Stochastic Programming on Optimal Drug Administration for Two Stage Cancer Treatment Problems

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ABSTRACT
Either Continuous drug administration or continuous drug vacation for long spells of cancer chemotherapy is not suggestive. Similarly the quantum of administered drug dose either above the required level or below the wanted level is also not advised. Effective drug administration has to consider the optimal threshold limits on the drug administration/drug vacation times; upper and lower limits of drug quantity; along with the suitable number of drug administration/drug vacation cycles; and the number of spells within the cycle of drug usage/stoppage. This paper develops an optimization programming problem for designing drug administration strategies for a cancer patient under chemotherapy. This study will help in exploring the decision parameters at the targeted objectives. Optimal decisions on drug dosage level, drug administration period, drug vacation period, number of drug administration cycles; number of drugs applied within a cycle, etc., can be obtained with the model. Sensitivity analysis is carried out for understanding the model behavior. This work has a scope for developing health care Decision Support Systems.

Keywords: Cancer Treatment, Decision Support Systems, Health Management, Optimal Drug Administration, Stochastic Programming

INTRODUCTION
A malignant tumor sometimes seems to show in grasping the tissues it invades. Cancer is a class of diseases characterized by out-of-control cell growth. It harms the body when damaged cells divide uncontrollably to form lumps or masses of tissue called tumors. Tumors can grow and interfere with the digestive, nervous, and circulatory systems and they can release hormones that alter body function. Malignant tumors form when two things occur as; a cancerous cell manages to move throughout the body using the blood or lymph systems, destroying healthy tissue in a process called invasion ;and that cell manages to divide and grow, making
new blood vessels to feed itself in a process called angiogenesis. When a tumor successfully spreads to other parts of the body and grows, invading and destroying other healthy tissues, it is said to have metastasized (http://www.medicalnewstoday.com/info/cancer).

Our bodies are composed of trillions of cells, all working together. In cancer, one of those cells stops paying attention to the normal signals that tell cells to grow, stop growing or even to die. Cancer cells still share many of the same needs and properties of normal cells but they become independent of the controls that make our body function smoothly. The process by which a normal cell changes into one that behaves so abnormally often triggered by outside influences. Normal cells in the body follow an orderly path of growth, division, and death. Programmed cell death is called apoptosis, and when this process breaks down, cancer begins to form. Unlike regular cells, cancer cells do not experience progmatic death and instead continue to grow and divide. This leads to a mass of abnormal cells that grows out of control. The frequency of a particular cancer may depend on many factors. Every case of cancer is unique, with its own set of genetic changes and growth properties. The many differences between cases of cancer, even of the same organ is one of the main reasons that treatment is so difficult (Warburg, 2007).

Usually the drug administration for cancer treatment can be done with the chemotherapy, in which the treatment consisting of induced chemicals to kill cancer causing cells. In practice the drug may target the normal cells also, so as it leads to loss of white blood cells. Continuous drug administration to a cancer patient may give adverse effects and health hazards due to loss of white blood cells. Therefore the patient may be allowed to drug vacation during this period he/she will get recovery from health hazards due to toxicity of the chemicals. Both of Continuous drug administration and Continuous drug vacation are unwanted. Threshold limits for minimum and maximum times of drug administration and vacation are very essential. The drug dosage levels less than the minimum required and the drug dose above the maximum required are also harmful as the former leads to drug resistance and the later leads to loss of white blood cells. In conventional methods of chemotherapy, the drug is administered in spells and different units of drug are administered within each spell. This sort of drug administration may be continued for successive days as per the baring abilities of the drug by the patient. Similarly the drug vacation includes number of time units of vacation per spell; number of spells per cycle and number of cycles in vacation during the total period of chemotherapy.

Much significant work has been reported on the contribution on formulations of optimization modeling for drug administration in the literature. The applications of engineering optimal control theory to investigate the drug regimen for reducing an exponential tumor cell populations (Bahrami et al., 1975; Swan et al., 1977). Cancer chemotherapy optimization computing models using branching processes (Baianu, 1986). A model on optimal control for cancer chemotherapy with toxicity limits (Murray, 1990). The various ways in which optimal control theory interacts with cancer chemotherapy (Swan, 1990). An optimal parameter selection model of cancer chemotherapy (Martin et al., 1990). A mathematical tumor model with immune resistance and drug therapy for protocols of optimal control (Radunskaya, 2000). An integer non-linear programming problem by assuming cancer and anti-cancer interaction is modeled as customer and server paradigm of Queuing theory (Çetin, 2007). A stochastic model for optimal drug administration in cancer chemotherapy (Rao et al., 2010).

Regular /periodical evaluation of health status of the patient during chemotherapy is very essential to understand the effectiveness of administered drug. The conventional approach of mathematical programming on deriving decision variables needs the attention of researchers as the complexity of problems in cancer. The contexts of chemotherapy related problems are stochastic rather than deterministic. Assessing the parameters like rates of arrivals of normal cells; rate of arrivals of cancer causing cells.