Available online at www.sciencedirect.com
ScienceDirect
Mathematics and Computers in Simulation 124 (2016) 1–15
MATHEMATICS AND COMPUTERS IN SIMULATION
www.elsevier.com/locate/matcom

Original articles

A mathematical model of cancer treatment by radiotherapy followed by chemotherapy

Zijian Liu[a,b,*], Chenxue Yang[c]

[a] *College of Mathematics and Statistics, Chongqing Jiaotong University, Chongqing 400074, PR China*
[b] *Department of Mathematics, Hangzhou Normal University, Hangzhou, Zhejiang 310036, PR China*
[c] *School of Computer Science and Engineering, University of Electronic Science and Technology of China, Chengdu 610054, PR China*

Received 27 November 2010; received in revised form 28 August 2015; accepted 23 December 2015
Available online 29 January 2016

Abstract

A periodic mathematical model of cancer treatment by radiotherapy followed by chemotherapy is presented and studied in this paper. Sufficient conditions on the coexistence of the healthy and cancer cells are obtained. Conditions on the existence and globally asymptotic stability of the positive periodic solution, the cancer eradication periodic solution and the cancer win periodic solution are derived. Numerical examples are shown to verify the validity of the results. A discussion is presented for further study.

Keywords: Radiotherapy; Chemotherapy; Coexistence; Cancer eradication periodic solution; Cancer win periodic solution

1. Introduction

Cancer is a well-known killer of humans world wide, and its treatments are varied and sporadically successful. The main types of cancer treatments involve surgery, chemotherapy, radiotherapy and immunotherapy, either in isolation, or in combination of two or more of these. In this paper, we consider cancer treatment by radiotherapy followed by chemotherapy.

Radiotherapy has been proven to be an effective tool in combating with cancer as a primary treatment strategy [18,22]. Radiation therapy uses radiation to kill malignant cells. This treatment targets rapidly reproducing cells such as those in cancer [23]. Therefore, when cancer cells are irradiated, there is a lesser effect on more slowly reproducing surrounding healthy cells. Recently, some mathematical models that focus on cancer treatment by radiotherapy have been presented and studied [12,3,4,8,11]. Liu and Zhong in [12] discussed dynamical behaviors of normal cells that affected by periodic radiation, they established conditions on the permanence and extinction of the normal and radiated cells and obtained criteria on the existence and globally asymptotic stability of unique positive periodic solutions of the

* Corresponding author at: College of Mathematics and Statistics, Chongqing Jiaotong University, Chongqing 400074, PR China. Tel.: +86 18225022503; fax: +86 23 62652254.
E-mail addresses: hbliuzijian@126.com (Z. Liu), yang.chenxue@163.com (C. Yang).

http://dx.doi.org/10.1016/j.matcom.2015.12.007
0378-4754/

system. Belostotski in [3] presented a mathematical model to represent the interactions between healthy and cancer cells subject to radiation, where the interactions between healthy and cancer cells were viewed as competition for bodily resources. Four different control mechanisms of radiation delivery: continuous constant radiation, continuous radiation that is proportional to the instantaneous cancer concentration, continuous radiation that is proportional to the ratio of cancer to healthy cell concentration, and periodic administration of radiation were featured and conditions on each case that guarantee the cancer to be cure or treatment were obtained under the hypothesis that the effect of radiation on healthy cells ideally is zero. In [4], Belostotski and Freedman developed and analyzed a mathematical model of cancer treatment by radiotherapy using control theory, where the radioactivity only affected the cancer cells. Later, considering the fact that the radiation also may affect the healthy cells to some extent during the radiotherapy, Freedman and Belostotski in [8] extended the previous study by perturbing the previous models. They considered four types of treatment delivery: constant, linear, feedback and perturbed periodic deliveries. For each case, they established sufficient conditions on the cure state and treatment state. However, paper [8] only considered the perturbed periodic radiation, although paper [4] investigated the periodic radiation, it was supposed that the effect of radiation on healthy cells is zero. Hence, Liu and Yang in paper [11] studied a periodic mathematical model of cancer treatment by radiotherapy. They established some sufficient conditions on the coexistence of the healthy and cancer cells, the existence and globally asymptotic stability of the positive periodic solution, the cancer eradication periodic solution and the cancer win periodic solution.

Chemotherapy, as one of cancer treatment methods, has also been investigated extensively from the perspective of mathematical modeling [6,27,19,16]. With respect to optimal control of drug treatment schedules, paper [6] investigated four different mathematical models that based on two different sets of ordinary differential equations containing either chemotherapy, immunotherapy, anti-angiogenic therapy or combinations of these. Different parameter sets, scenarios and objective functions optimal control problems were solved numerically using Bock's direct multiple shooting method. In paper [27], the effect of initial tumor biomass was studied applying numerical analysis method to a competition model describing tumor-normal cell interaction with periodically pulsed chemotherapy. Some properties of the set of initial tumor and normal cell biomasses for successful treatment were derived. On the basis of these properties, a numerical method was constructed for locating the boundary of such a set. Paper [16] modeled the response of spatially structured tumors to chemotherapy and investigated the action of a single chemotherapeutic drug on the tumor as well as explored how different drug kinetics and treatment regimes may affect the final treatment outcome. It obtained that a single infusion of drug is more effective than repeated short applications.

Naturally, cancer treatment using the combination of radiotherapy with chemotherapy were focused on by the subsequent research. Paper [5] reported some results observed in a large randomized study comparing radiotherapy alone to combined radiotherapy and chemotherapy in unresectable squamous cell and large cell lung carcinoma. 177 patients received radiotherapy alone, and 176 received the combined treatment. The 2-year survival rate was 14% for patients receiving radiotherapy vs. 21% for patients receiving the combined treatment and the distant metastasis rate was significantly lower in the group receiving the combined treatment. In [17], the authors revealed that adjuvant chemotherapy combined with postoperative radiotherapy could probably reduce disease progression and overall death in patients with advanced-stage disease. More literature about the combination of radiotherapy with chemotherapy could be seen [14,9,21,1,2]. It is worthy of noticing that nearly all of these studies are clinical trials.

No matter radiotherapy or chemotherapy always has harm to the healthy cells to some extent. The intent of this paper is to establish a model for cancer treatment with radiotherapy followed by chemotherapy and investigate its dynamical behaviors. It is rarely presented and studied from the view of mathematical modeling to cancer treatment by radiotherapy in combination with chemotherapy. Hence, the investigation of the mathematical model to cancer treatment with radiotherapy in combination with chemotherapy in this paper is of major importance.

This paper is organized as follows. In Section 2, the model of cancer treatment with radiotherapy followed by chemotherapy is presented and a basic Theorem is established. Conditions for the coexistence of the healthy and cancer cells are obtained in Section 3. In Section 4, sufficient conditions on the existence and globally asymptotic stability of the positive periodic solution, the cancer eradication periodic solution and the cancer win periodic solution are derived. Numerical simulations are shown to verify the validity of the Theorems in Section 5. Finally, the results are discussed and an interesting problem is presented for further study.