

Chemotherapy of vascularised tumours: role of vessel density and the effect of vascular “pruning”

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In this work we propose to model chemotherapy taking into account the mutual interaction between tumour growth and the development of tumour vasculature. By adopting a simple model for this interaction, and assuming that the efficacy of a drug can be modulated by the vessel density, we study the constant continuous therapy, the periodic bolus-based therapy, and combined therapy in which a chemotherapeutic drug is associated with an anti-angiogenic agent. The model allows to represent the vessel-disrupting activity of some standard chemotherapeutic drugs, and shows, in the case of constant continuous drug administration, the possibility of multiple stable equilibria. The multistability suggests an explanation for some sudden losses of control observed during therapy, and for the beneficial effect of vascular “pruning” exerted by anti-angiogenic agents in combined therapy. Moreover, in case of periodic therapies in which the drug amount administered per unit time is constant (“metronomic” delivery), the model predicts a response, as function of the bolus frequency, significantly influenced by the extent of the anti-angiogenic activity of the chemotherapeutic drug and by the dependence of the drug efficacy on the vessel density.