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Predicting the response of breast cancer to neoadjuvant chemotherapy with an imaging-driven, mechanics-coupled, reaction-diffusion model accounting for patient-specific therapeutic regimens

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Clinical methods for assessing tumour response to neoadjuvant therapy largely rely on monitoring the temporal changes in tumour size. Our goal is to predict tumour response to neoadjuvant therapy in breast cancer using a mathematical model that utilizes non-invasive imaging data obtained from individual patients. Previously, a mechanically-coupled, reaction-diffusion model with logistic growth for breast cancer was shown to outperform clinically used measures for predicting tumour response to therapy when initialized with patient specific magnetic resonance imaging (MRI) data. This model has since been extended to include patients' therapy using corresponding dynamic contrast-enhanced (DCE-) MRI data to determine areas for drug delivery, improving the concordance correlation coefficient of the predicted tumour cellularity compared to the calculated cellularity from 0.85 to 0.99 ($p<0.01$, N=5).

We use patient specific measurements from diffusion-weighted MRI data to calibrate tumour cell diffusion, carrying capacity, and proliferation values (on a per voxel basis) within each patient's tumour domain. The model is 3D and is mechanically coupled to the properties of the breast tissues by dampening the diffusivity of tumour cells based upon their growth and stresses induced in the breast. DCE-MRI data is used to identify spatiotemporal variations in tumour perfusion to approximate delivery of therapy within the tumour using the extended Kety-Tofts model. An explicit death term is incorporated into the tumour cell equation, where the amount of drug distributed in the tissue is spatially heterogeneous and dynamic in time according to the patient's therapy schedule. All model simulations were evaluated using a forward finite difference scheme.

For a cohort of breast cancer patients (N = 10), four MRI scans were collected over the course of their neoadjuvant therapy (pre-treatment, after one cycle of therapy, at the end of the first therapy, and after one cycle of the second therapy). Using this data, we assess the model's predictive ability in two different ways: 1) using the first two scans, the model is calibrated and simulated forward to the third scan time to assess the tumour cellularity, size, and heterogeneity predicted by the model in comparison with the calculated values from the patient's third scan; 2) the model is calibrated with the third and fourth scans and simulated forward to the time of surgery, where the model's results are compared to the patient's pathological response status. Using these metrics, we will report on and discuss ability of the modelling approach to predict tumour response to therapy in breast cancer.

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