AbstractID: 1828 Title: Increased Uptake of FDG in the Regions of Hypoxia

The purpose of this study is to investigate the causes of intratumoral variations of ^{18}F-fluorodeoxyglucose (^{18}F -FDG) uptake by correlating it with microenvironmental parameters of a tumor as imaged by a hypoxia marker pimonidazole, a cellular proliferation marker bromodeoxyuridine (BrdU), and a blood perfusion marker Hoechst 33342. Dunning rat prostate tumors (R3327-AT) were transplanted into four nude mice. When the tumors reached 10-15mm in diameter, the animals were injected with ^{18}F-FDG, pimonidazole, bromodeoxyuridine, and Hoechst 33342. Upon sacrifice, 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 Hoechst 33342 and by fluorescent antibodies raised against pimonidazole and bromodeoxyuridine were acquired from the adjacent sections and co-registered. Statistical analysis of the data demonstrated a positive pairwise correlation ($r=0.38$, $p<0.01$) between FDG uptake and BrdU staining intensity in the smallest analyzed tumor that had no visible necrosis. However, in the three other tumors, with a non-zero necrotic fraction, the correlation of FDG uptake and BrdU staining intensity was always negative ($r=-0.60$, $r=-0.71$, $r=-0.52$; all $p<0.01$). For all four tumors used in the study, FDG uptake was positively correlated with pimonidazole staining intensity ($r=0.43$, $r=0.73$, $r=0.50$, $r=0.49$; all $p<0.01$). Furthermore, in all the cases studied, the area of highest FDG uptake on a section was always in regions of hypoxia. Therefore, this study constitutes evidence of increased FDG uptake being caused mainly by upregulated glucose metabolism in the regions of hypoxia.