# Theoretically optimal chemotherapy protocols for drug resistant tumour growth under angiogenic signalling.

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We study a two-compartment model of drug-resistant tumour growth under angiogenic signalling. The main goal is to investigate how sensitive are the theoretically optimal protocols to changes in parameters quantifying the interactions between tumour cells in the sensitive and resistant compartments, i.e. he competition coefficients and mutation rates. Two optimisation problems are considered. In the first problem a constant, indefinite chemotherapy dose is optimised to maximise the time needed for the tumour to reach a critical (fatal) volume. It is shown that maximum survival time is generally obtained for intermediate drug dose. Moreover, the competition coefficients have a more visible influence on survival time than the mutation rates. In the second problem, an optimal dosage over a hort, 30-day time period, is found. An explicit running penalty for drug resistance is included in the objective functional. The problem is solved numerically and the properties of the numerical answer are verified against theoretical results obtained for a simplified model. It is concluded that, after an initial full dose interval, an administration of intermediate dose is optimal over a broad range of parameters. Moreover, mutation rates play an important role in deciding which short-term protocol is optimal.

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