Brain Tumor Simulation using a Hybrid Compartment-Continuum-Discrete Model

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Primary brain tumors are among the most aggressive and lethal forms of cancer. The most common and lethal are glioblastomas multiforme (GBM). Patients diagnosed with GBM have a median survival time of approximately 1 year despite the use of a variety of medical intervention (1). One reason for this poor prognosis is that GBMs are highly invasive and generate hair-like projections of migratory cells that invade healthy brain tissue. These projections cannot be completely removed surgically or through radiation therapy where the treatment is localized to a specific area. As a result, these migratory cells continue to invade the brain in spite of medical treatment and constitute a substrate for tumor re-growth.

Herein, we propose a hybrid compartment-continuum-discrete (CCD) model (2) to simulate glioma growth and cellular invasion. The discrete portion of the model is capable of capturing intercellular interactions including cell migration, intercellular communication, spatial cell population heterogeneity, phenotype differentiation, epigenetic events, proliferation, and apoptosis. Combining this with a compartment (3) and continuum model allows clinically significant tumor sizes to be evaluated.

Multiple simulations are performed to determine the sensitivity to changes in important model parameters, specifically, the fundamental length parameter, necrotic cell degradation rate, cell migration rate, and phenotype transformation rate. Using these values, the model is able to simulate tumor growth and invasion behavior observed clinically. This mathematical model provides a means to simulate various tumor development scenarios which may lead to a better understanding of how altering the fundamental parameters can influences neoplasm progression.

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