Combined Hyperpolarized $^{13}$C-pyruvate MRS and $^{18}$F-FDG PET (HyperPET) Estimates of Glycolysis in Canine Cancer Patients

Hyperpolarized $^{13}$C Magnetic Resonance Spectroscopy (MRS) using hyperpolarized $^{13}$C-labeled pyruvate as a substrate offers a measure of pyruvate-lactate interconversion and is thereby a marker of the elevated aerobic glycolysis (Warburg effect) generally exhibited by cancer cells. Here, we aim to compare hyperpolarized $^{[1-{^{13}}C]}$pyruvate MRS with simultaneous $^{18}$F-2-fluoro-2-deoxy-D-glucose (FDG) PET in a cross-sectional study of canine cancer patients. Methods: Canine cancer patients underwent integrated PET/MRI using a clinical whole-body system. Hyperpolarized $^{[1-{^{13}}C]}$pyruvate was obtained using dissolution-DNP. $^{18}$F-FDG PET, dynamic $^{13}$C MRS, $^{13}$C MRS Imaging (MRSI) and anatomical $^{1}$H MRI was acquired from 17 patients. Apparent pyruvate-to-lactate rate constants were estimated from dynamic $^{13}$C MRS. $^{18}$F-FDG Standard Uptake Values and maximum $^{[1-{^{13}}C]}$lactate-to-total-$^{13}$C ratios were obtained from tumor regions of interest. Following inspection of data, patients were grouped according to main cancer type and linear regression between measures of lactate generation and $^{18}$FFDG uptake were tested within groups. Between groups, the same measures were tested for group differences. Results: The main cancer types of the 17 patients were sarcoma (n = 11), carcinoma (n = 5) and mastocytoma (n = 1). Significant correlations between pyruvate-to-lactate rate constants and $^{18}$F-FDG uptake were found for sarcoma patients, whereas no significant correlations appeared for carcinoma patients. The sarcoma patients showed a non-significant trend towards lower $^{18}$F-FDG uptake and higher lactate generation than carcinoma patients. However, the ratio of lactate generation to $^{18}$F-FDG uptake was found to be significantly higher in sarcoma as compared to carcinoma. The results were found both when lactate generation was estimated as an apparent pyruvate-to-lactate rate constant from dynamic $^{13}$C MRS and as an $^{[1-{^{13}}C]}$lactate-to-total-$^{13}$C ratio from $^{13}$C MRSI. Conclusions: A comparison of hyperpolarized $^{[1-{^{13}}C]}$pyruvate MRS with simultaneous $^{18}$F-FDG PET indicate that lactate generation and $^{18}$F-FDG uptake in cancers can be related and that their relation depend on cancer type. This finding could be important for the interpretation and eventual clinical implementation of hyperpolarized $^{13}$C. In addition, the differences between the two modalities may allow for better metabolic phenotyping performing hybrid imaging in the form of hyperPET