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Data-driven motion correction in clinical PET - a joint accomplishment of creative academia and industry

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Dear Dr. Czernin,

I read with great interest the recent JNM article by Walker, et al. comparing data-driven and hardware-driven motion correction technologies in PET (*1*). The former is an important innovation, and it is exciting to see it transition into the market place. Publications like this one play a pivotal role in the technology's acceptance and broader dissemination. However, this work is very similar to work from our group published in 2016 (*2*) and unfortunately it was not properly referenced.

Like Walker et al., we compared head-to-head non-gated, software-gated, and hardware-gated images in a large set of clinical PET scans, using quantitative analysis of lesion uptake and qualitative blinded reviewer scoring of image quality, with similar results – a statistically significant preference of software-gated images over hardware-gated images and with similar ratios of performance metrics. There are, of course, subtle differences between the gating approaches, and the authors of the current manuscript note that their work validates newly available commercial technology. Given this work focused on commercial product testing, it should add to the scientific context to note that the key points they presented also describe our earlier findings.

Also, in their closing discussion the authors suggest data-driven gating with quiescent period sorting is a practical motion correction strategy, but that retention of more than 50% of coincidences may be required before respiratory gated PET imaging can dependably support the clinic. We are happy to share that we have also studied this, finding that PET data supports a spectrum of "ideal" or "optimal" bin sizes throughout a given population, and ultimately no single bin size will ensure maximum benefit, or even benefit, for any given patient (*3*). In our conclusion we proposed that a data-driven instance-specific binning strategy could be an effective way to overcome the instance-specific artifacts found in motion impacted PET scans.

The commercial technology discussed in Walker, el al.'s article is GE's *MotionFree™* product. To the company's credit they recognized the potential of data driven motion correction and developed a product to translate it to clinic settings. The algorithms used in GE's product, and in our 2016 and earlier publications *(2-5)*, are remarkably similar.

Data driven motion correction has evolved over the last decades, and our group has been active in its development. In 2007, we recognized that, at the data level, motion in PET is captured and recorded in localized signal fluctuations. We were the first demonstrate the ability to characterize patient motion through direct constructive combination of time-activity signal fluctuations in the data acquired, an original that idea at the time improved significantly upon the strategy of tracking geometric/center-of-mass type motion (*4-7*). In recognizing the importance of practicality, our group was also the first to consider and demonstrate that processing can be accelerated, to virtually real time, through strategic collapsing of raw (i.e., sinogram) data (*8*). Notably, these innovations provided proof of principle and formed the basis of most data-driven gating publications since. Additionally, our group was the first to discuss and demonstrate the concept of fully automated workflows as a uniquely practical strategy for bringing robust motion management into the clinic (*9-11*). We developed innovative spinoff concepts, such as using a "quality factor" (defined as the ratio of signal in respiratory and non-respiratory temporal frequencies in our collected motion trace) to determine a priori the capacity of the signal to usefully correct a patient scan (*7*), and to modulate bed acquisition times based on information from such signals for practical clinical integration (*10*). It is gratifying that GE's *MotionFree™* product integrates all the foregoing innovations originally presented in our earlier publications.

The absence of an acknowledgement of our previously published work and its relationship to that presented in the current manuscript is perhaps related to the assertion that the principle component analysis (PCA) algorithm is a different algorithm than the one our group developed. Both algorithms, in fact, are driven by using a weighted combination of spatially clustered time-activity signal to characterize patient motion. In 2007, 2009, and 2010, our group demonstrated the utility of this approach and suggested that it is likely that our methods could be improved with further development of signal weighting (*5,7,8*). In 2011, e.g., Thielemans, et al. investigated this possibility by integrating a well-established mathematical function of PCA to calculate these weighting factors (*12*). Our comparisons between PCA-based weighting and our original constructive combination-based methods have not yet been published, but they show that the two methods perform similarly, and in many cases virtually identically (*13*). It is therefore no surprise that the results of Walker, et al.'s clinical assessment and our work are similar because we both employed similar methods. This is an important result because it indicates that the data-driven gating technology, based on combining spatially clustered signal fluctuations, can perform comparably across different centers, vendors, and flavors of implementation.

In data-driven motion management, our field is witnessing the culmination of a physics innovation concept-to-impact cycle, with GE providing a first-to-market product (for general PET motion correction). Many research scientists who began this journey over a decade ago have contributed original ideas to this effort (*12,14-20*). Alongside others, our group contributed to inventing the technology, enabling its practicality, advocating for its consideration, and demonstrating its clinical utility. In the process, we found researchers eager to cooperate, vendors who offered support, an effective process for solution development that built off each other's accomplishments and ideas for even further development. We also found challenges, which illuminated opportunities to expand our field's infrastructure to better support data driven innovation, including evolving our understanding of data as a resource, solution development pathways, training and professional roles, and fostering a community that embraces new concepts for innovation, which we expect to come with a rapidly advancing digital landscape (*21-23*).

Ultimately, our goal should be to transition to a field where data science innovation is limited by our imagination and not a legacy infrastructure. To this end we have much work to do, and the path there is best supported with respectful co-leadership, acknowledgement, and cooperation.

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