

Purpose: To quantify and predict response to radiation therapy in vivo prior to treatment on a patient-specific basis using mathematical modeling.

Methods: Glioblastoma multiforme (GBM) are highly invasive primary brain tumors that diffusely invade the surrounding normal appearing tissue and yields short life expectancies despite aggressive treatment. The differential motility of glioma cells throughout the brain characterize tumor invasion. We present and apply a patient-specific, mathematical model for glioma growth that quantifies response to radiation therapy (RT) in vivo in the 3D anatomy of the human brain. The mathematical model uses net rates of proliferation and migration of tumor cells to characterize the tumor's growth and invasion along with the linear-quadratic model for response to radiation therapy.

Results: Patient individualized simulations of tumor growth and radiation response are performed in 9 GBM patients validating a predictive relationship between the net rate of proliferation rate and radiosensitivity. The simulations accurately predict the imageable tumor post-treatment within 2.4 mm. Because the patient-specific net proliferation rate of the tumor is calculated prior to treatment, this result provides quantitative predictions of radiosensitivity on a patient-by-patient basis.

Conclusions: This work presents the first mathematical model to quantify patient-specific radiosensitivity based on in vivo data. Our results indicate that, using our model, clinicians will be able to identify the degree to which any given glioma patient will respond to radiation therapy prior to treatment. That is, a virtual in silico tumor with the same growth kinetics as a particular patient combined with the complex anatomy of the brain can predict treatment response in individual patients in vivo. This work marks a paradigm shift in the quantification of treatment response and provides a basis for individualizing radiation treatment according to both the dynamics of each tumor but also their diffuse extent.