



First clinical experience of 106 cm, long axial field-of-view (LAFOV) PET/CT: an elegant balance between standard axial (23 cm) and total-body (194 cm) systems

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Conventional PET/CT scanners with standard axial field-of-view (SAFOV) usually cover around 23–26 cm [1, 2]. Over the last decade, however, there has been tremendous effort in the development of long axial field-of-view (LAFOV) PET/CT scanners, and several of them have entered the clinical arena [3–5]. It is well recognized that, with LAFOV PET/CT scanners, one could image better (e.g. reconstruct at higher resolution and detect smaller lesions), image faster, image longer after tracer injection, and image gently (e.g., at a much lower radiopharmaceutical dose than usual, which will enable more PET scans in the children population, as well as more repeated scans in the adult population) [1].

In the July issue of *European Journal of Nuclear Medicine and Molecular Imaging*, a superbly designed and executed study on the first clinical implementation of a LAFOV PET/CT scanner was reported by Dr. Rominger and colleagues from Bern University Hospital, University of Bern, Switzerland [5]. This is a prospective, non-randomized, dual-arm crossover, comparative imaging study with a clearly stated hypothesis and inclusion/exclusion criteria. The number of patients needed for the study (> 40) was calculated to provide robust statistical analysis. In addition, three PET tracers (¹⁸F-FDG, ¹⁸F-PSMA-1007, and ⁶⁸Ga-DOTA-TOC) and 2 PET isotopes (¹⁸F and ⁶⁸Ga)

were investigated, in order for the study to be more broadly applicable. The entire work was carried out in a very short time frame: the scanner was installed in October 2020, and the manuscript was received on January 25, 2021. This high efficiency is very impressive, especially considering that the COVID-19 pandemic in Switzerland was at its height during that time, not to mention that this was during the holiday season. While reading this manuscript in detail, one cannot help but think about the art of making Swiss watches. The study could not have been designed nor executed in a better way. Finally, the manuscript itself is highly satisfactory, from the presentation to the figures. All in all, this is an exemplary work on a topic that is truly state-of-the-art, which perfectly suits *EJNMMI*.

Two PET/CT systems from Siemens Healthineers were compared in this study [5]. One is the first Biograph Vision Quadra LAFOV PET/CT system (axial FOV 106 cm), with a sensitivity of ≥ 70 cps/kBq and a time resolution of 219 ps in ultra-high sensitivity mode. The other is the clinically well-established Biograph Vision 600 system (axial FOV 26.3 cm), with a sensitivity of ~ 16 cps/kBq and a time resolution of 214 ps [6]. Standardized doses of 3.5 MBq/kg of ¹⁸F-FDG, 250 MBq of ¹⁸F-PSMA-1007, or 150 MBq of ⁶⁸Ga-DOTA-TOC were administered intravenously into patients. Rather than total-body PET/CT scans from head to toe, regular whole-body scans (from skull-base to thighs on the SAFOV Biograph Vision scanner, or vertex to thighs on the LAFOV Biograph Vision Quadra scanner) were performed.

The technical and specific parameters for data acquisition, image reconstruction, data analysis, image interpretation, visual display (e.g., images were cropped to include only “eyes-to-thighs” to minimize differences between captured FOV in both systems to avoid potential bias from the two nuclear medicine physicians), statistical analysis, etc. were presented in exquisite detail in the manuscript, which will not be repeated here. In brief, PET/CT images were acquired

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on the SAFOV PET/CT scanner in continuous bed motion (CBM) with a table velocity of 1.1 mm/s, with an effective examination time of 16.06 min to capture a 106 cm FOV. In comparison, PET/CT images were acquired on the LAFOV PET/CT scanner in one-bed position for 10 min, and PET data were sampled to produce sinograms emulating 10-, 6-, 4-, 2-, 1-, and 0.5-min acquisitions. There was no difference between the CT scans for the two systems.

The key findings of this superb study are summarized below: (1) all 153 target lesions in 44 patients were identified in both scanners, with no observed difference. (2) The LAFOV PET/CT scan time that yielded equivalent target lesion integral activity (count statistics) to the 16.06 min SAFOV scan was 1.63 ± 0.19 min. When comparing ^{18}F - vs ^{68}Ga -based tracers for the LAFOV system, ^{18}F performed better (~ 1.5 vs ~ 2.3 min), which is expected since ^{18}F has much better decay characteristics for PET imaging than ^{68}Ga . (3) Signal-to-noise ratio (SNR) was the highest for long-duration (i.e., 10 min) LAFOV images, and equivalency between the LAFOV and SAFOV (16.06 min scan) was seen at 1.83 ± 1.00 min. (4) Target lesion-to-background ratio (TBR) was slightly better on the LAFOV at 10 min (mean value 2.27 ± 0.02) than the SAFOV (mean value 2.06 ± 0.02), although there was no statistically significant difference. (5) Ten-minute LAFOV PET images showed superior quality than 16.06 min SAFOV images, while those that showed equivalent quality (as the 16.06 min SAFOV PET images) had average scan times of about 1.5–2 min on the LAFOV scanner. Importantly, 0.5-min acquisitions on the LAFOV system did provide visualization of all target lesions and demonstrated acceptable quality for diagnostic purposes. (6) To achieve equivalent lesion measured integral activity as the SAFOV reference (16.06 min scan in CBM), if the LAFOV examination is maintained at 10 min, an approximately sixfold reduction in the injected tracer dose could be used, which can lead to \sim sixfold lower equivalent radiation dose (< 1 mSv vs. ~ 5 mSv for standard PET tracer dose). It is worth noting that these results were achieved on the LAFOV PET/CT scanner using a maximum ring difference (MRD) of 85. There is further potential to reduce imaging time and/or injected radioactivity with the ultra-high sensitivity mode (which has a MRD of 322, available now but not available at the time of this study), which has higher sensitivity (≥ 150 cps/kBq) than the LAFOV Biograph Vision Quadra scanner (≥ 70 cps/kBq) but the same time resolution.

One cannot talk about this LAFOV PET/CT scanner without mentioning the uEXPLORER PET/CT scanner (United Imaging Healthcare Co., Ltd.). In May 2018, the first total-body PET scanner was built by a consortium with aid from several industrial collaborators, which has a 194 cm axial FOV for PET imaging [4, 7]. Of note, the time resolution of the uEXPLORER PET/CT scanner was 430 ps, and

the sensitivity based on the NEMA NU-2 phantom was ~ 190 cps/kBq (70-cm length) and ~ 150 cps/kBq (200-cm length) respectively [8]. In November 2018, the first human images from the uEXPLORER scanner were presented at a total-body PET workshop, which were acquired at the Department of Nuclear Medicine, Zhongshan Hospital, Fudan University (Shanghai, China) [4]. Within a short period of time, a series of studies were reported to investigate the potential and future clinical applications of this total-body scanner [4, 9–20]. In one recent study, it was concluded that a fast PET protocol with a 30–45 s acquisition time in the uEXPLORER PET/CT can provide equivalent image quality as the conventional digital uMI 780 PET/CT (United Imaging Healthcare Co., Ltd.) with longer clinical acquisition settings.

There is likely no room for even faster PET scans, which will not be patient-friendly except in some very unusual circumstances (for example, a patient cannot hold still for more than 1 min due to certain diseases). Several reports (including this work [5]) showed that 1-min PET scan or low-dose PET scan had the same diagnostic performance as a typical 5–10 min PET scan with typical injected radiopharmaceutical dose. With the capability of acquiring superb quality PET images (e.g., HD or 4 K) using the LAFOV PET/CT scanner and 10 min (or longer) scan time, it will be very important to investigate whether higher quality PET images will lead to better clinical performance (e.g., diagnostic accuracy and detection of more lesions) than a standard PET scan. That is a critical question to answer, which is eagerly awaited by many in the field of nuclear medicine and molecular imaging, and we look forward to the findings in the near future. If the answer is no, it may dampen the enthusiasm for such LAFOV PET/CT scanner, just like a luxury car does not get one to the destination faster than a normal family car, which is much more affordable and cost-effective for the majority of the human population.

Currently, there is no head-to-head comparison between the 106 cm (Siemens Healthineers, USA) and 194 cm (United Imaging Healthcare Co., Ltd., China) LAFOV PET/CT systems. Both scanners have generally met the performance expectations for such an expensive system. The smaller footprint of the 106 cm LAFOV scanner may allow for easier clinical installation. Since we do not have detailed figures for cost comparison between the two systems, we cannot comment on this aspect, which will certainly be a major consideration when a hospital/institution decides on which system to procure. Another consideration is that bed movement will be needed for the 106-cm LAFOV system to scan the entire body, which may not be necessary for the 194-cm uEXPLORER system. There could be some error or artifacts caused by bed motion. However, such issues could/should be readily corrected with the modern state-of-the-art systems.

In the work of [5], attenuation correction was performed using low-dose non-enhanced CT data. Although the CT dose was not specifically stated, the effective radiation dose associated with this type of low-dose CT scan is approximately 2–3 mSv, which is significantly lower than a typical diagnostic body CT exam and the CT component of a typical modern PET/CT exam (~5–10 mSv) [21–23]. With the constant advancements of CT tube and detector technologies [24], as well as artificial intelligence (AI)-based CT dose reduction technologies (e.g., TrueFidelity Deep Learning Image Reconstruction from GE Healthcare [25, 26] and Advanced Intelligent Clear-IQ Engine from Canon Medical Systems USA Inc. [27–29]), it is very likely that the CT component of LAFOV PET/CT exam will be further reduced to the sub-mSv level in the near future, which means the entire whole-body PET/CT exam with a low dose of injected PET tracer can be achieved below 2 mSv. This will provide unprecedented possibilities for a variety of clinical scenarios such as longitudinal PET/CT scans of (cancer) patients to monitor the therapeutic response [30–32], routine PET/CT scans of non-cancer patients [33–36], and repeated scans in pediatric patients [37], among others.

Many aspects of the LAFOV PET/CT scanner deserve to be further explored in the future. For example, PET/CT scans with low tracer dose could provide important insight for first-in-human studies of novel tracers by enabling non-invasive whole-body pharmacokinetic analysis in all tissues. This is especially important for ^{11}C -/ ^{18}F -based tracers that require elaborate and lengthy syntheses, which may have low radiochemical yields and consequently are not amenable to human studies using a conventional PET/CT scanner. We look forward to future studies of many novel PET tracers in the metastatic cancer setting. In addition, PET/CT scans at later time points may offer important information, such as differentiating cancer from inflammation based on dual-time-point ^{18}F -FDG PET scans. In a recent study, the same group from Bern, Switzerland, reported that late acquisition ^{68}Ga -PSMA-11 PET/CT using the LAFOV system resulted in improvements in TBR and SNR for clinical diagnosis of recurrent prostate cancer, with only modest impairment in subjective visual imaging quality [38]. For future systematic and routine studies in these areas, scanner performance may not be the limiting factor. Instead, logistics and throughput will be the major considerations especially in medical centers with a high daily clinical workload.

Currently, LAFOV PET/CT scanners are much more expensive than SAFOV PET/CT and only available at a few major medical centers around the world. LAFOV PET is still in its early days, analogous to PET scanners in the 1970s when they were first reported [39, 40]. With continued development and optimization of the PET/CT scanner, as well as cost reduction, we believe LAFOV PET/CT scanners will become widely available in the future, just like PET/CT

scanners have replaced PET scanners more than a decade ago [41, 42]. Without any doubt, LAFOV PET/CT scanners hold tremendous potential for becoming an indispensable tool for humankind's ultimate victory over cancer, as well as catalyzing more preclinical/clinical applications in various disciplines (e.g., pediatric disorders, peripheral vascular diseases, tracking of transplanted cells, development of novel pharmaceuticals and radiopharmaceuticals, global disease assessment) [11, 34, 43–46].

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Declarations

Conflict of interest Weibo Cai is a scientific advisor, stockholder, and grantee of Focus-X Therapeutics, Inc. All other authors declare no conflict of interest.

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