Purpose: Statistical tools to derive imaging-based prescription functions linked to outcome data have great potential for dose painting. The predictive power of PET images was assessed in a veterinary dose escalation trial via voxel regression.

Methods: Ten canine patients with sinonasal tumors underwent pre-treatment PET/CT scans of [F-18]FDG, [F-18]FLT and [Cu-61]Cu-ATSM (PETpre). Following radiotherapy, nine patients underwent FDG PET/CT scans at three months (FDGpost). Multivariate voxel-based regression of PETpre images to the FDGpost image, a surrogate of local recurrence, was performed in each patient for linear, log-linear, log-ratio and generalized-linear models. Model predictions of patient FDGpost images were assessed by the coefficient of determination R-squared. Population predictive power was established for non-zero regression coefficients using one-sample t-tests, as well as for different coefficients between RECIST-classified responders and non-responders using two-sample t-tests.

Results: The log-ratio model achieved the best patient model fits (mean: R-squared=0.64, range: [0.22-0.85]). The population predictive power of FDGpre to FDGpost was statistically significant in all but the log-linear model (p=0.12 vs. p<0.03). The linear model classified the slope of 0.37 for RECIST non-responders to be different from the slope of 0.07 for RECIST responders (p=0.01). The generalized-linear model related FDGpre to FDGpost by a linear power law (coefficient = 0.93, p<0.01). FLTpre and Cu-ATSMpre had non-significant coefficients, though Cu-ATSMpre weakly classified RECIST response in the generalized-linear model (non-responders: coefficient = 0.68; responders: coefficient = -0.22; p=0.12).

Conclusions: Results from the majority of regression models indicate that pre-treatment FDG is an independent predictor of three month post-treatment FDG. The log-ratio model of relative PET uptake produced the best patient fits. The generalized-linear model characterized pre-treatment Cu-ATSM as a potential classifier of RECIST response. Further statistical analysis of the possible synergistic interactions between image parameters and radiation dose may lead to the discovery of a dose painting prescription function.