DEVELOPMENT OF PET IMAGING-BASED DOSE-PAINTING PRESCRIPTIONS

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ABSTRACT

Historically, prescriptions in radiation therapy are based on physician experience from extensive clinical trials in order to establish standard-of-care guidelines. The doses of radiation are generally uniform across target volumes to reflect a fixed level of local neoplastic disease control of the population mean. However, inter-patient and intra-tumor variation in response to uniform doses can result in diminished tumor control and poor clinical outcome for certain patients. Recent research endeavors are emphasizing the need to individualize prescriptions by incorporating patient-specific biological markers with prognostic and predictive value. Quantitative imaging with positron emission tomography (PET) of tumor glucose metabolism, cell proliferation, and hypoxia has been suggested as a sensitive and specific technique to tailor patient prescriptions in a manner that may significantly improve clinical outcome. The concept of prescribing and delivering non-uniform dose based on molecular imaging, termed dose painting, hinges on the establishment of a dose-response relationship at the image voxel scale that optimizes a particular clinical endpoint. This doctoral thesis presented two methods of defining dose-painting prescriptions based on PET imaging: the first was a heuristic model derivation of hypoxia dose-painting prescriptions in head-and-neck cancer patients (Chapter 3); the second was an empirical imaging surrogate endpoint derivation of dose-painting prescriptions in veterinary sinonasal cancer patients (Chapter 4). The clinical implementation of these dose-painting prescriptions was investigated, which emphasized treatment planning and delivery solutions (Chapter 5). Lastly, a summary and discussion of the future of dose painting to forge links between tumor biology and clinical outcome is presented (Chapter 6). The compelling dose painting concept is fast becoming a clinical reality that may positively impact cancer patient lives.