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Optimal and suboptimal treatment protocols for anti-angiogenic therapy

In 1971 Judah Folman discovered that growth of any tumour is strongly dependent on the amount of blood vessels that it induces to grow. He surmised that, if a tumour could be stopped from growing its own blood supply, it would wither and die. Anti-angiogenic therapy is a novel treatment approach that aims at preventing a tumour from developing its own blood supply system.

On the basis of the biologically validated model proposed by Hahnfeldt, Panigrahy, Folkman and Hlatky in 1999, with the usage of the optimal control theory, some protocols of anti-angiogenic treatment were proposed. However, in our opinion the formulation of that model is valid only for the anti-vascular treatment, that is treatment that is focused on destroying endothelial cells. Therefore, we propose a modification of the original model which is valid in the case of treatment which is focused on blocking angiogenic signaling.

We propose also a new mathematical description of the anti-angiogenic treatment goal. In current studies it is assumed that the main goal of anti-angiogenic treatment is to minimize the tumor volume at the end of treatment. On the other hand, chemotherapy is still the main kind of cancer treatment, while anti-angiogenic treatment is only a supplement. The efficient treatment with chemotherapy is possible only when the drug can be distributed evenly, that is when vessels penetrate most of the tumour regions.

Therefore, we assume that the main goal of anti-angiogenic treatment, despite the minimization of the tumour volume, is to maintain high ratio of vessels volume that support the tumour to the actual tumour volume. We analyze it as an optimal control problem and a solution of the problem is given in some cases.