Abstract

Recent advancements in computing power has allowed for the mathematical simulation of systems that are otherwise too complicated to solve analytically. This work will focus on the mathematical modeling and simulation of the solid tumor microenvironment and how various doses and infusion times will affect the solid tumor.

The first part of this work presents a brief literature review on the mathematical modeling of drug release from diffusion-controlled drug release devices. These are drug systems that are comprised of a polymer that encapsulates the drug in some form, and dictates the diffusion and release of drug. In many cases, the polymer can swell due to the increase in the volume of material due to absorption of solvent. Therefore, an investigation on the behavior of drug diffusion in a polymer-swelling system was performed. Sensitivity analysis revealed that the diffusion coefficients in played a major role in the drug release profiles in such systems.

The second part of this work models the diffusion of drug in solid tumors. Specifically, a mathematical model of drug behavior in solid tumors is performed in order to characterize the mass transport of drug in the solid tumor microenvironment. The equations used to model the system are based on the convection-diffusion equation. Clinical parameters such as dose and infusion time were varied to determine optimal tumor regression, and thus, optimal dose treatments. It was found that for drug efficacy could be maintained while reducing cardiotoxicity by two methods: (1) increase infusion times for large doses (e.g. 40 mins or greater for doses of 100 mg/m^2 or more), or (2) Fractionate a standard dose (approx. 40 – 100 mg/m^2) into several smaller doses (approx. 15 – 25 mg/m^2 each) which

favor quicker infusion times.

Based on the modeling framework presented in the second part, a mathematical model accounting for more complex biochemical phenomena, such as intracellular signaling, is presented. Intracellular signaling plays a major role in various pathways that regulate a cell's metabolism, gene expression, or the ability to undergo cell division. Clinically relevant parameters, such as dose and infusion time, were varied in order to characterize what affect various treatment regiments have on the biochemical response of solid tumor systems. It was found that higher infusion times had the most significant impact on tumor regression than any other parameter.