SYNERGY OF RADIATION AND IMMUNE SYSTEM: MATHEMATICAL MODELS TO ENHANCE CURRENT TREATMENT PROTOCOLS FOR METASTATIC CANCER PATIENTS

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Animal studies and clinical trials identified a synergy of irradiation and immunotherapy. This synergy stems from the fact that radiation induces cell stress and immunogenic cell death, thereby exposing a wealth of previously hidden tumor-associated antigens, stress proteins and danger associated molecular patterns (HSPs, DAMPs), which are endogenous immune adjuvants that can initiate and stimulate an immune response. What is the most important, local immune system stimulation is propagated systematically through the lymphatic system making other metastatic sites also susceptible to this new wave of locally-induced immune attack. Thus, immunotherapy can be more efficient after irradiation and it boosts radiation-induced immune system stimulation. There are, however, many clinically important questions about radiation-immune system synergy that remain unanswered: 1) irradiation of which metastatic lesion would result in the best overall response; 2) what is the optimal radiation dose to stimulate the biggest immune response; 3) which immunotherapy synergizes with radiation the most. The goal of the proposed PhD project is to develop a quantitative mathematical framework that predicts systemic response of metastatic tumors to focal radiotherapy – either alone or in combination with immunotherapy – that can be further used to provide at least partial answers to the abovestated questions. It is assumed that the framework will be expressed in terms of ordinary differential equations describing temporal evolution of various cellular populations, i.e. cancer cells and various types of immune cells. The framework will be calibrated with clinical/experimental data using appropriate optimization methods. An example of modeling systemic immune-mediated response after focal irradiation can be found in the paper by Poleszczuk et al. "Abscopal Benefits of Localized Radiotherapy Depend on Activated T-cell Trafficking and Distribution between Metastatic Lesions" (access from http://cancerres.aacrjournals.org).