PhD Thesis Title: Optimization and improving the precision of quantitative analysis in small animal PET imaging system (Xtrim-PET)

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ABSTRACT:

Xtrim-PET *(Parto Negar Persia Co., Ltd., Tehran, Iran)* is the first PET scanner manufactured in Iran and dedicated to the diverse research applications in the field of small animal imaging. This thesis outlines the development of the necessary corrections and the image reconstruction algorithms needed for conducting quantitative analysis through the Xtrim-PET system. We studied the degrading factors affecting the image quality and quantitative accuracy of the scanner and developed/tailored the algorithms considering the scanner design.

The first part of the thesis focuses on evaluating the performance of the system based on the National Electrical Manufacturers Association (NEMA) NU-4 2008 standards and defining the appropriate protocols for routine practices, as well. The second part of the work concerns the uncertainties related to normalization, gap correction, photon attenuation and scattering. In an effort to reduce human bias and increase the precision of the gap-correction technique in different situations, we developed a de novo and fully-automated normalization method of embedding dead areas between the adjacent Lutetium yttrium oxyorthosilicate (LYSO) detection blocks.

For correcting attenuated photons, an off-line registration framework was deployed in which anatomical images of a LOTUS-InVivo Micro-CT scanner *(Behin Negareh Co., Ltd., Tehran, Iran)* were used for the CT-based attenuation correction. An automated segmentation-based method was also deployed as a transmission-less attenuation correction approach. A convolution-subtraction method was also utilized for measuring and eliminating the scattered events. We used a double-exponential model to define the scatter contribution from the scanner while the non-stationary behaviour of the object scattering kernel was approximated through the asymmetric Laplace distribution.

The third section discusses the advanced image-reconstruction techniques of embedding the Xtrim-PET geometry and the blurring effect of the point spread function in different parts of the field of view. Moreover, we investigated the feasibility of several advanced deep-learning methods to eliminate gap-related artifacts and also improved the quantitation in low-dose preclinical PET studies. The last part of the dissertation studies the accuracy and precision of the algorithms developed in the previous sections. In addition to various phantom studies, PET and CT images of 14 rodents (8 normal mice/ 3 tumoral mice/ 3 normal rats) were acquired. Each animal was dissected and the actual activity values in different tissues (brain, lung, liver, Intestine, stomach, and spleen) were measured by the dose calibrator. The activity concentration calculated through the PET images was then compared to the actual values to validate the accuracy of the codes in real situations. This work demonstrates that absolute relative error in quantitative PET research could be decreased meaningfully by implementing customized yet effective algorithms.

References to author publications that relate specifically to the dissertation[1-7]:

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3. **Amirrashedi M**, Zaidi H, and Ay MR. "Towards quantitative small-animal imaging on hybrid PET/CT and PET/MRI systems." *Clin Transl Imaging*. July 2020; 8:243-263. https://doi.org/10.1007/s40336-020-00376-y
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5. **Amirrashedi M**, Sarkar S, Mamizadeh H, et al. "Leveraging deep neural networks to improve numerical and perceptual image quality in low-dose preclinical PET imaging." *Comput Med Imaging Graph*. Dec 2021;94:102010. doi:10.1016/j.compmedimag.2021.102010
6. **Amirrashedi M**, Sarkar S, Ghadiri H, Ghafarian P, and Ay MR. "Standard-dose PET reconstruction from low-dose preclinical images using an adopted all convolutional U-Net." Paper presented at: International Society for Optics and Photonics (SPIE Medical Imaging); 2021:116000P.
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