**Maciej Mrugala**
University of Washington Department of Neurology
e-mail: mmrugala@u.washington.edu
**Kristin Swanson**
University of Washington Department of Pathology, Department of Applied Mathematics
e-mail: krae@u.washington.edu
**Addie Boone**
University of Washington Department of Pathology
**Russell Rockne**
University of Washington Department of Pathology, Department of Applied Mathematics

# Predicting pseudoprogression in glioblastoma patients: A mathematical and clinical perspective

Background: Glioblastoma multiforme (GBM) is a highly invasive primary brain tumor that diffusely invades the surrounding normal appearing tissue and yields short life expectancies despite aggressive treatment. A combination of chemo and radiation therapies is the standard of care for newly diagnosed GBM. However, published data estimate that 20%-50% of progressive enhancement on MRI occurring within 12 weeks post chemoradiotherapy is the result of pseudoprogression (Psp) and does not indicate true progression (TP) of disease. Though many novel methods and modalities are currently being evaluated to distinguish Psp from TP, there is no widely accepted noninvasive mechanism to predict Psp in individual patients.

Methods: A reaction-diffusion model has effectively quantified the net proliferation () and invastion rate (D) (P-I) of untreated glioma growth and invasion. We investigate the application of the P-I model as a mechanism to predict which patents will be more likely to experience pseudoprogression and true progressive disease. The pre- and post-chemoradiotherapy MRI scans of 57 patients were reviewed retrospectively.

Results: Eleven of the 57 patients were clinically confirmed to exhibit pseudoprogression and 46 patients were confirmed to exhibit true progression. These patients were then evaluated based on model-generated parameters of the net migration (D) and proliferation rates () of each patients glioma tumor. Of the 11 Psp patients, 9 (82%) had pretreatment D/<1 mm2, and of the 46 TP patients, 33 (72%) had pretreatment D/>1 mm2.

Conclusion: A pre-treatment D/rho<1 mm2 reflects a more focal, less invasive tumor that is more likely to be highly vascularized and hypoxic. Thus, in a post chemotherapy environment, such tumors may be more prone to enhanced edema due to the increased permeability of the tumor vasculature and more likely to exhibit enhancement on radiographic imaging. Though additional investigation is necessary to determine if this relationship persists, preliminary results suggest the application of the P-I model to patient-specific pre-chemoradiotherapy MRI data provides model-derived parameters that may offer a quantitative mechanism to help predict which patients are more likely to experience pseudoprogression.