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An experimental-computational approach for predicting the spatial-temporal response of tumour and vasculature to radiation therapy

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Introduction. Radiation therapy is a critical portion of the standard-of-care for patients with brain tumours, as it targets residual disease and non-operable tumours. However, one of the shortcomings of radiation therapy is the heterogeneity of response observed in the patient population which may be due to fundamental limitations in the way radiation therapy plans are currently selected. To this end, we are developing a coupled system of biophysical models of tumour growth and angiogenesis to predict the spatial-temporal response to radiation therapy within a tumour that is initialized and calibrated on an individual basis from non-invasive magnetic resonance imaging (MRI) data.

Methods. To evaluate this model system, we use subject-specific diffusion-weighted MRI (DW-MRI) and dynamic contrast enhanced MRI (DCE-MRI) acquired at seven time points (collected every 48 hrs) in rats (n = 7) with C6 gliomas. Three imaging time points (t1-t3) were acquired before the rats received a single fraction of either 20 Gy (n = 4) or 40 Gy (n = 3) dose of x-ray radiation delivered over the whole brain, while the remaining time points (t4 - t7) were collected post-treatment. DCE-MRI data was used to identify tumour regions of interest and estimate the blood volume fraction (vb) on a voxel basis. Tumour cell number (Ntc) was estimated using DW-MRI data. The spatial-temporal evolution of Ntc and vb in 3D was described by two coupled, partial differential equations describing the motility, proliferation, and death of tumour cells and blood vessels. Model parameters were calibrated from data on t1-t4, which were then used in a forward evaluation of the model from t5-t7. Error was assessed by calculating the percent error in the predicted and observed tumour volume. Agreement between the spatial distributions of Ntc and vb was assessed be calculating the concordance correlation coefficient (CCC) between the measured and observed quantities.

Results. For the rats that received 20 Gy of radiation, the error between the predicted and observed tumour volume ranged from 6% to 13% from t5 to t7. Additionally, the CCC between the predicted and observed Ntc ranged from 0.65 to 0.73 for all rats, while the CCC for vb ranged from 0.47 to 0.85. Higher error was observed for the rats who received 40 Gy of radiation, where the error between the predicted and observed tumour volume ranged from 10% to 18% on days t5-t7. A high level of agreement CCC greater than 0.70 was observed on t5 for both the vb and Ntc, while CCCs less than 0.5 were observed on t6 and t7.

Conclusion and Discussion. The results of this study indicate the potential to accurately model the spatial-temporal evolution of tumour and blood volume fractions from clinically relevant imaging data following radiation therapy. Further development of subject-specific mathematical models, such as the one presented here, will facilitate individualized radiation therapy plans to address the heterogeneity of response to treatment.

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