Optimal Control Problem of Metronomic Chemotherapy

D. Grass[1] **and V. Lykina**[1]

Abstract: In recent years the question of modelling a low-dosed cancer treatment by means of chemotherapy agents has been paid a broad attention. It has become evident through numerous experiments that "more is not necessarily better" for certain type of cancers. The papers of KLEMENT ET AL. and BROWDER ET AL. gave birth to a new research field in medicine called metronomic chemotherapy. The two mostly spread definitions of what metronomic chemotherapy means say: "The frequent administration of chemotherapy drugs at relatively low, non-toxic doses, without prolonged drug-free breaks" and the recent one "the minimum biologically effective dose of a chemotherapeutic agent, which, when given at a regular dosing regiment with no prolonged drug-free breaks, leads to antitumor activity". The main assumption is that besides of a cytotoxic effect on tumor cells, small doses of a chemotherapeutic agent have both antiangiogenic and immune stimulatory effect, while toxicity level on healthy tissues stays low or even neglectful.

Our task in the present paper is to consider the problem of metronomic chemotherapy as an optimal control problem, where the tumor size and the side effects of the therapy are being minimized over the treatment horizon, which gives rise to an integral objective in Lagrange form. One of our key ideas is to assume that we have enough time to treat the patient and the goal is not to fight the cancer as fast as possible. Moreover, we consider the cancer as a chronic disease, which will be treated over the whole remaining future life time of the particular patient. The aim is to figure out whether such "chronic" formulation of control problem leads to considerably lower doses in comparison to the short fixed finite treatment horizons. We would like to mention that through minimizing the expectation value of the cost functional the optimal control problem becomes stochastic. Nevertheless, it can easily be transformed to a purely deterministic control problem with infinite horizon.

To handle the obtained infinite horizon optimal control problem we use on the one side its rigorous formulation in weighted functional spaces. On the other side, to obtain numerical solutions to the considered problem, the open source software package OCMat was applied, which is available at http://orcos.tuwien.ac.at/research/ocmat_software/.

[1] Research Unit Operations Research and Control of Systems
Vienna University of Technology
Wiedner Hauptstrasse 8, A-1040 Vienna, Austria
{*dieter.grass, valeriya.lykina*}*@tuwien.ac.at*