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A model for anti-angiogenic therapy

Since the proposal by J. Folkman in the 70's to use tumoral neo-angiogenesis as a therapeutic target, important efforts lead to the development of various anti-angiogenic drugs now used in the clinic. Though, the practical results obtained by these so-called "targeted therapies" are quite poor up to now and anti-angiogenic drugs are far from replacing the classical, very toxic, chemotherapies. In some cases, angiogenic drugs can even exhibit paroxystic effects such as metastatic acceleration [3]. It seems that the way of administering the drug, its *scheduling* is of fundamental importance and determining the best schedules for anti-angiogenic drugs alone or in combination with cytotoxic drugs is a clinical open question.

In order to give insights on these questions, we developed the model of [2] and included a module to incorporate the metastases [1]. We will present interesting simulations studying and optimizing efficient temporal administration protocols, and describing the paradoxal effect observed in [3].

In particular, we can give answers in an emerging area of clinical oncology named metronomic chemotherapy (or anti-angiogenic therapy) [4]. It consists in delivering the chemotherapy at doses below the maximum tolerated doses, with a frequent schedule and is based on the assumption that such a schedule would have an anti-angiogenic effect.

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