Development of a molecular imaging-based tumor simulation framework

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Computational tumor models have emerged as powerful tools to help identify, understand, test, and predict physiological and pathophysiological factors influencing the response to anti-cancer therapies. To date, however, most tumor modeling approaches are limited in their applicability to clinical patient data due to their reliance on arbitrary or non-measurable model parameters and the absence of biomarkers specific to the tumor tissue. Thus, in order to simulate the inter-patient and intra-tumor variability in response observed clinically, patient-specific, biological information characterizing the tumor microenvironment should be incorporated into tumor modeling approaches. Here, positron emission tomography (PET) constitutes an ideal imaging modality due to its high sensitivity, its non-invasive nature, and its ability to provide spatially-resolved, quantitative imaging data. This doctoral thesis presents the development of a stochastic, multiscale tumor modeling framework that is able to simulate tumor growth and treatment response based on PET imaging data of proliferation, hypoxia, and metabolic activity. In particular, two different anti-cancer therapy modules were developed and incorporated into the modeling framework presented in chapter 3: the first consists of a model to simulate response to radiation therapy (chapter 4); the second therapy module consists of a model simulating anti-angiogenic therapy (chapter 5). Both applications were tested and applied to clinical trial data. Lastly, an overall summary and discussion of model limitations and future modeling endeavors is presented (chapter 6). Ultimately, molecular imaging-based tumor models may provide a valuable tool to investigate different therapeutic scenarios and to accelerate the transition from population-based therapies towards personalized medicine.