Purpose: Quantitative imaging measures are essential for assessment of tumor response to therapy; however, systematic validation is required before imaging biomarkers can be successfully implemented. We performed preliminary validation of the optimal image reconstruction parameters to maximize the accuracy of PET-based imaging biomarkers.

Methods: Optimal PET reconstruction parameters were determined using four spheres of various sizes (10-22mm) containing 168 kBq/cc of [18F]FDG. Spheres were placed inside a NEMA IEC body phantom. Scans were acquired on a GE VCT PET/CT scanner in both 2D and 3D mode. Multiple images were reconstructed using OSEM by varying matrix dimensions, iteration number, and post-filtration. For each sphere, the recovery coefficient (RC) was used to measure quantitative image accuracy. Robustness of reconstruction parameters to sphere size changes was measured as the coefficient of variation (CV) of the RCs of the individual spheres within an image. Optimal reconstruction parameters were those which resulted in the highest average RC and lowest CV.

Results: RC averaged over all four spheres ranged from 0.72 - 0.95 for the image reconstructions investigated. Higher RCs were observed for 2D acquisition mode than 3D (0.91 vs. 0.80), and for 22mm spheres than 10mm spheres (0.99 vs. 0.74). No such trends were observed for CVs. CV values varied by a factor of two across the reconstructions investigated, ranging from 9% to 17%. Image accuracy and robustness to lesion size changes were highest for 2D acquisition, 256x256 matrix, 2 iterations, and 3mm post-filtration, yielding an RC of 0.92 and CV of  $\pm$ 9%.

Conclusions: We successfully optimized image reconstruction parameters to maximize quantitative imaging accuracy, which will increase reproducibility of biomarkers. Future work will include test-retest imaging of biomarkers in patients to quantify remaining uncertainties. This study represents a critical first step towards validation of imaging biomarkers of treatment response.