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Mathematical Modeling for the Tumor Growth in the Bladder

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Abstract

The early detection of bladder cancer is a challenging problem, due to structure of cancer cells. The aim of this paper is to presents mathematical modeling describe the tumor growth in the bladder. This model is used for detecting the cancer in its early stages. The segmentation results will be used as a base for a computer aided diagnosis (CAD) system for early detection of the cancer which will improve the chances of survival of patient.

Keywords: Cancer detection, Image segmentation.

1. Introduction

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer is the second leading cause of death in the Iraq. About one-half of all men and one-third of all women in the Iraq will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer [1].

Each year in the Iraq, bladder cancer is diagnosed in 38,000 men and 15,000 women. This is the most common type of cancer in men and the eighth most common in women. (According to a report from the National Cancer Institute) [2].

Before beginning to model diagrams of this disease, I would like to discuss the possible causes, symptoms, diagnosis, treatments and rehabilitation. In addition, I will provide information to help patients cope with bladder cancer [3].

Scientists throughout the world are learning more about bladder cancer and its causes. They are exploring new ways to prevent, detect, diagnose and treat this disease.

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2. The Bladder

The bladder is a hollow organ in the lower abdomen. It stores urine, the liquid waste produced by the kidneys. Urine passes from each kidney into the bladder through a tube called a urethra [4].

The inner lining of the bladder is surrounded by an outer layer of muscle. When the bladder is full, the muscles in the bladder wall tighten to allow for urination. Urine leaves the bladder through another tube, called the ureter [5].

3. Defining Parts of the Cancer

To define the parts of the cancer we have to better understand cancer.
Cancer is a group of many related diseases and which begin in cells, the body's basic unit of life. As seen in basic biology, cells make up the organs of the body. When functioning correctly, cells grow and divide to form new cells as the body needs them. Normally the new cells will take the place of the old cells when they die.

Sometimes this process breaks down. The new cells form when the body does not need them, and the old cells do not die when they should. These extra cells can form a mass of tissue called a growth, or tumor.
Tumors can be divided into two categories, benign and malignant [6].

3.1. Benign Tumors

Cells from benign tumors do not spread to other parts of the body. This type of tumor is not considered cancerous, and can be removed by a doctor. In most cases once benign tumors are removed they do not reappear.

3.2. Malignant Tumors

Cells from malignant tumors are considered cancer. This type of cell can invade and damage nearby tissues and organs. Cancer cells can break away from a malignant tumor and enter the bloodstream, or the lymphatic system. This is how cancer cells spread from the original (primary) tumor to form new tumors in other organs. The spread of cancer is called metastasis.

The wall of the bladder is lined with cells called transitional cells and squamous cells. Studies performed by The National Cancer Institute found that more than 90 percent of bladder cancers originate in the transitional cells. This type of bladder cancer is called transitional cell carcinoma. Squamous cell carcinoma accounts for eight percent of bladder cancer patients. When cancer is found only in the lining of the bladder, it is called superficial bladder cancer. Physicians often call this carcinoma in situ. This type of bladder cancer will often come back after treatment. If this happens, the disease most often recurs as another superficial cancer in the bladder.
In this type of cancer the superficial tumor may grow through the lining and into the muscular wall of the bladder.

This is known as invasive cancer. Invasive cancer may extend though the bladder wall. It may grow into a nearby organ such as the uterus or vagina (in women) or the prostate gland (in men). It also may invade the wall of the abdomen. When bladder cancer spreads outside the bladder, cancer cell often found in nearby lymph nodes. If cancer has reached these nodes, cancer cells may have spread to other lymph nodes or other organs, such as the lungs, liver, or bones.

If bladder cancer spreads to the lungs, the cancer cells in the lungs are actually ladder cancer cells. The disease is metastatic bladder cancer, not lung cancer.

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4. Description of Models for Tumor Growth

Instead of dealing with individual cells, this model represents the population of the tumor or the tumor's volume. We will consider the growth of a population as a function of time.

let x be the number of individual cells at time t.

We assume that the rate of change of the population is proportional to the number of individuals in it at any time, we have the following differential equation;

$\frac{dx}{dt} = \gamma x$ …….. (1),

where γ is a constant of proportionality. The population x is positive and is increasing.

Therefore, $\frac{dx}{dt} > 0$ and from equation (1) we must have $\gamma > 0$.

Suppose at time, t_0 the population of tumors is x_0,then in addition to the differential equation (1), we have the initial condition:

$x(t_0) = x_0$ …….. (2),

The differential equation (1) is separable. Separating variables, integrating and simplifying, we have:

$x = ce^{\gamma t}$ …… (3).

Applying the initial condition (2), i.e., $x = x_0$ at $t = t_0$ in equation (3) to this we have:

$x_0 = c\, e^{\gamma t_0}$ ……(4)

Solving equation (4) for c, we obtain:

$c = x_0\, e^{-\gamma t_0}$ …… (5)

Substitute equation (5) in equation (3) we get:

$x = x_0 e^{\gamma (t - t_0)}$ …… (6)

Equation (6) is the equation for exponential growth. Here γ is related to the tumor's doubling time.

Equation (6) is a good model for a tumor of the earliest stages of growth.

This model is not good for the steady state that is observed in more developed solid tumors supported by diffusion.

5. Logistic Law of Cancer Tumor Growth

The tumor's cell population growth is represented more realistically in many cases by assuming that the number x(t) of individual cells in the population at time t is: described by a differential equation of the form:

$\frac{dx}{dt} = \gamma x - \beta x^2$ …….. (7)

Where $\gamma > 0$ and $\beta > 0$ are constants.

The additional term - βx^2 is the result of some cause that tends to limit the ultimate growth of the population. For example, such a cause could be the radiation therapy,

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chemotherapy, or biological therapy when the population becomes sufficiently large, as the tumor grows.
Concerning the choice of - βx^2 for the term representing the effect of the cause, one can argue as follows:
Suppose the cause affects the entire cell population in the tumor with x members, then the effect on any one individual cell is proportional to x. Thus the effect on all x individuals in the population would be proportional to $x \cdot x = x^2$.

Assuming that the tumor cell population is described by a differential equation of the form (7) with constant $\gamma > 0$ and $\beta > 0$, and initial condition of the form (2).
In such cases, it turns out that the constant β is very small compared to the constant γ ($\gamma >> \beta$).
Thus, for a sufficiently small number x of cells, the term γx predominates, and so the tumor cell population grows very rapidly for a time.
However, as the tumor grows by diffusion and x becomes sufficiently large, the term $-\beta x^2$ (by radiation, chemo, or biological therapy) is of comparatively greater influence, and the result of this is a decrease in the rapid growth rate.
Note: The differential equation (7) is a separable equation, now, we solve this equation as follow:

$$\frac{dx}{dt} = \gamma x - \beta x^2$$

where γ and β are positive constant and $\gamma >> \beta$

$$\frac{dx}{\gamma x - \beta x^2} = dt \quad \ldots\ldots\ldots\ldots\ldots\ldots (8)$$

$$\frac{dx}{x(\gamma - \beta x)} = dt \quad \ldots\ldots\ldots\ldots\ldots\ldots (9)$$

and hence:

$$\frac{dx}{x\left[1 - \frac{\beta}{\gamma} x\right]} = dt \qquad \ldots\ldots\ldots\ldots (10)$$

using partial fraction, this becomes:

$$\left[\frac{1}{x} - \frac{-\beta}{\gamma - \beta x}\right] dx = dt \qquad \ldots\ldots\ldots\ldots\ldots\ldots (11)$$

By integrating and solving for x, we obtain:

$$\ln x - \ln(\gamma - \beta x) = t + c, \quad \ldots\ldots\ldots\ldots\ldots\ldots (12)$$

then;

$$\frac{x}{(\gamma - \beta x)} = e^{t+c} = c_1 e^t \text{, where } c_1 = e^c$$

so,

$$x = (\gamma - \beta x)\, c_1 e^t, \quad \ldots\ldots\ldots\ldots\ldots\ldots (13)$$

$$x + \beta c_1 x e^t = \gamma c_1 e^t \quad \ldots\ldots\ldots\ldots\ldots\ldots (14)$$

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and

$x(1 + \beta c_1 e^t) = \gamma c_1 e^t$ ..... (15)

hence:

$$x = \frac{\gamma c_1 e^t}{(1 + \beta c_1 e^t)} \text{ ..... (16)}$$

Applying the initial condition in equation (2) for equation (16), we obtain:

$$x_0 = \frac{\gamma c_1 e^{t_0}}{(1 + \beta c_1 e^{t_0})} \text{ ..... (17)}$$

Hence,

$$c_1 = \frac{x_0}{(\gamma - \beta x_0) e^{t_0}} \text{ ..... (18)}$$

Then substitute equation (18) in equation (16) we get:

$$x = \left(\frac{\gamma x_0}{(\gamma - \beta x_0)}\right) e^{t - t_0} / \{1 + \beta x_0 e^{t-t_0} / (\gamma - \beta x_0)\} \text{ ..... (19)}$$

Let $y_0 = \frac{x_0}{(\gamma - \beta x_0)}$

Then we have:

$$x = \frac{\gamma y_0 e^{(t - t_0)}}{(1 + \beta y_0 e^{(t - t_0)})} \text{ ..... (20)}$$

We see how large the cancer cell population will ultimately be.
We can assume that the differential equation (7) applies for time $t \to \infty$ then we can evaluate limx as $t \to \infty$ by using solution (20) of (7).

$$\lim_{t \to \infty} x = \lim_{t \to \infty} \frac{\gamma y_0 e^{\gamma (t - t_0)}}{1 + \beta y_0 e^{\gamma (t - t_0)}} = \frac{\gamma}{\beta}$$

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