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A FRACTIONAL-ORDER MODEL OF ADENOVIRUS INFECTION AND ONCOLYTIC CANCER THERAPY: STABILITY, BIFURCATION, AND OPTIMAL CONTROL

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ABSTRACT

Adenoviruses present a unique challenge in modern medicine due to their dual role as both infectious pathogens and promising agents in oncolytic cancer therapy. While adenovirus infections can spread within populations and cause significant health concerns, engineered adenoviruses have also been shown to selectively target tumor cells and stimulate antitumor immune responses. Motivated by this dual nature, we develop a novel fractional-order compartmental model that simultaneously describes adenovirus transmission dynamics and its therapeutic interaction with cancer. To the best of our knowledge, this study presents the first fractional-order framework that simultaneously captures adenovirus transmission dynamics and its oncolytic therapeutic effects within a unified population-level model. The proposed model divides the population into five compartments: healthy susceptible individuals, cancer patients susceptible to infection, infected individuals, recovered individuals with temporary immunity, and cancer patients in therapeutic remission induced by viral activity. The model is formulated using Caputo fractional derivatives to account for memory effects and hereditary properties that are commonly observed in biological and immunological systems. Theoretical analysis establishes the positivity and boundedness of solutions and derives the disease-free equilibrium and the basic reproduction number. Using the next-generation matrix approach and fractional stability theory, we show that the disease-free equilibrium is locally asymptotically stable when the basic reproduction number is less than one and unstable when it is greater than one. Furthermore, the model exhibits the possibility of backward bifurcation, indicating that adenovirus persistence may occur even when the reproduction number is below unity. This result reveals a more complex disease-control scenario than that predicted by classical epidemic models. A sensitivity analysis identifies the transmission rate, recovery rate, and increased susceptibility of cancer patients as the most influential parameters governing disease dynamics. To investigate effective intervention strategies, an optimal control framework is formulated by incorporating preventive measures, enhanced virotherapy, and immunotherapy. The resulting optimality system is derived using Pontryagin's Maximum Principle. The optimal strategy suggests that combining preventive measures with therapeutic interventions yields the most effective outcomes. Numerical simulations support the analytical findings and demonstrate that combining preventive interventions with therapeutic strategies can substantially reduce infection prevalence while increasing cancer remission outcomes. The proposed framework provides a new perspective on the interaction between infectious disease dynamics and cancer treatment and highlights the potential of fractional-order modeling in analyzing complex biomedical systems.

***K*eywords** Adenovirus Dynamics, Fractional-Order Modeling, Oncolytic Virotherapy, Cancer Immunotherapy, Bifurcation Analysis, Optimal Control

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