Optimal Fractionation in Radiotherapy

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Abstract:
The goal in radiotherapy for cancer is to maximize the biological effect of radiation on the tumor while limiting its toxic effects on nearby healthy anatomies. This is attempted by following a two-pronged approach: spatial localization of radiation dose, and temporal dispersion of radiation dose.

The spatial component of the problem involves prescribing a high dose to the tumor and putting upper limits on the dose delivered to the healthy anatomies. The radiation field's intensity profile is then optimized to meet this treatment protocol as closely as possible. This is called fluence-map optimization. The temporal component of the problem involves breaking the total planned dose into several equal-dose treatment sessions called fractions that are administered over several weeks. This is designed to give the healthy tissue some time to recover between sessions, as it possesses better damage-repair capabilities than the tumor. The key challenge on this temporal side is to choose an optimal number of fractions and the corresponding dosing schedule. This is called the optimal fractionation problem.

We will discuss the optimal fractionation problem from a mathematical viewpoint by using the standard linear-quadratic model of dose-response. We will introduce stylized as well as computationally challenging full-scale optimization models for this problem. Our stylized models assume that a fluence-map optimization problem has been solved a priori and then we will show that it is possible to solve the optimal fractionation problem essentially in closed-form. Our full-scale model attempts to simultaneously optimize the fluence-map as well as the number of fractions. This results in a non-convex problem that includes thousands of variables and a similar number of constraints. We will present an efficient convex optimization algorithm for approximate solution of our spatiotemporally integrated model. Numerical experiments and sensitivity analyses on head-and-neck and prostate cancer test cases will be discussed. The potential benefit of solving the spatiotemporally integrated model as compared to solving the stylized model will be quantified.

A variation of this problem, where the dose-response is stochastic will also be discussed. The talk will conclude by connecting this stochastic problem to the idea of response-guided dosing, which has recently seen a surge of clinical interest in diseases such as rheumatoid arthritis, hepatitis C, AIDS, and coronary heart disease.

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