The potential of a medium-cost long axial FOV PET system for nuclear medicine departments

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None.

Abstract

Purpose: Total-body positron emission tomography (TB-PET) has recently been introduced in nuclear medicine departments. There is a large interest in these systems but the high cost may prevent widespread as it cannot be financially justified by the higher throughput and large research grants are not widely available. Here we propose medium-cost long axial FOV scanners as an alternative.

Methods: Several medium-cost long axial FOV designs are described with their advantages and drawbacks. We describe their potential for higher throughput, more cost-effective scans, a larger group of indications, and novel research options. A wider spread of TB-PET can also lead to the fast introduction of new tracers (at low dose) and new methodologies.

Conclusions: A medium-cost TB-PET would cost-wise be positioned between the current standard PET-CT and the full TB-PET systems. The advantage of these designs is that they could be more easily justified financially in a standard academic nuclear medicine department and still have plenty of research options.

Keywords:
Positron Emission Tomography, Total-body PET, Deep learning, Dose reduction

1. Introduction

Total-body positron emission tomography (TB-PET) has evolved from a very promising concept (1990-2000) via first prototypes (2000-2010) into an approved system for clinical use [1,2,3]. Two PET/CT systems are commercially available: United Imaging (UI) uExplorer^{TM} (194 cm long and 505 ps TOF) [4] and the Siemens Biograph Vision Quadra^{TM} (106 cm long and 225-230 ps TOF) [5]. These systems have each their own advantages: the Quadra has a very compact footprint equal to the standard Siemens Vision and an excellent TOF, resulting in high effective sensitivity. The UI uExplorer has the ~2 m length axial field-of-view (FOV), enabling full-body dynamic acquisitions and ultra-high sensitivity for body imaging applications. Besides these commercial systems, UPENN has developed its own PennPET Explorer of 142 cm and 240 ps [6]. This system is based on modified Philips Vereos^{TM} detector technology (with improved TOF resolution). Several installations (Bern, Groningen, Amsterdam, Pittsburgh, Sydney, Tuebingen, Copenhagen, Heidelberg, Turku…) for Siemens Quadra and for United Imaging (UC Davis, BAMF Health, Sydney, Beijing Cancer Hospital, Zhongshan Hospital, Henan Provincial People's Hospital, Renji Hospital, Sun Yat-sen University Cancer Center,…) have been accomplished in a relatively short time since the first install. The total number of clinical TB-PET systems installed worldwide is already more than 20; the systems installed in Europe seem to be in centers with an active tracer development program and the sites in China are more focused on high clinical throughput.

In general, the nuclear medicine community is very positive and excited about these new systems which offer gains in the range of 10-40 x in system sensitivity for body imaging. This gain depends strongly on the acceptance angle, the patient's body mass index (BMI), and the length of the scanned subject. Important to note that the gain for single organ imaging (eg cardiac or brain scan) is more in the range of 2- to 3- fold [1]. The high number of detectors (about four and eight times that of PET/CT systems with conventional axial FOVs for the Biograph Quadra and uExplorer respectively) however results in a proportional multi-fold increase in the corresponding costs.

As the current standard axial FOV PET/CT market price is already 2-3 MEuro, the budget required for a TB-PET system is around 8-12 MEuro for 1-2 m long axial FOVs. Most of the centers will, however not be able to allocate a budget of that range for a single system. These systems not only have significant benefits for clinical body imaging (e.g. improved image quality with lower injected doses/shorter scan times), but can also enable research opportunities that are simply not possible with standard axial FOV systems (e.g., simultaneous measurements of distant organs kinetics). Moreover, novel tracers and protocols are also often first tested with preclinical mouse TB-PET systems as these are available at a reasonable budget (range of 0.4-0.7 MEuro). This translational research opportunity could be a drive for more sites to share an expensive TB-PET/CT equipment for both research and clinical studies, thus enhancing its utilization and helping share the burden of the associated large capital investment. Many countries may, however, not have the budget of that range; while for countries that can offer this size of grants, it would likely be allocated for 1-2 medical research/hospital centers. Despite TB-PET enabling a set of very interesting and important applications that were previously not possible, such long axial FOV systems are currently only affordable by a quite limited number of well-resourced imaging centers and healthcare systems. This considerably limits the dissemination of TB-PET imaging benefits to wider populations across the world. Although it is very interesting for many nuclear medicine departments, especially those with their own cyclotron and developments of novel tracers to have a TB-PET system, one of the risks is that new human or preclinical TB-PET findings/protocols will remain within those few departments with a TB-PET system, which will not translate into the larger nuclear medicine community. In general novel technology is often introduced at an initial high price setting (early adaptors) but the second generation of systems will only spread widely if there is a more affordable version available.

In this opinion paper, we want to propose potential designs for a medium-cost TB-PET about double the cost of a current standard limited axial FOV PET/CT, which can bridge the gap between nowadays long axial FOV (high-cost) systems and the widely available standard axial FOV PET/CT systems. We also propose ways to use these designs in a combined clinical and research setting in a cost-effective way using an efficient combination of tracer dose reduction and faster image acquisition for higher utilization and daily studies throughput. In this way, the medium cost for such a system would be easily justified by hospitals and/or research authorities, as smaller grants would need to be allocated. Such a system would still have good gains in sensitivity and have the full body (or torso) imaging potential enabling translation into the clinic.

2. Advantages and benefits of a medium-cost TB-PET

2.1 Major factors influencing the cost of a PET scanner

Looking at the different factors contributing to the cost of a PET/CT, the dominant components are the scintillators, the photosensors (SiPMs nowadays), the electronics readout, and the CT scanner, with scintillators making the largest contribution.

The main reason for the high cost of current TB-PET systems is the multi-fold increase in axial length, which leads to a roughly proportional increase in the manufacturing cost of scintillator crystals, SiPMs, and electronics readout. To provide a perspective on absolute and relative costs in this manuscript, let us assume that a standard SiPM-based PET/CT system of 25 cm axial FOV costs about 3 M Euro/USD, of which about 500 k Euro/USD would be for the CT (in addition to the gantry, couch, etc.), and 2.5 M Euro/USD would account for the detector material and readout. Then, TB-PET/CT of 4 times the length (1m in total) would require a budget of around 10.5 M Euro/USD assuming that the cost of ordered materials is linear to their amount, which may not always be the case due to unique manufacturing processes or marketing policies.

At this point, we should note that all our cost estimates are based on reasonable assumptions driven by our limited knowledge of the global policies in the manufacturing and marketing of clinical PET systems and their sub-systems and are only intended to be used as examples to develop our arguments here. We, therefore, acknowledge that it may not necessarily reflect the actual marketing prices of those PET systems across the different vendors.

2.2 Sensitivity gains with a Total Body PET scanner

The sensitivity of TB-PET systems dramatically outperforms the standard 25 cm PET-CT for long objects (body imaging): A system of 1 m length will attain approximately 10-20 times higher system sensitivity depending on the axial extent of the tracer distribution within the scanned subject's body, and the overall tissue attenuation of the subject and the scanner axial acceptance angle. The system sensitivity gain is higher than the increase in axial length because coincidences are formed by a combination of two singles (which increases linearly with the length). Going to greater lengths (e.g., 2 m), the gains can increase further but are ultimately limited due to the considerable degree of body attenuation along the highly oblique detection angles formed with long axial FOV PET scanners for subjects with medium or high BMI or/and less height. It is important to note that for organ-specific imaging (e.g., brain, heart, prostate) the sensitivity gain for that targeted axial range of interest, is limited to around a factor of 2-3, even as the axial FOV increases > 1m due to increased attenuation along the oblique axial acceptance angles.

2.3 A medium-cost Total Body PET scanner

We propose here different design options for a potential medium-cost clinical PET system. First of all, it was proposed to call a TB-PET system any system with > 60 cm AFOV [7]. Based on this, several designs with each their own specific advantages are possible; these are also illustrated in Table 1, with each their own advantages and disadvantages:

1. A medium axial FOV scanner of about 60-70 cm axial length (this would cover the torso)

This design ensures an axial FOV length that covers the majority of the average human body torso in a compact, thick detectors configuration; therefore, it attains most of the highest possible axial slice sensitivity gain (~ 2-3 times) for single-organ imaging and delivers high system sensitivity gains for body imaging. Moreover, it has the capability of performing high-quality static or dynamic multi-organ imaging across its axial FOV, e.g., brain-heart imaging, without bed motion, thus enabling simultaneous data acquisitions from both brain and heart regions (static scans) and with zero temporal acquisition gaps between the frames (dynamic scans)[8]. However, if dynamic scans are required with longer axial coverage, such as across the whole-torso or total body region, this can be achieved by scanning across two bed positions with an axial overlap between them [9,10], thus introducing axial non-uniformities in the axial sensitivity profile. This issue could be addressed with solutions like continuous bed motion static or dynamic scan protocols [11,12].

2. A sparse long axial FOV PET design of about 1 – 1.4 m, but with ~50% reduced manufacturing cost, by eliminating ~50 % of the detector elements or blocks omitted.

This design concept delivers large system sensitivity gains in body imaging, about 4 x less than a fully populated 1 m axial FOV TB-PET system, but still 4 x higher than a standard 25 cm axial FOV scanner [13-17]. Regarding peak axial slice sensitivity, a gain reduced by 2 times relative to a full 100 cm but still 2 times higher than a full 25 cm axial FOV PET system is expected. Thanks to its sparse 1 m axial FOV and sufficiently high total and peak axial slice sensitivity, the system allows for simultaneous static and dynamic torso imaging, from head to thigh, without temporal acquisition gaps between frames. Furthermore, thanks to the above sensitivity performance specifications, the sparse configuration attains the smallest axial variance in axial slice sensitivity between the center and the edges of the axial FOV, thus resulting in the smallest axial noise variance in the reconstructed images, compared to a full 100 cm long TB-PET system. These studies have shown that the introduction of a relatively large number of small axial gaps uniformly distributed between the existing detector elements or blocks can result in artifact-less reconstructed images of nearly double the axial FOV, similar NEMA contrast recovery and only a slightly elevated background image noise [13-17]. These results are a consequence of sparse detector designs taking advantage of the redundancy of data used in the 3D reconstruction. In fact, the PennPET Explorer has demonstrated the utility of a sparse detector geometry for TB-PET, operating until recently with inter-ring gaps equal to 30% of the active detector length. This affected the overall sensitivity, but neither image quality nor quantitative accuracy for both clinical and research applications, even though the gaps are relatively large (7.6 cm gap between each 16.4 cm active detector ring) [18]. It was shown that larger gaps are possible to save greater cost, despite the larger variation in the axial sensitivity [19], and suggests a relatively simple solution to reduce the number of detector rings (or units) and incorporate a fixed axial gap between adjacent rings to achieve a similar axial FOV (uExplorer has 8 ring units, PennPET Explorer has 6, Vision Quadra has 4).

3. A long axial FOV PET design of about 1 – 1.4 m, but with ~50% reduced scintillator cost, by reducing the scintillator thickness by ~one-half while retaining their original cross-section to maintain similar spatial resolution

The impact of this design modification is also a drop in total sensitivity of about 4 times compared to TB-PET systems with original crystal thickness, typically ~20-mm. One disadvantage is that it requires the same amount of SiPMs and electronics as a TB-PET with a thicker scintillator. A system with 1-m axial FOV would, however, still be 4-5x more sensitive than a current short axial FOV of 25 cm (2-3x for single organ imaging). It was shown that a longer axial FOV system, with thinner crystals, could improve clinical metrics such as lesion contrast and detectability [20]. A further advantage of using thinner crystals is that they have less light attenuation and exhibit less light dispersion as measured by the SiPM. Therefore, a significant improvement in TOF performance and effective sensitivity (with TOF gain) could be expected in this configuration, which could partially compensate for the sensitivity drop.

4. A long axial FOV PET design of ~50-70% reduced scintillator cost by using a more cost-effective scintillator. Different scintillators have been proposed, but the most practical choice is BGO which is readily available at a relatively low cost (estimated to be 30% of LYSO). BGO also has the advantage of higher stopping power; TOF is possible but depends on the instant Cherenkov light, and despite promising results [21], will clearly be inferior to L(Y)SO. Till now, BGO has been read out with PMTs: the lower light also impacts the crystal identification. Coupling BGO to SiPMs will likely result in better crystal identification (Less light spread), and TOF may also become possible with SiPMs having a good efficiency for the Cherenkov light.

5. An adaptively sparse long axial FOV PET design of ~50% the number of detector elements or blocks, which adopts the same sparse detector configuration as design #2 above, but with the ability of all of its detectors to also retract to the compact configuration of design #1, depending on the imaging task.

This involves a previously proposed concept [22,23] of adaptive axial FOV PET by adjusting the degree of sparsity between the basic detector elements depending on the imaging task, e.g., use of the compact retracted mode for single-organ imaging and of its extended sparse mode for body imaging, to attain the optimal axial slice sensitivity profile for each imaging application. However, this design also requires the use of a streamlined, robust, and reliable detector motion mechanism that would allow the frequent retraction and extension of the detectors at high accuracy and precision, as well as additional quality assurance/control methods to calibrate and validate the reproducibility of detectors positioning in each of their two configurations. The same concept could also be applied to nearly double the limited (~25 cm) axial FOV of current commercial PET scanners or extend the already long 1 m axial FOV of a compact PET system to a total-body 2 m long axial FOV PET system with a sparse detectors configuration.

Based on our initial assumptions, we expect that the cost of any of these configurations would be in the range of 4-6 M Euro/USD. This budget range is much more within reach of most clinical imaging centers, particularly those with high clinical throughput. If it is also combined with a strategic plan to exploit the unique capabilities of long axial FOV PET imaging to attract extramular funding and enable a wide range of novel research applications that were previously not possible, then the utility and potential of such a cost-effective PET system as an integrated clinical and research resource in large medical centers across the world becomes more apparent.

2.4 Integrating a medium-cost TB-PET scanner in a typical department

Here we explain the potential of a medium-cost TB-PET for a typical department owning its own cyclotron and two standard PET/CT (20-25 cm). Typically such a department will scan 30-50 patients (mostly FDG, PSMA, and other tracers) daily. To have sufficient tracer available for the whole day of scanning, typically 1 or 2 irradiation runs of the cyclotron are required (one in the early morning and one in the late afternoon). Assuming one run produces about 100 GBq (2700 mCi). In an optimal setting of 3 patients/hour (8-hour working day) on each scanner and dose usage per patient of about 185MBq (5mCi) (about 3 MBq/kg), this enables to scan about 48 patients per day (two scanners).

An important factor in the patient throughput is that this does not solely depend on the PET acquisition time but also on the patient preparation and positioning (which we cannot easily reduce for the typical PET population). A patient throughput shorter than 10-15 min (4-6 patients per hour) does not seem feasible, regardless of the PET sensitivity, as every patient will need bed positioning on the bed, a scout view, and a CT scan, all of which could take as much as 10 min dead time per patient. A PET-CT scan throughput of 3 patients per hour is therefore only feasible with a PET net acquisition time below 10 min. Assuming we can bring the PET acquisition time below 5 min, this will only deliver a 25 % gain in patient throughput (4 patients per hour, 5 min net + 10 min dead time = 15 min total time). Even a super sensitive and fast PET system (<1min per patient) and very optimized workflow would maximally reach 6 patients per hour (10 min total time per patient).

Assume one of the standard systems in such a department gets replaced by a medium-cost TB-PET. One can benefit from the 4 x higher sensitivity in different ways. We start from the assumption of 20 min per patient, 15 min total scan time for the PET-CT body exam.

1. 50 % of the higher sensitivity can be used for faster scanning. This should result in a 5 min PET-CT scan time reduction, so one patient every 15 min instead of every 20 min (4 patients per hour) → 25 % (6) more patients with the medium-cost TB-PET scanner can be examined in the same workday. Alternatively, this 25% 'extra time' (2 h per day) could be used to extend ongoing research programs (novel tracers, protocols) using the medium-cost TB-PET scanner.

2. Additionally, one can reduce the dose by a factor of 2. This should preferably be done in patients for which radiation dose is a concern (children, non-radiotherapy patients, …). Having one scanner of each (a standard and a medium-cost TB-PET) would enable planning the patients with a radiation concern on the TB-PET.

3. Less activity needs to be produced by the cyclotron as imaging is performed 25 % faster or at a lower dose (50% less). Cyclotron irradiation costs (molecule + target) depend on the amount of tracer required and the number of irradiations per day It is also estimated that these costs can be reduced by 25-50%. Daily irradiation costs can go above 1000 Euro/day.

This example shows that a medium-cost long axial FOV PET could become quite effective (25 % higher throughput and lower daily cyclotron costs) even in a standard academic clinical setting. In this scenario, one can scan more patients (up to 25 % extra) or reduce radiotracer production cost and subject's dose by 50 % for the exams of the medium-cost TB-PET scanner. This shows just a possible scenario, and evidently, this dose/scan time reduction can be adapted to the department's needs. What is important is that in such a design, the 4-5 times sensitivity gains can be easily translated into higher clinical throughput or lower tracer costs. This is, of course also true for a full TB-PET, but throughput gain and tracer reduction costs will not be much higher in a practical clinical setting as they can be limited by subjects availability, personnel efficiency and radiation-shielded waiting rooms). It seems quite hard, in that case, to come up with a scenario in which the financial benefits could bring in enough revenue to compensate for the higher acquisition and service costs of a 10 M Euro/USD system.

Alternative options are the replacement of 2 standard PET-CTs (reduction in personnel costs + space) by one medium-cost long axial FOV PET; this would however pose the risk of not having a backup scanner if the long axial FOV system goes down, while it would also require an extension of the working day to keep the same number of patients/day. There would be clear advantages in the space gained in the department, but a drawback would of course be that if the medium-

cost TB-PET required service, there would be no second system available. Interesting is that a nuclear medicine department without a cyclotron would even benefit more from the reduction in tracer costs as they often rely on commercial production at cyclotrons, often not close by (driving up the tracer cost per patient). So the budget reduction for tracer production in these centers would even be larger than for cyclotron-owning academic sites. In the US, even clinic sites with their own cyclotron may get their FDG from outside vendors.

Besides the conventional PET/CT studies, it is also interesting to look a the potential of TB-PET for current general nuclear medicine exams or novel exams. Evidently, paediatric patients would be scanned easier and more frequently on a TB-PET as radiation dose can be much lower (also, in CT, we see a trend towards very low dose CT scans). Also, SPECT exams could be shifted towards PET to reduce the dose to the patient (and personnel), most evident group of exams seems to be the conventional planar bone + SPECT. Using low dose Na-F and a TB-PET, one should be able to do quick full tomographic scans (around 10 min) of higher quality. Also, the uptake time of Na-F is much shorter (30 min instead of 3 hrs), which would make the waiting rooms less occupied.

Expensive imaging systems should also be used more efficiently, e.g. in MRI it is quite common to scan quite late in the evening. Now, this is not so often done in PET-CT as it would require an extra delivery of dose and more personnel hours. With TB-PET, it should be possible as even very low doses could be imaged in a reasonable acquisition time.

3. Discussion

Here we propose the two most straightforward ways (based on existing TOF-PET technology) to achieve a medium-cost TB-PET system. The first one is a medium axial length (60-70 cm), and the second one is a longer axial length (1 – 1.4 m) but with a sparse ring design (removal of up to 50 % of its detector blocks), which has a clear cost reduction equal to the fraction of removed detectors. Experimental evidence shows that this does not lead to uniformity artefacts but only a slight increase in image noise, provided the gaps are not too large. This is logical because 3D PET data are highly redundant. The third proposed one is using a thinner scintillator with the same readout. Reducing the number of rings or detector thickness both by 50% would lead to roughly 75% loss in sensitivity. For the third option (although not the cheapest), one would expect a better TOF for a thinner scintillator, which could partially compensate for the sensitivity loss since better TOF resolution helps to improve effective sensitivity. The TOF gain equation shows that a direct gain in sensitivity proportional to the improvement in TOF performance (e.g., 200 ps vs. 400 ps leads to a factor 2 increase in effective sensitivity. This can be significant and is potentially another direction that improves sensitivity at a lower cost (using better SiPMs, and/or with more scintillator coverage) than adding detectors (both scintillator plus SiPMs).

Another way to reduce the cost is to replace the LYSO scintillator with a lower-cost one. The most evident choice seems to be BGO (which was and is still used in existing PET systems). Interestingly, several groups have shown that BGO has potential for TOF measurements using the prompt Cherenkov light. Up to now, BGO has not been combined with SiPMs in a commercially available clinical system. The scintillator is less costly (BGO costs about 30 % of LYSO for the same volume), but likely SiPM + electronics capable of exploiting the fast (and weak) Cherenkov light will be more costly. Therefore it is unlikely that TOF with BGO will be as beneficial as with L(Y)SO. BGO time kernels also tend to have long tails. Other alternatives like axial side-end readout and/or plastic scintillators could further reduce the cost of TB-PET, but these systems also have lower sensitivity and spatial resolution and have not yet become commercially available.

Nowadays, artificial intelligence (AI) Deep Learning is more and more introduced to improve the acquisition performance and the image quality of reconstructed images [24], especially for sparse PET configurations [25]. This can be done using a trained convolutional neural network (CNN) to predict from low count reconstructions the high count reconstructions. Several papers and companies have shown gains of about a factor of 3-6 in dose reduction/scan time [26,27]. This concept may also apply to medium-cost TB-PET and can 'boost' the image quality to the level obtained on our current TB- PET systems (not using AI). Recently, a paper showed that non-TOF PET reconstructions could be upgraded with TOF information [28]. Deep learning-based image enhancement models may provide converged TOF-equivalent image quality without using TOF information in the reconstruction.

Of course, these techniques can also be applied to current high-end TB-PET systems to improve image quality. However, it is reasonable to expect the gap in various clinical tasks performance (e.g., lesion detectability and/or quantification) to become smaller between the AI-enhanced version of the two system classes as we approach lower noise levels. So there surely remains a gap between those two groups of systems. Anyhow, AI seems promising to deliver 'for free' higher image quality for lower cost (TB)-PET systems.

The introduction and acceptance of novel technology are often going through different phases. After a peak of inflated expectations, there is often a trough of disillusionment. In the case of TB-PET, there seems to be the potential for a relatively quick introduction in the clinical departments. This is not a new imaging modality but a further extension of what has happened for several decades (longer axial FOV, faster scanning). The only bottleneck for TB-PET and its wide

clinical adoption seems, therefore now the high acquisition price combined with the difficulties in justifying this high cost (and associated service contracts).

4. Conclusions

A medium-cost TB-PET with either an axial length of about 60-70 cm or 1–1.4 m with a uniformly sparse configuration of about 50% of the original compact detectors or a thinner scintillator would cost-wise be positioned between the current standard PET-CT and the full TB-PET systems. The advantage of one of those designs is that it could be more easily justified financially in a standard academic nuclear medicine department. The considerably smaller budget required for obtaining this type of system (in the range of 5.5 - 6 M Euro/USD) would also be easier to claim and justify than a fully populated TB-PET system. As the total sensitivity is about 4-5 times higher, this gain can be spent on either a more efficient imaging/higher throughput or a reduced tracer production. Additional available acquisition time becomes then available for TB-PET research. The primary benefit of more sites with a medium-cost TB-PET system is its greater affordability to a larger number of PET imaging sites across the globe to enable the assessment and application of the potential of total body imaging and that it could complement or follow up ongoing pioneering studies initiated at sites which have a full total body system.

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References

1. Vandenberghe S, Moskal P, Karp JS. State of the art in total body PET. EJNMMI Phys. 2020;7(1):35. https://doi: 10.1186/s40658-020-00290-2
2. Pantel AR, Mankoff DA, Karp JS. Total Body PET – Will it Change Science and Practice? J Nucl Med. 2022, 63 (5) 646-648. https://doi.org/10.2967/jnumed.121.263481
3. Cherry SR, Badawi RD, Karp JS, Moses WW, Price P, Jones T. Total-body imaging: Transforming the role of positron emission tomography, Sci Transl Med, 2017, 9, (381)
4. Spencer BA, Berg E, Schmall JP, Omidvari N, Leung EK, Abdelhafez YG, Tang S, Deng Z, Dong Y, Lv Y, Bao J, Liu W, Li H, Jones T, Badawi RD, Cherry SR. Performance evaluation of the uEXPLORER Total-body PET/CT scanner based on NEMA NU 2-2018 with additional tests to characterize long axial field-of-view PET scanners with a long axial field-of-view. J Nucl Med. 2021; 62:861-70. https://doi.org/10.2967/jnumed.120.250597
5. Prenosil GA, Sari H, Fürstner M, Afshar-Oromieh A, Shi K, Rominger A, Hentschel M. Performance Characteristics of the Biograph Vision Quadra PET/CT system with long axial field of view using the NEMA NU 2-2018 Standard. J Nucl Med. 2022;63(3):476-484. Htpps://doi:10.2967/jnumed.121.261972
6. Dai B, Daube-Witherspoon ME, McDonald ME, Werner ME, Parma MJ, Geagan MJ, Viswanath V, Karp JS. Performance evaluation of the PennPET Explorer with expanded axial coverage. Journal of Nuclear Medicine, May 2022.
7. Daube-Witherspoon ME, Pantel AR, Pryma DA, Karp JS. Total-Body PET: A New Paradigm for Molecular Imaging, British Journal of Radiology (in press).
8. Pantel AR, Viswanath V, Daube-Witherspoon ME, Dubroff JG, Muehllehner G, Parma MJ, Pryma DA, Schubert EK, Mankoff DA, Karp JS. PennPET Explorer: Human Imaging on a Whole-Body Imager. J Nucl Med. 2020;61(1):144-151. doi:10.2967/jnumed.119.231845.
9. Karakatsanis NA, Lodge MA, Zhou Y, Mhlanga J, Chaudhry MA, Tahari AK, Segars WP, Wahl RL, Rahmim A. Dynamic Multi-Bed FDG PET imaging: Feasibility and optimization. 2011 IEEE Nuclear Science Symposium Conference Record 2011; pp. 3863-3870. doi:10.1109/NSSMIC.2011.6153735
10. Karakatsanis NA, Lodge MA, Tahari AK, Zhou Y, Wahl RL, Rahmim A. Dynamic whole-body PET parametric imaging: I. Concept, acquisition protocol optimization and clinical application. Phys Med Biol. 2013;58(20):7391-418. doi:10.1088/0031-9155/58/20/7391
11. Karakatsanis NA, Garibotto V, Rager O, Zaidi H. Continuous bed motion Vs. Step-and-shoot acquisition on clinical whole-body dynamic and parametric PET imaging. 2015 IEEE Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), 2015, pp. 1-6. doi:10.1109/NSSMIC.2015.7582184
12. Osborne DR, Acuff S. Whole-body dynamic imaging with continuous bed motion PET/CT. Nucl Med Commun. 2016 37(4):428-31. doi:10.1097/MNM.0000000000000455

13. Karakatsanis NA, Nehmeh MH, Conti M, Bal G, González AJ, Nehmeh SA. Physical performance of adaptive axial FOV PET scanners with a sparse detector block rings or a checkerboard configuration. Phys Med Biol. 2022;67(10):10.1088/1361-6560/ac6aa1. doi:10.1088/1361-6560/ac6aa1
14. Karakatsanis NA, Zein SA, Nehmeh SA. Evaluation of Image Quality and Quantitation in a Clinical PET Scanner with a Uniformly Sparse Detector Rings Configuration. 2018 IEEE Nuclear Science Symposium and Medical Imaging Conference Proceedings (NSS/MIC), 1-9.
15. Zhang J, Knopp MI, Knopp MV. Sparse Detector Configuration in SiPM Digital Photon Counting PET: a Feasibility Study. MoI Imaging Biol. 2019;21(3):447-453. doi:10.1007/s11307-018-1250-7
16. Zein SA, Karakatsanis NA, Issa M, Haj-Ali AA, Nehmeh SA. Physical performance of a long axial FOV PET scanner prototype with sparse rings configuration: A Monte Carlo simulation study. Med Phys. 2020;47(4):1949-1957. doi:10.1002/mp.14046
17. Zein SA, Karakatsanis NA, Conti M, Nehmeh SA. Monte Carlo simulation of the Siemens Vision PET With Extended Field of View Using Sparse Detector Module Rings Configuration. IEEE Transactions on Radiation and Plasma Medical Sciences. 2021, vol. 5, no. 3, pp. 331-342. doi:10.1109/TRPMS.2020.3034676
18. Karp JS, Viswanath V, Geagan MJ, Muehllehner G, Panterl AR, Parma MJ, Perkins AE, Schmall JP, Werner ME, Daube-Witherspoon ME. PennPET Explorer: Design and Preliminary Performance of a Whole-Body Imager. J Nucl Med. 2020; 61(1):136-143. doi:10.2967/jnumed.119.229997
19. Daube-Witherspoon ME, Viswanath, Werner ME, Karp JS. Performance Characteristics of Long Axial Field-of-View PET Scanners with Axial Gaps. IEEE Trans Radiat Plasma Med Sci. 2021;5(3):322-330. DOI:10.1109/trpms.2020.3027257
20. Surti S, Werner ME, Karp JS. Study of PET scanner designs using clinical metrics to optimize the scanner axial FOV and crystal thickness. Phys Med Biol. 2013;58(12):3995-4012. DOI:10.1088/0031-9155/58/12/3995
21. Kwon SI, Gola A, Ferri A, Piemonte C, Cherry SR. Bismuth germanate coupled to near ultraviolet silicon photomultipliers for time-of-flight PET. Phys Med Biol. 2016;61(18):L38-L47. doi:10.1088/0031-9155/61/18/L38
22. S.Vandenberghe et al., PET20.0: a cost efficient, 2mm spatial resolution Total Body PET with point sensitivity up to 22% and adaptive axial FOV of maximum 2.00m *European Journal of Nuclear Medicine and Molecular Imaging* **volume 44**, pages119–956 (2017) doi.org/10.1007/s00259-017-3822-1
23. Nehmeh, S.A., Karakatsanis, N.A. (2022) "Positron emission tomography system with adaptive field of view" US2022/0022834 A1
24. Decuyper M, Maebe J, Van Holen R, Vandenberghe S. Artificial intelligence with deep learning in nuclear medicine and radiology', EJNMMI Physics, 2021, 8, (1), pp. 81
25. Feng T, Wang J, Li H. Sensitivity Estimation and Image Reconstruction for Sparse PET with Deep Learning. IEEE Nuclear Science Symposium and Medical Imaging Conference Proceedings (NSS/MIC), 2018, pp. 1-4, doi:10.1109/NSSMIC.2018.8824633
26. Katsari K, Penna D, Arena V, Polverari G, Ianniello A, Italiano D, Milani R, Roncacci A, Illing RO, Pelosi E. Artificial intelligence for reduced dose 18F-FDG PET examinations: a real-world deployment through a standardized framework and business case assessment. EJNMMI Phys. 2021;8(1):25. doi:10.1186/s40658-021-00374-7
27. Vangu M, Purbhoo K, Liu H. Clinical Potential for Artificial Intelligence in PET Imaging: Phase 1 Result of Dose Reduction using Deep Learning Reconstruction. Journal of Nuclear Medicine. 2021, 62 (supplement 1) 1179
28. Mehranian A, Wollenweber SD, Walker MD, Bradley KM, Fielding PA, Huellner M, Kotasidis F, Su KH, Johnsen R, Jansen FP, McGowan DR. Deep learning–based time-of-flight (ToF) image enhancement of non-ToF PET scans. *Eur J Nucl Med Mol Imaging* (2022). https://doi.org/10.1007/s00259-022-05824-7

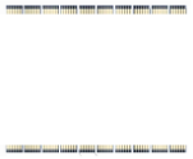
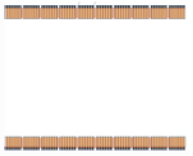
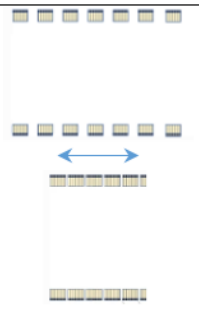
Configuration	Design	Detector	Expected performance	Pro/Contra
Medium axial FOV PET (50-60 cm, 100 % detectors)		LYSO + SiPM	200-400 ps 4-6 x more sensitive	Easy extension of current PET Optimal for standard routine Limited part of body
Split axial ring PET (100-120 cm, 50% detectors)		LYSO + SiPM	200-400 ps 4-6 x more sensitive	Easy extension of current PET Full torso Limited sensitivity gain
Thin crystal 100-120 cm, 50 % thickness		LYSO + SiPM	150-300 ps 4-6 x more sensitive	Better TOF More SiPMs + electronics
Thick crystal 100-120 cm 100 % thickness No axial gaps		BGO + PMT/SiPM	No or limited TOF 8-20 x more sensitive	Higher sensitivity Cheap Scintillation crystal No intrinsic Lu background Non-standard detector More SiPMs + electronics
Adaptive PET 100-120 cm 100 % thickness Axial and/or transvers gaps		Any	150-300 ps 4-6 x more sensitive	Higher sensitivity in organ imaging Moving parts extra calibrations

Table 1: Different Medium Cost TB-PET designs with their advantages and disadvantages