AbstractID: 12897 Title: Characterizing uncertainties in hypoxia imaging-based dose painting prescriptions

Purpose: Inadequate characterization of variability from dose escalation models limits the precise definition of dose painting prescriptions. The purpose of this study was to quantify uncertainties in hypoxia imaging-based prescriptions using an empirically-driven and patient-specific model.

Materials and Methods: The model coupled an electrochemical formalism, which related Cu-ATSM (hypoxia surrogate) uptake and pO_2, with a modified oxygen enhancement ratio (OER) equation to yield non-uniform dose prescriptions. This methodology was applied to eight head and neck cancer patients who underwent Cu-ATSM PET/CT scans. Integral dose escalation was determined as a function of tumor hypoxic proportion ($HP_{2.5}$ = percent tumor voxels with pO_2 < 2.5 mmHg). Model parameters included intracellular acidity – *pH*, dose boost as a function of hypoxic proportion – $D_{\text{boost}}(HP_{2.5})$, max OER – OER_{max}, and half-max sensitization oxygen tension – P_{mid}. Parameters were varied within published ranges for this patient population, and uncertainties were propagated to variations in the maximum dose heterogeneity ($MDH = \frac{D_{\text{max}} - D_{\text{min}}}{D_{mean}}$).

Results: Model parameters had differing impact on dose prescription uncertainties. Over the range of *pH* values [7.1-7.3], variation in *MDH* was 4 percent (maximum 9 percent). Within the 95 percent confidence intervals of the $D_{\text{boost}}(HP_{2.5})$ functional fit, variability in *MDH* was 5 percent (maximum 14 percent). Between the limits of OER_{max} values [1.4-3.0], variation in *MDH* was 1 percent (maximum 2 percent). From the array of P_{mid} values [2-5 mmHg], variability in *MDH* was 1 percent (maximum 2 percent). The total variation in *MDH* for all parameters was 10 percent (maximum 17 percent).

Conclusions: Dose prescription variability was on the order of 10 percent. Variations were due primarily to uncertainties in cellular acidity and dose boost functional fit, which are parameters governing calculated oxygen tension distributions. Ultimately, the derivation of a hypoxia imaging-based prescription function will require fitting model parameters to outcome data in dose escalation clinical trials.