Mathematical modeling of tumor-immune interactions and immunological consequences of radiotherapy

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Tumors grow in a complex ecosystem that is the result of co-evolution of the tumor with its host environment, and therefore highly patient-specific. Radiation is not only targeting individual cancer cells but the complex tumor-immune microenvironment in the treatment field. It is increasingly appreciated that radiation therapy (RT) can induce a robust anti-tumor immune response that provides a second wave of cell kill and tumor regression. However, current radiation has not specifically focused on enhancing immunity. It remains unclear, however, what are the best radiation dose and dose fractionation protocols to maximize the therapeutic benefits of this synergy. Only few protocols have been modeled experimentally due to logistic limitations, end even fewer have been evaluated prospectively in the clinic. Of utmost importance in the immediate future becomes the search for the optimal radiation protocol. We developed a mathematical model that simulates tumor-immune interactions, radiation response, immune checkpoint blockade therapy, and inter-exchange of activated T cells between multiple tumor sites. From experimental and tumor volume measurements, the calibrated model suggests that current daily radiation may be inferior to shorter treatment schema with larger doses. Furthermore, radiation prior to surgery may induce more robust immune responses than radiation after surgery.

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