AbstractID: 4807 Title: Intratumoral Pattern of FDG Uptake in Human Xenograft Models

Purpose: To investigate the spatial association between intratumoral uptake of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) and the following characteristics of the tumor microenvironment: hypoxia, cellular proliferation, and blood flow; and to evaluate the potential impact of this association on the use of ^{18}F-FDG images in radiation oncology treatment planning for target volume delineation.

Method and Materials: Six nude rats were inoculated with the following human tumor cells: HT-29 (colon adenocarcinoma), DU-145 (prostate carcinoma), and A549 (NSCLC). When the tumors reached 20-25mm in diameter, the animals were injected with ^{18}F-FDG, pimonidazole, and bromodeoxyuridine. 1hr post injection animals were imaged on animal PET scanner. Upon completion of imaging, animals were injected with Hoechst33342 and sacrificed with CO_2 5-10min later. Tumors were immediately dissected, frozen and cut into 8μm thick sections. One section from each tumor was placed onto a phosphor plate for autoradiography. The images of the fluorescence produced by Hoechst33342 and by fluorescent antibodies raised against pimonidazole and bromodeoxyuridine were acquired from the adjacent sections and co-registered. The statistical analysis of association between PET tracer uptake and microenvironmental markers was then performed on a pixel-by-pixel basis.

Results: In all the tumor models studied, we observed positive pixel-by-pixel correlation between FDG uptake and pimonidazole staining intensity (correlation coefficients ranged from 0.46 to 0.87, $p<0.001$). At the same time, correlation with bromodeoxyuridine was always negative (ranged from -0.50 to -0.78, $p<0.001$).

Conclusions: This study further confirms association between foci of increased intratumoral FDG uptake and regions of hypoxia. In addition, it demonstrates reduced FDG uptake in actively growing parts of the tumor. Therefore, the use of FDG uptake iso-contours to delineate lesions and, especially, to reduce target volume with respect to CT-defined volume should be approached very carefully, since it might potentially result in exclusion of areas of active tumor growth from the target volume.