An adaptive patient-specific treatment approach for EGFR driven lung cancer

Lung cancer is the leading cause of cancer-related mortality in Canada and the United States. It can typically be classified at the molecular level by oncogene mutations that drive the cancer, with one such mutation occurring in the EGFR oncogene. Standard of care for patients suffering from stage IV (metastatic) non-small cell lung cancer (NSCLC) that is being driven by an EGFR oncogene mutation is to give the patient an EGFR tyrosine kinase inhibitor (TKI) such as Erlotnib, but unfortunately most patients develop acquired resistance to the drug within a year or so, and survival rates are poor, with median survival time less than two years. I will present a mathematical model developed to predict an optimal patient specific treatment plan. Initially the EGFR pathway is simplified down to five key genes and an ODE model is constructed that describes the evolutionary dynamics of the number of cell clones harbouring various combinations of gene mutations or amplifications. Using a threshold tumour burden as an indicator of patient death, a genetic algorithm is used to predict a locally optimal sequence of drug combination therapies to maximize patients’ survival times. When simulated on a cohort of 100 virtual patients, the model’s selected treatment schedule predicted a prolongation of survival compared with standard of care (Erlotnib). Moreover, the model allows for new patient data to be fed back into the model every time new data (e.g. imaging) is available from a patient, thus allowing the model to be continually refined and increasingly personalized for individual patients.