Title: Prediction of breast tumor response to neoadjuvant chemotherapy using a mechanically coupled tumor growth model.

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Clinical observations have long suggested that cancer progression is strongly accompanied by extracellular matrix remodeling and concomitant increases in tissue mechanical stiffness. Elucidation of the cell and molecular mechanobiology basis supporting the association between tumor growth and tissue mechanics continues at the microscale level; however, there is a fundamental need to understand translation of measurable macroscale structural tissue biomarkers into the clinical setting. This is especially important in the neoadjuvant setting for breast cancer, where response to therapy is currently monitored by changes in tumor size as measured by conventional imaging, which generally does not show whether a tumor is responding until the patient has received many, potentially ineffective, treatment cycles. In this work, we link macroscale tissue mechanical properties to a tumor growth model through the use of a reaction-diffusion tumor growth model that is mechanically coupled to the surrounding tissue stiffness via restricted tumor cell motility/diffusivity and informed by quantitative magnetic resonance imaging data (dynamic contrast enhanced MRI, diffusion weighted MRI, and high-resolution structural MRI). This approach is used to model and predict patient-specific tumor response to neoadjuvant chemotherapy with the goal of predicting, early in the course of therapy, whether a patient is responding to a particular therapeutic regimen. Tumor growth model parameters within the model are reconstructed by utilizing differences in tumor cell distributions measured early in the course of therapy (i.e., before and after one cycle of neoadjuvant therapy). Following parameter estimation, we then use the model to predict the tumor burden at the conclusion of neoadjuvant therapy and compare to experimental observations. We apply the approach to a database of breast cancer patients exhibiting a varying degree of response to neoadjuvant chemotherapy, and show that predictions for the mechanically coupled model have a significant correlation with experimental data (PCC = 0.84, $p < 0.01$).

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