HPM OF ESTROGEN MODEL ON THE DYNAMICS OF BREAST CANCER

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Abstract. We enhance a deterministic mathematical model involving universal dynamics on breast cancer with immune response. This is population model so includes Normal cells class, Tumor cells, Immune cells and Estrogen. The effects regarding Estrogen are below incorporated in the model. The effects show to that amount the arrival of greater Estrogen increases the danger over growing breast cancer. Furthermore, approximate solution regarding nonlinear differential equations is arrived by Homotopy Perturbation Method (HPM). Hence HPM is good and correct technique after solve nonlinear differential equation directly. Approximate solution learnt with the support of that method is suitable same as like the actual results in accordance with this models.

Keywords: HPM, Estrogen model, breast cancer.
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1. Introduction
A basic mathematical model of the immune response when breast cancer cells are recognized is proposed. The model consists of four ordinary differential equations. It is extended by taking into account two types of analysis: equilibrium and stability analysis. There are many factors that affect the chance of an individual developing breast cancer, some of which one can change and some cannot be changed. Having a risk factor, or even several, does not mean that one will automatically develop the disease. Women have a higher risk of developing breast cancer although in men it has been discovered too. Some of these factors include use of alcohol with the risk increasing relative to the amount of alcohol consumed, overweight or obese, especially for women after menopause. Obesity increases estrogen levels due to fat tissue producing small amounts of estrogen. High doses of radiation are also known to increase breast cancer risk. In women, estrogen is produced mainly in the ovaries; it is also produced by fat cells and the adrenal gland. At the onset of puberty, estrogen plays a role in the development of so-called secondary sex characteristics, such as breasts, pubic hair and armpit hair.

Among many cancer types, breast cancer is the second most common cancer in women, exceeded only by skin cancers [1]. Being exceeded only by lung cancer, breast cancer is the second leading cause of cancer deaths in women. Breast cancer is currently the third leading cancer responsible for deaths of women of all ages with crude mortality rate of 5.6 per 100 000, exceeded only by Cervical cancer [2-4]. The chance of developing invasive breast cancer at some time in
a woman’s life is a little less than about 12%. A single genetically altered cell then grows into a tumor in a stepwise progression. There are several types of breast cancer, but some of them are quite rare [5]. In some cases a single breast tumor can be a combination of these types or be a mixture of invasive and in situ cancer. Breast cancer is a malignant tumor that starts in the cells of the breast, that is, a group of cancer cells that can grow into surrounding tissues or spread to distant areas of the body. It begins when breast cells start to grow out of control due to DNA damage which controls all cell actions in the body tissues [6]. However, with pregnancy, estrogen levels rise stimulating the dormant cancer cell to grow into a clinically detectable cancer. Breast cancer incidence rates are higher in non-Hispanic white women compared to African American women for most age groups. Incidence and death rates for breast cancer are lower among women of other racial and ethnic groups [7].

2. Mathematical Modeling of Estrogen

Based on many previous useful models done on tumour growth we here consider a model which subdivides the total population \( N(t) \) of cells of the breast tissue at any given time \( t \) into three groups which include normal or host cells, tumor cells and immune cells classes. The normal cells class, denoted by \( H(t) \) is in form of epithelial cells that make up the breast tissue. The cells differentiate and die normally as they have unaltered DNA which controls all cell actions. We assumed that the normal and tumor cells compete for space and resources in a small volume and therefore assumed a competition model. The normal cells grow exponentially at a per capita growth rate of \( \alpha_1 \) as a result of DNA initiation. \( \beta_1 \) is the depletion rate resulting from competition for resources such as nutrients and oxygen or the accumulation of substances released from cell metabolism within themselves. Tumor cells, denoted by \( T(t) \) at any time \( t \), represent a class of breast cancer cells with damaged DNA.

We assume the presence of a small tumor mass, that is, a tumor size that is close to zero relative to carrying capacity, and therefore the choice of growth law does not significantly affect the qualitative behaviour of the model since they only differ for large tumor sizes. We therefore assume an exponential growth of tumor cells with per capita rate of \( \alpha_2 \) which results from the damaged DNA. Analogously \( \beta_2 \) is a factor restricting their growth competition for space and food within themselves. The normal cells \( H(t) \) and tumor cells \( T(t) \) also compete for space and natural cell requirements like oxygen as they are supplied by the blood vessels. We assume cancer cells have uncontrolled cycle than the normal cells due to changed DNA which makes them fail to regulate a cell cycle and thus their interaction with normal cells results in an inhibitory effect on normal cells at rate \( \delta_1 \). The model includes an immune cells class, \( I(t) \), in form of Natural Killer (NK) cells and CD8 + T cells.

The population of immune cells is considered to be outside of the system and we assume a background level of NK cells, even in the absence of tumor with CD8+ T cells only present as a result of activation. It is therefore reasonable to assume a constant source, \( s \), of the immune cells from the thymus gland. Furthermore, in the absence of any tumour, the cells will die off naturally at a per capita rate of \( \mu \). The presence of tumor cells stimulates the immune response resulting in growth of immune cells. This is represented by a positive nonlinear growth term for immune cells which as a function of \( T(t) \), is positive, increasing and concave with the form \( \rho I(t)T(t)/(\omega + T(t)) \), where \( \rho \) is the immune response rate and \( \omega \) is the immune threshold rate, which is inversely proportional to the steepness of the immune response curve [5]. Furthermore, the reaction of immune cells and tumour cells can result in either the death of tumor cells at a rate \( \gamma_2 \) or the inactivation of the immune cells, with \( \gamma_3 \) as the interaction coefficient. After considering all these aspects, we present the following system of Lotka-Volterra type of differential equations to determine the dynamics of breast cancer cells [8]:
\[
\frac{dH}{dt} = H(\alpha_1 - \beta_1 H - \delta_1 T) - \alpha_1 HE \\
\frac{dT}{dt} = T(\alpha_3 - \beta_2 T) - \gamma_2 IT + \delta_2 HE \\
\frac{dI}{dt} = S + \frac{\mu IT}{\omega + T} - \gamma_3 IT - \mu I - \frac{\sigma_1 I E}{\sqrt{\omega + E}} \\
\frac{dE}{dt} = \pi - \theta E
\]

Initial and boundary conditions are \(H(0) = 1; T(0) = 10; I(0) = 1.4; E(0) = 2\).

3. Solution of Estrogen Model
The analytic solutions of the above equations are as follows:
\[
\frac{dH}{dt} - H\alpha_1 + \beta_1 H^2 + \delta_1 HT + \alpha_1 HE = 0 \\
\frac{dT}{dt} - T\alpha_3 + \beta_2 T^2 + \gamma_2 IT - \sigma_2 HE = 0 \\
\frac{dI}{dt} - S - \frac{\mu IT}{\omega + T} + \gamma_3 IT + \mu I - \frac{\sigma_1 I E}{\sqrt{\omega + E}} = 0 \\
\frac{dE}{dt} - \pi + \theta E = 0
\]

We construct a Homotopy as follows:
\[
(1 - \rho) \left( \frac{dH}{dt} - H\alpha_1 \right) + \rho \left( \frac{dH}{dt} - H\alpha_1 + \beta_1 H^2 + \delta_1 HT + \alpha_1 HE \right) = 0
\]
\[
(1 - \rho) \left( \frac{dT}{dt} - T\alpha_3 \right) + \rho \left( \frac{dT}{dt} - T\alpha_3 + \beta_2 T^2 + \gamma_2 IT - \sigma_2 HE \right) = 0
\]
\[
(1 - \rho) \left( \frac{dI}{dt} - S + \mu I \right) + \rho \left( \frac{dI}{dt} - S - \frac{\mu IT}{\omega + T} + \gamma_3 IT + \mu I - \frac{\sigma_1 I E}{\sqrt{\omega + E}} \right) = 0
\]
\[
(1 - \rho) \left( \frac{dE}{dt} + \pi + \theta E \right) + \rho \left( \frac{dE}{dt} - \pi + \theta E \right) = 0
\]

Let \(H = H_0 + H_1 \rho + H_2 \rho^2 + \cdots\)
\(T = T_0 + T_1 \rho + T_2 \rho^2 + \cdots\)
\(I = I_0 + I_1 \rho + I_2 \rho^2 + \cdots\)
\(E = E_0 + E_1 \rho + E_2 \rho^2 + \cdots\)

\(\rho^0: dH_0 dt - \alpha_1 H_0 = 0\)
\(\frac{dH_0}{dt} - \alpha_3 T_0 = 0\)
\(\frac{dT_0}{dt} - S + \mu I_0 = 0\)
\(\frac{dI_0}{dt} - \pi + \theta E_0 = 0\)

\(\rho^1: dH_1 dt - \alpha_1 H_1 = -\beta_1 e^{2\alpha_1 t}\)
\(\frac{dH_1}{dt} - \alpha_3 T_1 = -\beta_2 (100 e^{2\alpha_1 t})\)
\(\frac{dT_1}{dt} + \mu I_1 = 0\)
\(\frac{dI_1}{dt} + \theta E_1 = 0\)

Therefore the approximate solutions are
\[H(t) = e^{\alpha_1 t} + \left(1 + \frac{\beta_1}{\alpha_1}\right)\]
\[T(t) = 10 e^{\alpha_3 t} + 10 \left(1 + \frac{\beta_2}{\alpha_3}\right) e^{\alpha_3 t} - \frac{100 \beta_2}{\alpha_3} e^{2\alpha_3 t}\]
\[I(t) = (1.4 - \frac{S}{\mu}) e^{-\mu t} + \frac{S}{\mu} + 1.4 e^{-\mu t}\]
\[E(t) = \frac{\pi}{\theta} (1 - e^{-\theta t}) + 2 e^{-\theta t}\]

4. Conclusion
The mathematical modeling arises which of the HPM methods is better. The models should be improved to better reflect the breast cancer evolution and its therapy using vaccine. The results clearly show a negative relationship of estrogen amounts and tumor cell development. The development of tumor cells depends on the ability of the normal cells to combat tumor cells in the absence of excess estrogen and on estrogen levels plus immune compatibility in case of excess estrogen levels. However, it must be noted that it may also depend on genetics of an individual like the ability of DNA to resist change in structure and amount of estrogen released during natural biological processes like menopause and premenopause stages.
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