Purpose:
High precision within quantitative imaging studies is required to define biological targets for dose painting, and to evaluate responses to therapy. However, within PET imaging systems there are position-dependent systematic fluctuations in contrast-recovery. The objective of this study was to determine the impact of patient set-up on PET-based quantification of heterogeneous tumors.

Methods:
Ten dogs with sinonasal tumors received six repeated [18F]FDG-PET scans. Between each PET acquisition, known set-up errors were produced by varying patient position in precisely controlled 1.0±0.5 mm steps. Image noise was investigated by retrospectively varying acquisition time of a stationary scan. Resulting changes in SUVmax and PET-based target volumes were evaluated. Correlation between corresponding voxels of co-registered images determined repeatability of spatial distributions. A theoretical upper limit of repeatability was estimated from simulated PET images using empirical models of position-dependent contrast-recovery.

Results:
From the simulated PET images, a theoretical upper limit of 0.90 was estimated for the repeatability of spatial distributions when set-up errors are present. When only image noise was varied between [18F]FDG-PET scans, repeatability of spatial distributions was measured at 0.95. However, set-up errors lead to significant decreases ($p < 0.01$) in voxel correlations. Introducing set-up errors between [18F]FDG-PET acquisitions reduced the repeatability of spatial distributions to 0.80, and caused changes of 5% in SUVmax and 10% in volumes of PET-based targets.

Conclusions:
Set-up errors as small as a few millimeters (< 3mm) reduced the reproducibility of quantitative PET imaging of heterogeneous tumors. PET-based quantitative values generally varied within 10%, but target volumes within some tumors changed by 30%. Errors during PET acquisition will lead to uncertainty in quantifying changes in tumor function, and to limited accuracy and precision of PET-based biological target volumes. Therefore, tumor delineation must be independent of SUV thresholds and uncertainty margins are required for PET-based response quantification.