Mathematical and optimal control analysis of a model for tumour growth under chemovirotherapy

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Current clinical and experimental research on cancer treatments shows that combination therapies are the cutting edge for cancer treatment. However, the design of an optimal protocol remains an open question. In this paper, we address the question on:"*what is the optimal chemotherapeutic drug and virus dosage combination for the elimination of tumour cells in body tissue*?" To this end, We construct an ODE based mathematical model describing the interactions between tumour cells, the immune response, and a treatment combination with chemotherapy and oncolytic viruses.

Stability analysis of the model with constant chemotherapy treatment rates shows that without any form of treatment, a tumour would grow to its maximum size. It also demonstrates that chemotherapy alone is capable of clearing tumour cells provided that the drug efficacy is greater than the intrinsic tumour growth rate. Furthermore, virotherapy alone may not be able to clear tumour cells from body tissue but would rather enhance chemotherapy if viruses with high viral potency are used. To assess the combined effect of virotherapy and chemotherapy we use the forward sensitivity index to perform a sensitivity analysis, with respect to chemotherapy key parameters, of the virus basic reproductive number and the tumour endemic equilibrium. The results from this sensitivity analysis indicate the existence of a *critical* dose of chemotherapy above which no further significant reduction in the tumour population can be observed. Numerical simulations show that a successful combinational therapy of the chemotherapeutic drugs and viruses depends mostly on the virus burst size, infection rate, and the amount of drugs supplied.

Optimal control analysis was performed, by means of the Pontryagin's maximum principle, to further refine the predictions of the model with constant treatment rates by accounting for the treatment costs and sides effects. Results from this analysis suggest that the optimal drug and virus combination correspond to half their maximum tolerated doses. This is in agreement with the results from stability and sensitivity analyses.