**Iterative PET Reconstruction Algorithms followed by Non-Local Means Denoising for Improved Quantitative Imaging**

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**Objectives**: To test the use of non-local means (NLM) as a method to improve the quantitative performance of various iterative PET reconstruction algorithms using a python-based framework.

**Methods:** Realistic simulated PET images were generated from first principles using radiopharmaceutical coupled to attenuation maps. We specifically focused on modeling of three distinct regions: lesions, liver, and background. The number of decays from each pixel was Poisson with mean proportional to the true radiopharmaceutical concentration at that location. Attenuation maps were then used to simulate detection; the detected decays were used to generate sinograms.

A variety of iterative PET image reconstruction techniques from the python library tomopy were used to obtain estimates for the original radiopharmaceutical distribution, including the analytical reconstruction technique (ART), the simultaneous iterative reconstructive technique (SIRT), the total variation reconstruction technique (TV), and variations of maximum-likelihood expectation maximum (MLEM) and ordered-subset expectation maximum (OSEM), including those with linear and quadratic penalty terms . With increasing iterations, bias and variance trade-off curves were generated for different algorithms, enabling comparison between different methods.

An NLM framework for denoising was applied to generate images at each stage of the iterative process, yielding updated bias-variance trade-off curves. The purpose of such modification was to (i) compare the relative improvements across algorithms, and (ii) compare relative improvements between the background, liver, and lesions of each image.

**Results:** Analysis of bias-variance curves suggests that NLM improves the reconstructive capabilities of all iterative algorithms considered. All algorithms saw a reduction in both bias and variance of background predictions: the most significant examples were ART with an average reduction in variance from 0.76% to 0.31% (-0.45%) and OSEM with an average reduction in bias from 1.07% to 0.76% (-0.31%) throughout their iterations. For liver predictions, all algorithms saw a decrease in variance with a slight increase in bias: the most significant examples were OSEM with an average decrease in variance from 0.81% to 0.26% (-0.55%) but corresponding increase in bias of 2.67% to 3.05% (+0.37%) throughout its iterations. For tumor regions, the ART, MLEM, OSEM, SIRT, and TV algorithms all saw a reduction in variance; the most significant was ART with an average decrease of 1.27% to 1.01% (-0.26%) throughout its iterations. Variations of MLEM and OSEM with penalized linear and quadratic components saw an increase in variance in tumour regions. In addition, all algorithms except ART saw an increase in the bias of tumour regions. In the attached document, Figures 1 and 2 show bias variance trade-off curves for all algorithms, Figure 3 shows a sample curve comparing standard and NLM adjustment to the SIRT algorithm, and Figure 4 displays the original PET image, and image reconstructed using SIRT, and an image reconstructed using SIRT and NLM.

**Conclusion:** For the realistically simulated dataset, use of a non-local means denoising framework on predicted PET images reconstructed with iterative reconstruction algorithms was shown to improve quantitative performance. While the results are most notable in background and liver regions, improvements in tumor regions are also observed for certain algorithms.