Title: Virtual Cancer Patient (VCP) for treatment personalization: prediction accuracy in metastatic breast cancer (MBC) patients

Authors

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Abstract:

To aid oncologists in predicting individual patient response to different drugs, the interplay between biological, pathological and pharmacological processes underlying drug-patient interactions have been mathematically modelled. These models have been computer-implemented for creating the Virtual Cancer Patient (VCP) engine. This trial was aimed at testing the accuracy of the VCP in predicting response to single agent docetaxel or doxorubicin treatment in MBC patients. The primary end-point was to determine whether the VCP simulations retrieved the clinical scenario in terms of both response and toxicities.

Clinical, radiological and pathological parameters, including pre-metastatic and metastatic treatment profiles, were retrospectively collected from 33 MBC patients with liver, lung and lymph node metastases, treated by either doxorubicin (9) or docetaxel (24). Patients’ data were divided into a validation set and a training set. Training set response parameters were input for calibrating the VCP. The VCP engine thus created an individual pharmacodynamics function characterising the relationships between histopathological parameters, taken from initial tumour biopsies, and the effect of each drug on metastatic growth. This function was then implemented in the VCP with the initial data of the validation set, and disease course and response to chemotherapy regimens simulated. The computed treatment (virtual) effects were compared with the actual clinical response. Proper blinding was ensured between data collection and modelling.

Predictions of response of individual metastases in the validation set to each particular treatment were clustered into “response” and “no response” groups. Our preliminary result of the prediction accuracy of VCP to actual response was 70%. Analysis of accuracy in predicting myelo-suppression is ongoing. The VCP appears to have the potential to be a powerful tool for treatment individualisation and a prospective study is warranted for further refinement and validation of the model. (NB: This work was supported by a CRUK pilot project grant).

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