AbstractID: 12904 Title: Characterizing inter-patient and intra-patient variability in hypoxia imaging-based dose painting prescriptions

**Purpose:** Heterogeneity in tumor hypoxia between and within patients may have significant impact on target prescription definition. The purpose of this study was to characterize inter-patient and intra-patient variations in hypoxia-based dose painting prescriptions.

**Materials and Methods:** A model was developed to relate Cu-ATSM (hypoxia surrogate) uptake and prescribed dose via a modified oxygen enhancement ratio (OER) equation. It was applied to eight head and neck (HN) cancer patients who underwent Cu-ATSM PET/CT scans. Integral dose escalation was based on tumor hypoxic proportion ($HP_{2.5}$ = percent tumor voxels with $pO_2$ < 2.5 mmHg). Model parameter values were fixed across the population: acidity ($pH$ = 7.2), max OER ($OER_{max}$ = 1.4), and half-max sensitization $pO_2$ ($P_{mid}$ = 3 mmHg). The population deviation of patient means (inter-patient variation $\sigma_{inter}$) and the population pooled deviation (intra-patient variation $\sigma_{intra}$) were calculated. Similar analysis was applied to 69 HN patients receiving microelectrode $pO_2$ measurements for statistical comparison.

**Results:** In imaging patients, $\sigma_{inter}$(dose) was 4.6 Gy and $\sigma_{intra}$(dose) was 2.7 Gy relative to a population mean dose of 63 Gy. Across microelectrode patients, $\sigma_{inter}$(dose) was 5.3 Gy and $\sigma_{intra}$(dose) was 3.0 Gy relative to a mean dose of 63 Gy. Neither inter-patient nor intra-patient dose variations were significantly different between populations ($p$ > 0.8). Inter-patient variability was higher than intra-patient variability in microelectrode patients ($p$ < 0.01) but insignificantly different in imaging patients ($p$ = 0.3). Patients receiving at least 10 Gy dose boosts comprised 13 percent of the imaging population and 9 percent of the microelectrode population.

**Conclusions:** Inter-patient dose variations equaled or exceeded intra-patient dose variations. Approximately 10 percent of patients required significant dose escalation and redistribution due to high hypoxic proportion and heterogeneity. Minimizing variations through robust hypoxia-based target prescription definitions has potential to judiciously individualize treatment protocols in resistant subpopulations.