AbstractID: 10810 Title: Comparison of Cu-ATSM and FMISO uptake to variations in oxygen tension

Purpose: Unique uptake and retention mechanisms of PET hypoxia tracers make comparison between them challenging. Two common hypoxia surrogates, [^{61}Cu]Cu-ATSM and [^{18}F]FMISO, were compared by modeling their uptake as a function of local oxygen tension and comparing these with clinical measurements.

Materials and Methods: An electrochemical formalism describing bioreductive retention mechanisms under equilibrium conditions was adopted to relate time-averaged tracer concentration to tissue partial oxygen tension (pO_2). Chemical equilibrium constants describing product concentration to reactant concentration ratios were determined from free energy changes and reduction-oxidation potentials of the most probable reactions. Calculated pO_2 distributions from imaged Cu-ATSM tracer activity concentrations of head and neck squamous cell carcinoma (HNSCC) patients were compared to microelectrode pO_2 measurements in 69 patients with HNSCC. Additionally, simulated Cu-ATSM and FMISO uptake distributions were derived from the mean HNSCC population pO_2 distribution.

Results: Cu-ATSM and FMISO uptake differ in sensitivity to changes in oxygen tension, as Cu-ATSM finely samples low pO_2 over broad uptake ranges while FMISO uniformly samples pO_2 above low pO_2 distribution peaks. Cu-ATSM uptake is higher than FMISO uptake under severe hypoxia ($pO_2 < 2.5$ mmHg), but under moderately hypoxic conditions ($pO_2 > 10$ mmHg) FMISO is retained more than Cu-ATSM. Based on population averages, clinical hypoxia thresholds (5 mmHg and 2.5 mmHg) correspond to higher Cu-ATSM SUV (3.1 and 3.7) and lower FMISO SUV (1.2 and 2.4).

Conclusions: Differing retention mechanisms of Cu-ATSM and FMISO make direct comparison inaccurate without relating their uptake to common metrics. Results indicate that Cu-ATSM is more selective for low pO_2 than FMISO and may explain the relatively low correlation between uptakes of these tracers in certain small animal models. When using various hypoxia tracers as a basis for dose painting, uptake and resulting dose distributions should not be interpreted interchangeably but rather as yielding complementary information.