Imaging-based modeling of vasculature growth and response to anti-angiogenic therapy

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Vasculature supplying oxygen and nutrients to cancerous tumors is essential for their growth. An emergent therapeutic modality is anti-angiogenic therapy which targets this vasculature in order to eradicate the tumor. For decades now, computational modeling focused on tumor-vasculature dynamics has been used as a cheaper and alternative method to probe this system in addition to the experimental studies. However, the results of such models are generic since the parameters are population-based and not patient-specific. Imaging offers a unique opportunity to non-invasively acquire patient- and tumor-specific information about the current tumor condition. In this work, we present the first computational model for explicit vasculature simulation based on functional and molecular imaging data. Firstly, the model simulates a stochastic vasculature that appropriately represents the hypoxia imaged in the tumor. Then the temporal changes in tumor vasculature system are simulated; firstly without therapy and subsequently with anti-angiogenic therapy intervention. At each stage, the model is benchmarked to literature data to validate the parameters involved. Keeping imaging in perspective, explicit application to imaging data is demonstrated at each stage. While the parameters required to simulate a stochastically reproducible vasculature have been elicited, sensitivity studies quantifying the impact of critical model parameters on tumor hypoxia have been also been performed. The presented framework can be applied to any generic anti-angiogenic drug and is a potent tool to further explore the intricacies involved in the mechanisms of anti-angiogenic therapy. Future directions of model improvement have been indicated along with therapeutic and research-oriented applications of the model.