AbstractID: 10565 Title: Simulating the effects of anti-angiogenic therapy using voxel-based biological parameters derived from functional imaging

Purpose: Although anti-angiogenic agents are being used in combination with standard radiotherapy or radiochemotherapy, the biological response mechanisms are currently not well understood. This study investigates therapeutic response to bevacizumab, a monoclonal antibody to VEGF-A, using a functional imaging-based tumor simulation model.

Method and Materials: A multiscale tumor growth and radiation therapy response model based upon patient-specific parameters was extended by implementing response mechanisms to bevacizumab. PET/CT images of cellular proliferation ([^{18}F]FLT) and hypoxia ([^{61}Cu]Cu-ATSM) in human HNSCC tumors served as simulation input. Treatment with bevacizumab according to a clinical treatment regimen was simulated as an example of anti-angiogenic therapy. Heterogeneous drug delivery within the tumors was simulated using a four-compartment pharmacokinetic model coupled with perfusion parameters assessed by DCE-CT. Within each voxel, response was modeled based on changes in VEGF-A levels, simulated changes in microvessel density (MVD), and resulting changes in oxygenation levels. Results were compared to follow-up PET/CT scans of hypoxia and proliferation.

Results: Simulating response to a single bevacizumab dose of 10 mg/kg yielded decreased [^{18}F]FLT uptake values as observed in all follow-up scans. The mean correlation coefficient between simulated and follow-up [^{18}F]FLT scans was 0.79. However, trends in [^{61}Cu]Cu-ATSM uptake values could not be reproduced in all simulation cases, indicating that response time, as well as quantitative changes in hypoxia might depend on additional patient-specific biological parameters. Simulated MVDs were found to be highly time-dependent.

Conclusion: The implemented model successfully reproduced trends in proliferative response following bevacizumab monotherapy and can be readily integrated into a previously developed radiation response model. Results also suggest that MVD should be used carefully when characterizing treatment response to anti-angiogenic therapy due to a strong time-dependence. Upon successful validation, the implemented model could serve as a prospective tool to help identify personalized dosing and sequencing of combination therapies.