Purpose: To investigate the feasibility of decomposition of differential uptake volume histograms (UVH) derived from FDG-PET and CT data for uncovering tumor sub-volumes as a novel approach for defining biological target volumes (BTV) for use in radiotherapy treatment planning.

Methods: For a cohort of 27 histopathologically proven non-small cell lung carcinoma (NSCLC) patients, background uptake values were sampled within contra-lateral healthy lung over PET slices containing tumor and then scaled by the ratio of tissue densities between healthy lung and tumor derived from CT data. Signal-to-background uptake values within volumes of interest encompassing the tumor were scored from which differential uptake volume histograms were constructed. These were subsequently decomposed into the minimum number of analytical functions that yielded acceptable net fits, as assessed by chi^2 values.

Results: Based on the assumption that each function used to decompose the UVH may correspond to a single sub-volume comprising the volume of interest sampled, at least four sub-volumes consistently evolved for our patient population. Furthermore, if crossing points between adjacent functions are interpreted as threshold values that differentiate sub-volumes, average threshold values between the four sub-volumes were found to be 0.80±0.21, 1.56±0.48, and 2.96±1.04 for adenocarcinomas, 0.89±0.48, 1.60±0.40, and 2.85±0.75 for large cell carcinomas, and 0.84±0.31, 1.70±0.58, and 3.72±1.68 for squamous cell carcinomas.

Conclusions: Our study suggests that FDG-based PET data could be used to identify biological sub-volumes within tumor in NSCLC patients. Significant fluctuations in threshold values throughout the patient cohort can be explained as a consequence of large variability in physiological status of the tumor volume for each patient at the time of the PET/CT scan. This further suggests that BTV threshold values may be rather patient-specific, and could be determined by creation and curve fitting of differential uptake volume histograms on a patient-specific basis.