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Novel Virtual Patient technology for predicting response of breast cancer and mesenchymal chondrosarcoma patients to mono- and combination therapy by cytotoxic and targeted drugs

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Introduction: Lack of tools for predicting response of individual patients to pharmacotherapy is a significant impediment to providing improved, personalized medical treatments. The Virtual Patient (VP) is a predictive biosimulation technology, comprising computer-implemented mathematical algorithms of key physiological, pathological and pharmacological processes in the body of the patient. Calibrated with available patient-specific data, the VP can accurately retrieve preclinical and clinical reality and predict short- and long-term *in vivo* effects of drugs. **Materials & Methods**: The VP's solid tumor model was calibrated to retrieve the dynamics of breast cancer (BC) and mesenchymal chondrosarcoma (MCS) xenografts. Published tumor growth curves were used in the BC case, while growth curves of untreated human tumor xenografts, derived from a lung metastasis of an MCS patient and histopathological results of this metastasis were used to create the MCS model. Published data were used to model PK/PD of three targeted therapies (Bevacizumab, Sunitinib, Sorafenib), as well as PK of four chemotherapeutic drugs (Docetaxel, Gemcitabine, Doxorubicin and Irinotecan) in mice. *In vitro* proliferation assays of the MCS patient's tumor cells were employed for establishing patient-specific concentration-effect curves for the chemotherapeutics. The virtual drugs were then 'administered' to the virtual BC and MCS xenografts as single-agents and in combinations, and short term tumor growth dynamics were simulated under different regimens. Simulation results of the MCS xenograft were compared to corresponding experimental growth curves of treated and untreated tumors for evaluating prediction accuracy. **Results**: Predictions indicate several therapies, namely, Bevacizumab +Docetaxel combination, Sunitinib, to be significantly superior to others, notably Gemcitabine, in the MCS patient's xenografts. Over the simulated treatment period of up to 41 days, combinations with Bevacizumab are predicted to greatly enhance the treatment efficacy in comparison to the corresponding monotherapies in both cancer types. The average accuracy of the VP's predictions is 82%. **Conclusions**: The Virtual Cancer Patient's showed high precision in predicting the growth pattern and response of xenografted MCS patient's tumor cells to various mono- or combination therapies. Our results suggest that, in general, treatments involving antiangiogenic drugs greatly improve MCS as well as BC tumor growth inhibition. In particular, Bevacizumab+Docetaxel regimens of reduced doses and inter-dosing intervals proved superior to other tested regimens for both indications. These results support the use of the Virtual Cancer Patient as a powerful tool for personalizing patients' treatment, especially when the application of new drugs is anticipated or when treatment of patients with rare diseases is considered.