Inverse optimization for imputing radiobiological parameters of the linear-quadratic dose-response model from a radiotherapy fractionation plan

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Abstract: The objective in cancer radiotherapy is to maximize tumor-kill while limiting toxic effects of radiation dose on nearby organs-at-risk. Given a fixed number of treatment sessions, planners thus face the problem of finding a dosing sequence that achieves this goal. This is called the fractionation problem, and has received steady attention over a long history in the clinical literature. Mathematical formulations of the resulting optimization problem utilize the linear-quadratic (LQ) framework to characterize radiation dose-response of tumors and OAR. This yields a nonconvex quadratically constrained quadratic program. The optimal dosing plan in this forward problem crucially depends on the parameters of the LQ model. Unfortunately, these parameters are difficult to estimate via *in vitro* or *in vivo* studies, and as such, their values are unknown to treatment planners. The clinical literature is thus replete with debates about what parameter values will make specific dosing plans effective.

In this talk, I will formulate this as an inverse optimization problem. The LQ dose-response parameters appear in the objective function, the left hand side, and the right hand side of the forward problem, and none of the existing generic methods can provide an exact solution of the inverse problem. I will exploit the structure of the problem and identify all possible parameter values that render the given dosing plan optimal, in closed-form. This closed-form formula will be applied to dosing-plans from three clinical studies published within the last two years.

Bio: Archis is a Professor and Associate Chair in the Department of Industrial & Systems Engineering at the University of Washington in Seattle, where he currently holds the College of Engineering Endowed Professorship in Healthcare Operations Research. He joined the University of Washington as an Assistant Professor in 2006 after receiving a PhD in Industrial and Operations Engineering from the University of Michigan in 2006, and an MS in Management Science and Engineering from Stanford in 2003. He completed his undergraduate education at the Indian Institute of Technology, Bombay, India, in 2001. Archis is a recipient of the NSF CAREER award, and of the award for Excellence in Teaching Operations Research from the Institute of Industrial Engineers. Archis has served on the editorial boards of several journals.