

## ABSTRACT

### Event-by-Event Motion Correction in Positron Emission Tomography: Development, Evaluation and Applications

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Positron Emission Tomography (PET) is a powerful metabolic and pharmacological imaging technique with a broad range of applications in Neuropsychiatry, Cardiology and Oncology. As the system resolution of PET imaging has improved, motion correction has become essential to eliminate image blurring and artifacts due to subject motion. This work develops, applies, and assesses the accuracy of both frame-based and event-by-event motion correction methods. Human and non-human primate (NHP) brain and whole-body PET studies were employed with 3 different scanners.

We first investigated the accuracy of frame-based motion correction and event-by-event motion correction methods in human brain PET imaging. Static and dynamic list-mode PET data were simulated using the forward projection model of MOLAR (Motion-Compensation OSEM List-mode Algorithm for Resolution-Recovery Reconstruction), incorporating a wide range of real subject head motion. Image intensities in high-contrast regions of interest (ROI) and estimates of volume of distribution and binding potential from tracer kinetic models were assessed to evaluate the accuracy of each motion correction method. The results showed that event-by-event motion correction can reliably correct for all head motions. With the attenuation map correctly aligned, frame-based motion correction produced ~9% bias in ROI intensities, ~5% in volume of distribution and ~10% in binding potential estimates for large motions (>5 mm).

We then developed, implemented, and evaluated both frame-based motion correction and event-by-event motion correction for awake NHP brain PET imaging on the microPET scanner FOCUS-220. For frame-based motion correction, a strategy for dividing PET list-mode data into sub-frames was developed. For event-by-event motion correction, the MOLAR platform was adapted for the FOCUS-220. Both motion correction algorithms were applied to awake NHP PET studies with a GABA<sub>A</sub>-benzodiazepine receptor ligand [<sup>11</sup>C]flumazenil. The results showed that event-by-event motion correction noticeably eliminates image blurring due to intra-frame motion and improves statistics over frame-based motion correction method in awake NHP brain PET imaging.

We finally developed event-by-event motion correction for respiratory motion in whole-body PET studies on the Biograph mCT scanner, based on MOLAR. Application of MOLAR for the mCT required two novel algorithmic developments. First, in routine studies, the mCT collects list-mode data in 32-bit packets, where averaging of lines of response (LORs) reduced the number of LORs so that 32 bits are sufficient to address all sinogram bins. This degrades the spatial resolution. In this work, a probabilistic assignment of LOR positions (pLOR) was developed to address LOR grouping in 32-bit data. Second, two approaches for 3D time-of-flight (TOF) scatter estimation were developed to accelerate the computationally intensive calculation. The proposed list-mode reconstruction algorithm was compared to the manufacturer's point spread function + time-of-flight (PSF+TOF) algorithm. Moving phantom, animal, and human studies demonstrated that event-by-event motion correction noticeably reduces image blurring caused by respiratory motion.

The results from human brain studies, NHP brain studies, and whole-body studies indicate that, while frame-based motion correction methods may be suitable for human brain PET studies with

small motion, the event-by-event motion correction method is clearly superior to the frame-based methods when large motion is present, e.g., in NHP brain studies and whole-body studies.