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Mathematical modeling and optimal control of glioma dynamics under combined therapy

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Abstract

Low-grade gliomas (LGGs) are slow-growing but infiltrative brain tumors characterized by long-term persistence and frequent progression. In this work, we develop and analyze a compartmental mathematical model describing LGG dynamics under combination therapy involving cytotoxic chemotherapy and targeted molecular treatment. The tumor population is structured into proliferating, quiescent, and damaged compartments, and therapeutic interventions are incorporated through bilinear control terms accounting for temozolomide chemotherapy and isocitrate dehydrogenase (IDH) inhibition, a molecular target present in the majority of LGG cases. We first establish the well-posedness of the model by proving existence, uniqueness, positivity, and boundedness of solutions. The dynamics of untreated glioma growth are then analyzed, revealing that the tumor-free equilibrium is always unstable in the absence of therapy, leading to exponential tumor expansion. Under constant treatment regimens, we derive an explicit controlled reproduction number that governs tumor persistence or eradication.

References

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