On the Structure of Optimal Controls for Combined Radiotherapy and Anti-Angiogenic Treatments

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Abstract: We consider mathematical models for the optimal control problem of minimizing the tumor volume under combined anti-angiogenic and radiotherapy treatment with a priori restrictions on the amount of anti-angiogenic agents and damage done by radiation ionization. These become challenging, high-dimensional, multi-input optimal control problems. We are using a Lie derivative based analysis of the dynamics to compute explicit formulas for singular dosages of the anti-angiogenic agent and a singular radiotherapy fractionation schedule that allow for a quick and efficient computation of these controls. Totally singular controls, i.e, controls that are simultaneously singular over an interval, are a rather unusual structure, but for this problem they are supported by numerical results in the literature. Based on the explicit formulas for these controls, we explore the structure of optimal controlled trajectories in the state-space through numerical computations. Our results provide guidelines for the design of dosages for these two treatment protocols.

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