 0.94$ for the prostate cancer growth model (14) and presented the chaotic graphical results. The results obtained are more reasonable and reliable than the integer order models and will be more helpful regarding the controlling of prostate cancer growth. These graphical results show the importance of the fractional calculus for such applications model of cancer growth.
6. Conclusion. The present paper explores the dynamics of prostate cancer growth model within the scope of fractional calculus. Initially, we obtained the model formulation in detailed and some mathematical results associated to the model are presented. Then, we obtained the model in the Atangana-Baleanu form and then the existence and uniqueness results are provided. The prostate cancer growth model is then solved numerically by using a new iterative scheme. We obtained various graphical results for different values of the fractional order parameter $\alpha$ and the results are discussed in detail. The chaotic attractivity of the model is achieved by considering various values of the fractional order parameter $\alpha$. The graphical results compared to the integer case show that the fractional order model is more helpful for the infection eradication in cancer growth by decreasing the value of $\alpha$. The fractional model considered in this paper in Atangana-Baleanu derivative could be more useful for public health authorities and other researchers who working on control of cancer growth. Therefore, on the basis of the results obtained in this paper we suggest that cancer growth could be decreased efficiently by using the

Figure 10. Phase portraits of the model considering different variables with $\alpha = 0.96$. 
proper management and treatment of infected individuals. In future, this important cancer prostate growth problem will be solved by some new numerical scheme available in literature.

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