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MATHEMATICAL MODELING OF MALIGNANT GLIOMAS: TREATMENT DYNAMICS AND IN SILICO TRIALS

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ABSTRACT

Malignant gliomas (MGs), particularly glioblastoma, are among the most aggressive brain tumors, with limited treatment options and a poor prognosis. Current first-line therapy consists of maximal safe resection followed by the Stupp protocol—an intensive combination of radiotherapy and chemotherapy—which only modestly extends survival. This highlights the urgent need for new therapeutic strategies.

In this work, we present and validate an ordinary differential equation–based mathematical model that captures key features of MG dynamics, including cancer cell dormancy, phenotypic switching, drug persistence, and treatment-induced effects. The model was calibrated with in vivo data from animal studies and used to design and test alternative treatment schedules through in silico trials. Notably, we found that less aggressive, protracted dosing regimens may significantly outperform the standard protocol, potentially delaying resistance, reducing side effects, and extending survival. Extrapolating our findings to humans, our simulations suggest up to a fourfold increase in median survival with optimized regimens.

Although further experimental and clinical validation is required, this framework illustrates how mathematical modeling and in silico trials can guide the design of more effective and personalized treatment strategies for malignant gliomas and related cancers.