Modeling the combined therapies against cancer using virus and inhibitor (or radioiodide)[1]

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Abstract This talk deals with two new treatment approaches against cancer. One is the combined therapies against cancer using oncolytic viruses and inhibitors. Replicating genetically modified adenoviruses infect cancer cells, reproduce inside them and eventually cause their death (lysis). As infected cells die, the viruses inside them are released and then proceed to infect other tumor cells. The successful entry of virus into cancer cells is related to the presence of the coxsackie-adenovirus receptor (CAR). Mitogen-activated protein kinase kinase (known as MEK) inhibitors can promote CAR expression, resulting in enhanced adenovirus entry into cancer cells. However, MEK inhibitors can also cause G1 cell cycle arrest, inhibiting reproduction of the virus. To design an effective synergistic therapy, the promotion of virus infection must be optimally balanced with inhibition of virus production. We introduce a mathematical model to describe the effects of MEK inhibitors and viruses on tumor cells, and use it to explore the reduction of the tumor size that can be achieved by this therapy. Furthermore, we analytically find an optimal dose of inhibitor for a certain initial density of cells. The optimal timing of MEK inhibitors is also numerically studied.

The other is cancer radiovirotherapy which requires not only injection of replication-competent viruses but also administration of radioiodide. Radioiodide is in a continuous state of flux between the tumor and the remaining part. Iodide undergoes beta particle decay and the emitted beta particles have a significant effect on tumor cells. The combination of virotherapy with radiotherapy has been recently shown to be significantly more effective than treatment with virotherapy alone. Cancer radiovirotherapy can be described by a free boundary problem for a nonlinear system of partial differential equations, where the free boundary is the surface of a tumor. Global existence and uniqueness of solutions to this free boundary problem is proved, and a *new* explicit parameter condition corresponding to success of therapy is also found. Furthermore, numerical simulations are given to show that there is an optimal timing for radio-iodine administration, and that there is an optimal dose for the radioactive iodide.

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