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# Scope of Nanotechnology in Radiation Treatment Planning

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**Abstract**

In this paper an attempt has been made to study some of the elements of mathematical modeling in solid tumor growth. We present simple deterministic mathematical models used to describe tumor growth. Radiation therapy can be made very effective through the use of nanoscale particles such as gold nanoparticles, carbon nanotubes and magnetic nanoparticles. Development of a model using all the necessary biological assumption has been illustrated through an example. A large number of drug delivery systems have been developed over the years to overcome the challenges in cancer treatment and hence improve the right balance between effectiveness and toxicity. Finally we present various aspects of our methods and their results .The results demonstrate that the use of nanoscale particles in radiation treatment planning holds a lot of potential to improve the efficiency of the treatment.

*Keywords:* mathematical modelling; nanotechnology; radiation therapy, gold nanoparticles (GNPs) ;carbon nanotubes (CNT).

## 1. Introduction

A Mathematical model is an abstract mathematical expression used to describe the behaviour of the system. A tumor growth model gives the measure of tumour volume at a specified period of time. In this section we discuss some of the deterministic and probabilistic mathematical models currently in use to understand the growth of tumor. Mathematical modelling problems are classified as white box or black box models. Mathematical modelling in general consists of three stages:

- defining the problem
- testing the model
- acceptance or rejection of model

In the first stage, model is defined considering all the necessary biological assumptions. In the second stage the model is tested against the experimental data by selecting a suitable test statistic. The model evaluation part is one of the crucial parts in modelling as it shows whether the data suffice to explain the model accurately or not. In the third stage we draw all the inferences and conclude by accepting or rejecting a model. If a model is rejected then necessary changes are made in assumptions. Sometimes a model is rejected if there is inadequate number of assumptions or wrong assumption(s).

Radiation treatment planning to a cancer patient has been improving all the time and it shows a lot of promise in near future. Tumors are treated primarily using one or combination of the following methods: chemotherapy, surgery, radiotherapy (internal and external beam radiotherapy).There are some more methods used to treat cancerous tumors like thermotherapy, biological therapy, hormone therapy and stem cell therapy.

In the current scenario of radiation treatment nano particles have a huge role to play because of its unexpected optical, mechanical and magnetic properties. Nowadays nanotechnology is used in almost all the areas of health care and particularly so in radiotherapy. The medical application of nanotechnology is also referred as nanomedicine. Cancer Nanotechnology provides a larger picture of the methods currently used in cancer therapy and to an extent provides promising solutions to many of the therapies. Radiotherapy can be made effective through the use of nanoscale particles. The major aim in developing a nanoscale particle in drug delivery system is to enhance the therapeutic effect and in turn reduce the toxicity of other active materials. Gold nanoparticles have the potential to be useful in therapeutic situations as they come with a size of 50 nm. Carbon nanotubes are generally used in photodynamic irradiation therapy of targeted cancerous cells.In photodynamic irradiation therapy,carbon nanotubes are targeted to tumor tissues using a small molecular compound or a specific tumor antibody and are irradiated with an near infra-red lasers(NIR).carbon nanotubes are synthesized mainly by the methods, laser ablation,arc discharge synthesis and chemical vapour deposition. The size of carbon nanotubes is less than 100 nm. Magnetic nanoparticles have a size of 10 nm and are synthesized by co-precipitation of $Fe^{2+}$ and $Fe^{3+}$ aqueous salts and by adding a suitable base.

## 2. Some Mathematical Models

The mathematical models are generally divided into three categories: Empirical models, Functional models and structural models. In this paper a study has been made of empirical models with respect to their metabolic considerations.

Simple Exponential growth curve is given by

$$\frac{dL}{dt} = \lambda L \quad ; \lambda > 0$$

(1)

where L denotes the total number of carcinogenic cells and $\lambda$ denotes the intrinsic growth rate. Equation (1) has a solution

$$L(t) = L(t_0)e^{\lambda(t-t_0)}$$

(2)

where $L(t_0)$ is the tumor size at time $t = t_0$.

Since the growth is unrestricted verhulst *et al.*considered that for a stable growth a saturation level has to be achieved. To achieve this tumor growth model a multiplier $\frac{K-N}{K}$ is used which represents the fraction of the current size from the saturation level $K$ .The well known logistic growth equation can be obtained by expanding $f(L)$ by Taylor series method at origin. The Taylor series in one variable is given by

$$f(L) = f(0) + Lf'(0) + \frac{L^2}{2!}f''(0) + \frac{L^2}{3!}f'''(0) + ......$$

(3)

Neglecting the higher order terms, we get

$$f(L) = f(0) + Lf'(0) + \frac{L^2}{2!}f''(0)$$

(4)

Since, initially a zero population has a zero growth, we have $f(0) = 0$

Therefore, we obtain

$$f(L) = L\left[f'(0) + \frac{L}{2}f''(0)\right]$$

(5)

By setting $f'(0) = \lambda$ and $f''(0) = \frac{-2\lambda}{k}$ ,one obtains the Logistic growth equation

$$\frac{dL}{dt} = \lambda L\left[1 - \frac{L}{K}\right]$$

(6)

where $\lambda$ and $K$ are constants.

This logistic differential equation gives the recovery time of the non cancerous cells after they have been distributed by the same internal and external forces. If initially at $t = t_0$ ,we have $L(t_0) = L_0$ ,then $L_0 > K$ or $L_0 < K$ ,where $K$ is the carrying capacity. The tumor growth level for the time $t > t_0$ is given by the solution of the logistic differential equation (6)

$$L(t) = \frac{1}{\frac{1}{K} + \left(\frac{1}{L_0} - \frac{1}{K}\right)e^{-\lambda(t-t_0)}}$$

(7)

shows the graph of the solution of the logistic equation when $L_0$ is greater than, is equal to or is less than the saturation level. The expression (7) is assumed to hold good after a single irradiation of normal cells. In the procedure of radiation treatment planning the restitution of normal cells is incomplete and this will affect the carrying capacity $K$ .

The growth pattern in all the tumors is more or less the same. All the tumors increase rapidly in the beginning, till they reach the maximum size. The main disadvantage in simple exponential growth model is that it is unable to model the behavior *in vivo*.

The generalized Logistic equation is given by

$$\frac{dL}{dt} = \lambda L^\alpha \left[1 - \left(\frac{L}{K}\right)^\beta\right]^\nu$$

(8)

Equation (8) includes as a special case the well known logistic differential equation $(\alpha = 1, \beta = 1, \nu = 1)$ , Blumberg's growth equation $(\beta = 1)$ and the Richard equation $(\alpha = 1, \nu = 1)$ .All the three models have been used to describe the tumor growth. It is very interesting to note that the generalized logistic growth equation gives arise to two important models of tumor growth based on their metabolic considerations .For $\nu = 1$ , the generalized logistic growth equation reduces to Von Bertalanffy equation $(\alpha = \frac{2}{3}, \beta = \frac{1}{3})$ , given by

$$\frac{dL}{dt} = \lambda L^{\frac{2}{3}} \left[ 1 - \left( \frac{L}{K} \right)^{\frac{1}{3}} \right]$$

(9)

Solution of the differential equation (4) gives

$$L(t) = K \left\{ 1 - \left[ 1 - \left( \frac{L_0}{K} \right)^{\frac{1}{3}} \right] e^{\left( \frac{-\lambda t}{3K^{\frac{1}{3}}} \right)} \right\}^3$$

(10)

According to Von Bertalanffy *et al.* the rate of degradation and the rate of growth are proportional to the power of the tumor volume. Based on the metabolic considerations we have considered two more growth models, The first growth model is given by

$$\frac{dL}{dt} = \lambda L^{\frac{3}{4}} \left[ 1 - \left( \frac{L}{K} \right)^{\frac{1}{4}} \right]$$

(11)

and the solution of the differential equation (11) is obtained by setting $L = L_0$ at $t = 0$, and it can be written as

$$L(t) = K \left\{ 1 - \left[ 1 - \left( \frac{L_0}{K} \right)^{\frac{1}{4}} \right] e^{\left( \frac{-\lambda t}{4K^{\frac{1}{4}}} \right)} \right\}^4$$

(12)

The second growth model is given by

$$\frac{dL}{dt} = \lambda L^{\frac{1}{4}} \left[ 1 - \left( \frac{L}{K} \right)^{\frac{3}{4}} \right]$$

(13)

and the solution of the differential equation (13) is obtained by setting $L = L_0$ at $t = 0$, and can be written as

$$L(t) = K \left\{ 1 - \left[ 1 - \left( \frac{L_0}{K} \right)^{\frac{3}{4}} \right] e^{\left( \frac{-\lambda t}{4K^{\frac{3}{4}}} \right)} \right\}^4$$

(14)

Gompertz growth curve can be derived as a special case of the generalized two parameter model of growth. It is described by the equation

$$\frac{dL}{dt} = \lambda L \left[ \ln \frac{K}{L} \right]$$

(15)

George W Swan *et al.* reduced the non linear differential equation (7) to a linear one by the transformation

$$X = \ln \frac{K}{L}$$

(16)

and the solution of the differential equation (16) can be written in the form of

$$L = Ke^{-\ln\left(\frac{K}{L_0}\right)e^{-\lambda(t-t_0)}}$$

(17)

## 3. Gold Nanoparicles (GNPs)

Nanoscale particles exhibit a lot of unusual optical, electronic and magnetic properties .Interestingly GNPs have attracted a lot of attention in health care system because of its physicochemical properties.GNPs efficiency has already been demonstrated *in vitro* and *in vivo* in a mathematical model on mice.GNPs have been synthesized from the 19th century, they can enter into the cells and act as novel agents in cancer therapy. The two common methods for the production of GNPs are

- Produced in a liquid by citrate reduction of $Au^{3+}$ such as aurochloric acid ($Haucl_4$) in water to $Au^{0+}$

- Two phase synthesis and stabilization by thiols.

## 4. Carbon Nanotubes(CNTs)

Carbon nanotubes are synthesized mainly by the methods, laser ablation, arc discharge synthesis, plasma torch, removal of catalysts and chemical vapour deposition. CNTs can be categorized by their structure as single- wall, double-wall and Multi-wall Nanotubes. Additionally, there are some of the the carbon nanotubes which are biodegradable such as polyhydroxyalkanoates.The strength and flexibility of CNTs make them of potential use and has garnered a lot of attention in real time research because of its mechanical, electrical,physical and chemical properties. As more and more CNTs will be produced in near future, the main goal would be to understand the toxicity of it. To obtain more accurate results researchers should use more reliable methods for detection. However, long term application of carbon nanotubes may be associated with cancer risk. Table 1 briefly depicts the Applications and toxicity of GNPs and CNTs.

|  | Applications | Toxicity |
|---|---|---|
| Gold Nanoparticles | <ul><li>Photo thermal therapy</li><li>Specific target tissues or cells in radiotherapy</li><li>Used as radiosensitisers</li><li>Excellent drug delivery vehicles</li><li>Cancer imaging</li><li>Anti-cancer conjugates</li></ul> | S  kin reactions |
| Carbon Nanotubes | <ul><li>Micro beam  radiotherapy</li><li>Used in biomedical applications</li><li>*In vivo* and *in vitro* analysis, they move into cells by receptor mediated endocytosis</li><li>X-ray source array surrounding the target of irradiation</li><li>Low cost MRT devices</li></ul> | <ul><li>Oxidation stress</li><li>Inflammatory responses</li><li>Malignant transformation</li><li>Interstitial fibrosis</li><li>DNA damage and mutation</li></ul> |

## 5. Conclusions

It is significant to mention that the models used here to describe tumor growth are capable enough to be evaluated. Some other basis, such as estimation of parameters, biological considerations and prediction of the growth of the curve by calculating the tumor doubling time can be used for selecting an appropriate model.

Since GNPs have a high atomic number, so they have more capacity of absorption of kilo voltage X- rays, which helps us to use them as contrast agents. GNPs come in lot of sizes varying from 1 nm to 50 nm, so they can easily penetrate throughout the body and can easily accumulated at the tumor site  At kilo voltage photon energy, nanoparticles of gold can cause radiosensitisation.Lot of research is been carried in checking the toxicity of GNPs, so it has got the potential to be used in clinical trials. On a global scale, lot of efforts in nanotechnology has been seen, so a lot of scope there and the questions pertaining to GNPs will be addressed in a rigorous way in future by keeping a check on its toxicity.CNTs are extremely versatile as they can be used in many fields owing to their excellent material properties. Therefore more study on toxicity of GNPs and CNTs are recommended so that they can augment the available data. Nanotechnology in radiotherapy is a relatively unexplored area and the rate at which the research is been carried out is highly commendable, so in near future a lot of nano materials will be used in cancer treatment.

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