AbstractID: 12978 Title: Classification and Characterization of Tumor Subpopulations Using Molecular Imaging

Purpose: Distinct subpopulations of tumor cells with varying characteristics exist within a single neoplasm. The aim of this study was to develop a classification scheme for tumor subpopulations and investigate their characteristics and spatial distributions. **Method and Materials:** Eight HNSCC patients underwent PET/CT scans with [^{18}F]FDG (a surrogate of metabolism), [^{18}F]FLT (cell proliferation), and [^{61}Cu]CuATSM (hypoxia). CT images were co-registered and transformation matrices were applied to corresponding PET images. Five different clustering algorithms were utilized to classify voxels within a tumor ROI. By using the Silhouette validity index, performance of the clustering algorithms was evaluated and the optimal number of clusters was determined for each tumor. Mean SUVs were calculated for each subpopulation and then normalized to the mean SUV for an entire tumor. **Results:** The k-means algorithm was used in this study since it gave the highest value of the Silhouette validity index. Seven tumors were partitioned: one into two subpopulations and six into three subpopulations. The number of clusters for the remaining tumor was much greater than those for the others, which might be caused by the misregistration between CT and PET. For the three partition cases, the subpopulations were found to be spatially separated into peripheral, central and intermediate regions. FDG uptake was 55% lower for the peripheral subpopulations and 19% lower for central subpopulations relative to the overall mean. On the other hand, FLT uptake was 51% lower for the peripheral subpopulations but 52% higher for the central subpopulations. However, no significant difference in CuATSM uptake among subpopulations was observed. **Conclusion:** We demonstrated that tumors can be partitioned into multiple subpopulations with distinct characteristics using multi-phenotypic molecular imaging. This subpopulation-based study may lead to better understanding in designing personalized cancer therapy.