Available online at www.sciencedirect.com
ScienceDirect
Applied Mathematics and Computation 189 (2007) 1246–1254
APPLIED MATHEMATICS AND COMPUTATION
www.elsevier.com/locate/amc

Mathematical modeling of chemotherapy strategies in vascular tumor growth using nanoparticles

Somna Mishra [a,*], V.K. Katiyar [b], V. Arora [a]

[a] Department of Mathematics and Statistics, Gurukula Kangri Vishwavidyalaya, Haridwar, Uttaranchal, India
[b] Department of Mathematics, Indian Institute of Technology, Roorkee, Uttaranchal, India

Abstract

Throughout various fields of science and technology, a push towards the use of nanoscale technology is well underway. One area where nanoscale work is already well underway is within the field of drug delivery. Nanoscale devices carrying chemotherapeutic drugs could extravasate from blood vessels and even diffuse through the tissue and enter tumor cells. Drug delivery through nanoparticles presents significant potential advantages over traditional delivery via bolus injection. Drug release kinetics at the tumor site is an important aspect of chemotherapy.

In this paper, we have developed a mathematical model that describes the chemotherapy strategies in spherically symmetric tumor. A system of partial differential equations is used to describe the drug concentration in the tumor cell, the cell movement whose divergence defines the local specific mass growth rate and the expression for the radius of the tumor cell.

The analytical and numerical techniques are used to illustrate the tumor's response to various chemotherapeutic strategies (i.e. for 10 nm and 100 nm) and the analytic expressions are also developed.

Keywords: Tumor; Chemotherapy; Nanoparticles

1. Introduction

Nanotechnology is the frontier research area of the twenty first century. In recent years, we have gained a better understanding of the mechanism responsible for cell recognition, transport of biological molecules across membranes and the mechanisms that regulate cell function. The concurrent progress and sophistication of organic synthetic chemistry, has sparked optimism for the development of 'intelligent medicines'' (i.e. drugs that are actively directed to the target cell, actively translocated across the membrane, and specifically intervene with a particular function in the cell). One area where nanoscale work is well underway is within the field of drug delivery. In drug delivery, nanoparticles are fabricated in order to entrap and deliver specific pharmaceutical agents to various locations in the body.

* Corresponding author.
E-mail address: mishra_somna@yahoo.com (S. Mishra).

0096-3003/$ - see front matter
doi:10.1016/j.amc.2006.12.057

Traditional drug delivery methods include oral and intravenous routes of administration. Oral delivery via tablets or capsules is largely inefficient due to exposure of the pharmaceutical agent to the metabolic processes of the body. Therefore a larger than necessary dose is often required and the maximum effectiveness of the drug is limited. Traditional intravenous (IV) administration is much more problematic. Specificity for IV injectable drugs is often low, necessitating large amounts of a drug to be injected into a patient, creating a high concentration of the drug in the blood stream that could potentially lead to toxic side effects. Nanoparticle drug delivery provides a more efficient, less risky solution to many drug delivery challenges. Nanoparticles are generally defined as particles between 10 nm and 1000 nm in size. Applications of nanotechnologies in medicines are especially promising in the longer term. These can be expected to enable drug delivery targeted at specific sites in the body so that, chemotherapy is less invasive.

There are numerous models that describe the tumor behavior. Anderson and Chaplain [1] presented both continuous and discrete mathematical models, which described the formation of capillary sprout network in response to chemical stimuli (tumor angiogenic factor, TAF) supplied by a tumor. McDougall et al. [2] generated theoretical capillary networks using the discrete mathematical model of Anderson and Chaplain [1]. Byrne and Chaplain [3] described the growth of non-necrotic tumors in the presence and absence of inhibitors. Cui and Friedman [4] also studied the model of Necrotic tumor growth. Later Zheng et al. [5] presented a full non-linear, two-dimensional simulation, showing the potential of virtual cancer simulator. Sinek et al. [6] developed a model for two-dimensional chemotherapy simulations that demonstrate fundamental transport and tumor response limitations involving nanoparticles.

Although the clinical arsenal in treating tumor has been greatly extended in recent years with the application of new drugs and therapeutic modalities, the three basic approaches continue to be surgical resection, radiation, and chemotherapy. A significance proportion of research is focused on improving the efficacy of chemotherapy and the drug release kinetics at the tumor site is an important aspect of chemotherapy [7]. In this paper, we have proposed a mathematical model that describes the nanodrug delivery in a vascular tumor using the nanoparticles on the order of 10 nm and 100 nm.

2. Mathematical formulation

Over the past two decades, tumor growth has been fertile for mathematical modeling and many models have appeared in this era. Treating the tumor as a growing spherical mass, with radial symmetry [4], a one-space-dimensional model is used to describe the tumor response to the Nanodrug delivery. The tumor consists of a spherical core of dead cells (necrotic core) and a spherical shell of life-proliferating cells surrounding the core (non-necrotic shell). The non-necrotic region receives its blood supply through a developed network of capillary vessels (vascularized tumor). The blood supply provides the non-necrotic region with nutrients. Across the microvascular wall, the transport of molecules is mainly due to convection while diffusion is also important. Convection depends on the nutrient concentration in the blood stream, while the diffusion is proportional to the difference of the vascular and interstitial concentration [6]. We assume that 1–10 nm particles convect from the vasculature, diffuse through the tumor interstitial, and enter cancer cells just as do nutrients or drug molecules, and so the net local rate of chemotherapeutic nanodrug delivery from the neo-vasculature and uptake by the tumor cells as [6]

$$S = v_1\left(\frac{s_v - s}{n_v}\right)\delta - \eta\frac{s}{n_v},$$

where s is the local chemotherapeutic carrier concentration; s_v, the chemotherapeutic carrier concentration in vasculature; n_v, the nutrient and chemotherapeutic carrier concentration in the vasculature; η, the rate of drug loss due to decay, cellular uptake and metabolism; v_1, the transfer coefficient from the vasculature and δ is the indicator function of vasculature (1 where it exists, 0 otherwise).

Consider an spherically symmetric tumor of radius $R(t)$. The local volume changes accompanying cell proliferation and death produce cell movement. So we associate a local cell velocity $u(r,t)$ with cell movement.