AbstractID: 12796 Title: Functional relationships between imaging and biological markers for the purpose of dose painting using the example of FLT-PET and the Ki-67 labeling index

Purpose: To develop a Monte Carlo simulation based parameter estimation procedure to obtain and assess functional relationships between imaging data and an underlying biological property that are necessary for dose prescription strategies such as dose painting.

Method and Materials: An example of such a relationship is the correlation of FLT tracer uptake in the tumor and the fraction of proliferating cells as measured by the labeling index (LI) of the Ki-67 protein. Lung tumor xenografts (H520) in 6 mice were irradiated on a small animal irradiator and FLT-PET/CT imaged pre- and 24 hours post-irradiation. Tumors were harvested after the second imaging session, processed and stained for Ki-67. The post-irradiation FLT uptake distributions were analyzed within the boundary of the tumors as segmented on the CT images. For 4/6 tumors 2 ROIs each and corresponding uptake distributions were identified, resulting in a total of 10 FLT distributions and associated Ki-67 LI. For every FLT uptake distribution a test statistic and its probability density function (pdf) was computed that mimicks the measurement of the LI using 4 non-overlapping fields. A likelihood function from the test statistics of each tumor ROI was maximized to obtain the parameters of an assumed linear relationship between FLT uptake in units of %ID/g and the LI.

Results: A linear relationship is compatible with the measured LI, however the likelihood function demonstrates a broad maximum if the pdfs are generated from purely random samples within the ROIs. More samples and additional information about the location of the sample fields narrows the width of the pdfs and enhances the maximum likelihood.

Conclusion: The advantage of the proposed parameter estimation is that it simulates the LI analysis process and does not rely on any summary metric of the FLT uptake distributions, such as the maximum or a tail-mean value.