



Hypoxic Cell Waves around Necrotic Cores in Glioblastoma: A Biomathematical Model and its Therapeutic Implications

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Glioblastoma is a rapidly evolving high-grade astrocytoma that is distinguished pathologically from lower grade gliomas by the presence of necrosis and microvascular hiperplasia. Necrotic areas are typically surrounded by hypercellular regions known as "pseudopalisades" originated by local tumor vessel occlusions that induce collective cellular migration events. This leads to the formation of waves of tumor cells actively migrating away from central hypoxia. We present a mathematical model that incorporates the interplay among two tumor cell phenotypes, a necrotic core and the oxygen distribution. Our simulations reveal the formation of a traveling wave of tumor cells that reproduces the observed histologic patterns of pseudopalisades. Additional simulations of the model equations show that preventing the collapse of tumor microvessels leads to slower glioma invasion, a fact that might be exploited for therapeutic purposes.

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