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SHORT COMMUNICATION

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

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## 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 for many centers, the high acquisition cost makes it very difficult to justify their current operational budget. 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 scanning, a larger group of indications, and novel research opportunities. The wider spread of TB-PET can also lead to the fast introduction of new tracers (at a low dose), new methodologies, and optimized workflows.

**Conclusions** A medium-cost TB-PET would be positioned between the current standard PET-CT and the full TB-PET systems in investment but recapitulate most advantages of full TB-PET. These systems could be more easily justified financially in a standard academic or large private nuclear medicine department and still have ample research options.

**Keywords** Positron emission tomography · Total-body PET · Deep learning · Dose reduction

## Introduction

Total body positron emission tomography (TB-PET) has evolved from a very promising concept (1990–2000) via the first prototypes (2000–2010) into an approved system for clinical use [1–3]. Two PET/CT systems are commercially available: United Imaging (UI) uExplorer™ (194-cm long and 505 ps TOF) [4] and the Siemens Biograph Vision Quadra™ (106-cm long and 225–230 ps TOF) [5]. These systems each have 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.

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The UI uExplorer has the ~ 2-m-length axial field-of-view (FOV), enabling full-body dynamic acquisitions and high sensitivity over a long axial FOV, suitable for full-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™ detector technology (with an 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 installation. 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 × 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. It is important to note that the gain for single-organ imaging (e.g., cardiac or brain scan) is more in the range of 2- to threefold [1]. The reason is that the organ is typically embedded in the tissue, and therefore, the oblique lines (which would lead to 4–5 × gain) are heavily attenuated. The brain is more free of attenuation, and therefore, likely a higher gain (in between 2–3- and 4–fivefold can be expected. 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 system 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 centers will not, however, be able to allocate a budget of that range for a single system. One of the challenges for current TB-PET systems is also that the latest PET-CT is already quite fast (15–20 min between 2 patients). And this seems to justify rather 2 PET-CT than one TB-PET, with a disadvantage of requiring 2 rooms and a bit more personnel. An advantage of 2 standard PET-CT systems is sure to have a backup solution when there are 2 systems.

Our analysis (outside of this paper) shows that the high investment and service costs for a 10-M Euro TB-PET CT are very difficult and almost impossible to earn back over a 10-year period even if we can almost double the number of patients (very hard as patient positioning/scout and CT become a good fraction of the time). This analysis does not even take into account that more personnel will be required for a TB-PET-CT (more patients). For this budget, 2 × a standard PET-CT is the better choice for clinical routine. Reducing the dose and associated costs (especially for non-cyclotron owners, these may be high) may help to make a 10-M Euro TB-PET-CT more financially viable.

These systems not only have significant benefits for clinical body imaging (e.g., improved the one 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 organ 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 M Euro). This translational research opportunity could be a driver for more sites to share 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 do not have the budget of that range; while for countries that can offer this size of grants, it would likely be allocated for only 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 novel tracer development 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 adoptors), but the second generation of systems will only spread widely if there is a more affordable version available. Because of the high raw material costs of current TB-PET systems, the price cannot meaningfully decrease without design changes.

In this opinion paper, we propose potential designs for a medium-cost TB-PET about doubling the cost of a current standard limited axial FOV PET/CT, which can bridge the gap between current long axial FOV (high-cost) systems and the widely available standard axial FOV PET/CT systems (15–30-cm axial length). 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 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.

## Advantages and benefits of a medium-cost TB-PET

### 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 raw material and 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 (1 m in total) would require a budget of around 10M 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. We, therefore, acknowledge that it may not necessarily reflect the actual marketing prices of those PET systems across the different vendors.

### 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 > 1 m due to increased attenuation along the oblique axial acceptance angles.

### A medium-cost total-body PET scanner

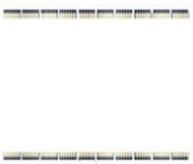
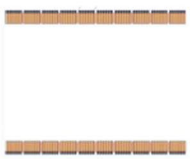
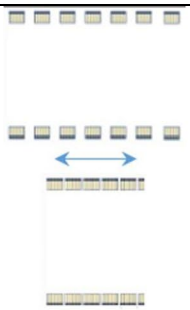
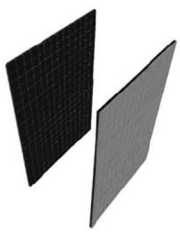
We propose different design options for a potential medium-cost clinical PET system. First of all, it was proposed to call a TB-PET system any system with > 60 cm AFOV [7]. Based on this, several designs are possible; these are also illustrated in Table 1, with each their own advantages and disadvantages:

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 detector 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 (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]. Ultimately, this will still require multi-bed scanning protocols to cover the major organs and so has the least potential for paradigm-shifting acquisitions compared to axial FOV of 1–1.4 m + .
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

   This design concept delivers large system sensitivity gains in body imaging, about 4 × less than a fully populated 1-m axial FOV TB-PET system, but still 4 × 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

**Table 1** Different medium-cost TB-PET designs with their advantages and disadvantages. A conventional 25-cm axial FOV PET system was considered as our reference design

| Configuration | Design | Detector | Expected performance | Pro/Contra |
|---|---|---|---|---|
| **Medium axial FOV**<br>**Axial: 50–60 cm,**<br>**100% detectors** |  | LYSO + SiPMs | 200–400 ps<br>4–6 more sensitive | Easy extension of current PET<br>Optimal for standard routine<br>Limited part of body (2 bed positions for TB-PET) |
| **Split axial ring PET**<br>**Axial: 100–120 cm**<br>**50% detectors** |  | LYSO + SiPMs | 200–400 ps<br>4–6 more sensitive | Easy extension of current PET<br>Full torso<br>Limited sensitivity gain |
| **Thin crystal**<br>**Axial: 100–120 cm**<br>**50% thickness** |  | LYSO + SiPMs | 150–300 ps<br>4–6 more sensitive | Better TOF<br>More SiPMs + electronics |
| **Thick lower cost crystal**<br>**Axial:100–120 cm**<br>**100% thickness** |  | BGO + SiPMs | No TOF<br>400–600 ps (Cherenkov + optimal SiPMs<br>8–20 × more sensitive | Higher sensitivity cheap scintillation crystal<br>No intrinsic Lu background<br>Non-standard detector<br>More SiPMs + electronics |
| **Adaptive PET**<br>**Axial (top): 100–120 cm**<br>**Axial (top): 50–60 cm**<br>**100% thickness**<br>**Axial sparse PET and/or transverse gaps** |  | LYSO/BGO + SiPMs | 200–400 ps<br>4–6 × more sensitive | Higher sensitivity in organ imaging in second mode<br>Moving parts<br>Extra calibrations |
| **Flat panel PET**<br>**Axial: 100–120 cm**<br>**100% thickness** |  | LYSO/BGO + SiPM | 200–400 ps (LYSO)<br>400–600 ps (BGO)<br>8–20 × more sensitive | Smaller detector surface for same FOV<br>Effects of limited angle |

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 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 centers 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. 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 doubling 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 4–5 × more sensitive than a current short axial FOV of 25 cm (2–3 × 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 L(Y)SO). BGO also has the advantage of higher stopping power; TOF is possible but depends on the instant Cherenkov light. *Recent publications* [21] *have shown that BGO of 15 mm can achieve less than 300 ps which will likely at the system level become around 400–500 ps. Using AI at the optical photons processing can further improve this.* Despite promising results [21], it will clearly be inferior to L(Y)SO. Until 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. However, several plausible, but significant, advances would be required to make this a viable option. *The recent results of 300–400 ps are very promising but should however be taken with caution. As the Cherenkov light is not always sufficient to give fast timing* via *the SiPMs, there is also a quite large slow component in the timing (causing a kind of double Gaussian curve). But indeed, the combination of great TOF for a good section of the events and 3–4 × lower cost and higher photo-fraction surely brings BGO in a very competitive situation with L(Y)SO. It can therefore be expected that BGO will re-appear in systems with a large quantity of scintillators.*

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., the 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 detector configuration.

6. Flat panel (close to the patient) based TOF TB PET is an old idea first presented at IEEE MIC 1990 (Terry Jones) and was recently proposed by Ghent university in a design with the patient in a standing position. One major advantage is to reduce the cost without reduced performance. There are also practical advantages as improved spatial resolution should be achievable due to the reduced. One of the challenges in such a design is the missing data in the transverse direction. However, Surti et al. (limited angle TOF PET) have already shown this to be a small effect when a TOF resolution of around 300 ps is available. A rotating flat panel would evidently also solve this problem at the expense of the additional complexity due to rotation.

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 and even lower for combinations of BGO with designs with gaps or flat panels (smaller detector surface). 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 wider 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.

## 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 (the number also depends on the number of hours scanned per day). 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 afternoon), assuming one run produces about 100 GBq (2700 mCi). In an optimal setting of 3 patients/hour (8-h working day) on each scanner and dose usage per patient of about 185 MBq (5 mCi) (about 3 MBq/kg), this enables to scan of 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 positioning on the bed, a scout view, a CT scan, and table cleaning after the scan, all of which could take typically at least 10 min 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 about 25% gain in patient throughput (4 patients per hour, 5 min PET + 10 min positioning/CT = 15 min total time). Even a super sensitive and fast PET system (< 1 min per patient) and very optimized workflow would maximally reach 6 patients per hour (10 min total time per patient). However, such a model is not practically feasible when scanning humans. Many patients are infirm and cannot move quickly. Toileting prior to scanning takes highly variable amounts of time. Maximizing throughput may require additional technologist staff. Finally, compressing a clinical schedule into a shorter duration will require additional uptake rooms. A more interesting scenario is to combine the limited faster scanning with high dose reduction. For sites ordering the dose, the costs can go up to 200 Euro per patient and this can lead to a significantly reduced budget. For sites already owning a cyclotron, the tracer cost will however be much lower and this scenario may be not interesting.

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

1. Fifty percent 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. Furthermore, for studies requiring fasting (i.e., FDG scans), patients greatly prefer early morning appointments and such a system would allow more of these preferred early slots.
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, patients whose disease typically requires multiple lifetime scans). Having one scanner of each (a stand-

ard 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 one 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, lower tracer costs, or a custom combination of both.

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 subject 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, in addition to the extra space costs for a full 2-m system. Furthermore, patient intolerance of a full 2-m system due to claustrophobia is a considerable issue.

Alternative options are the replacement of 2 standard PET-CTs (reduction in personnel costs + space) with 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. Interestingly, 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, particularly if all doses for the day could be made in a single delivery. In the US, even sites with their own cyclotron frequently obtain clinical (non-research) radiopharmaceuticals from outside vendors.

Besides the conventional PET/CT studies, it is also interesting to look at the potential of TB-PET for current general nuclear medicine exams or novel exams. Evidently, pediatric 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). Furthermore, the shorter scan duration may obviate the need for sedation in some cases. Also, SPECT exams could be shifted towards PET to reduce the dose to the patient (and personnel), and the 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 2–3 h), 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 doses and more personnel hours. With TB-PET, it should be possible as even very low doses could be imaged in a reasonable acquisition time.

These examples all imagine utilizing TB-PET to re-implement current workflows more efficiently. However, the potential to do dynamic imaging of all organs of interest or to perform ultra-low radiation exposure PET imaging could open the door to new indications and techniques. For example, rather than reporting SUV one could envision reporting SUV slope which may provide better tissue characterization. By potentially reducing cost, time and radiation exposure from studies, PET could be expanded to many benign diseases resulting in new revenue streams to offset the initial investment. Brief serial scans of all organs at risk could inform dosimetry for theranostics.

## Discussion

Here, we first propose the two most straightforward ways (based on existing TOF-PET technology) to achieve a medium-cost TB-PET system using the available detector technology. 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 artifacts 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. No spatial resolution changes are expected as these systems are based on the same detector technology.

The third proposed option 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 is significant and 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). *A small improvement in spatial resolution can be expected as there will be less depth of interaction.*

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 the potential for TOF measurements using the prompt Cerenkov 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) Cerenkov 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. One can expect a similar or even better spatial resolution (for the same pixel size) as the photofraction is higher. 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 increasingly being 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) or further reduce required detectors. Recently, a paper showed that non-TOF PET reconstructions could be upgraded with TOF information [28]. This is a very recent technique, and it remains to be evaluated how AI can help in obtaining TOF quality in non-TOF scanners. If it works reliably, it can then likely also improve data from TOF scanners into even better image quality.

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 task 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. AI seems promising to deliver "for free" higher image quality for lower cost (TB)-PET systems. Therefore, concurrent axial coverage of all organs of interest (which can be achieved with 1–1.4-m axial FOV) seems the most beneficial aspect of TB-PET and compromises needed to achieve this at an acceptable cost will be mitigated with further AI refinements.

The introduction and acceptance of novel technology go 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 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, the high acquisition price combined with the difficulties in justifying this high cost (and associated service contracts). Reducing the initial investment while maintaining most of the benefits will speed the adoption of this promising novel imaging method.

## Conclusions

A medium-cost TB-PET with an axial length of 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. Such a design could be more easily justified financially in a standard nuclear medicine department (in the range of 5.5–6 M Euro/USD). As the total sensitivity is about 4–5 times higher, this gain can be spent on either a more efficient imaging/higher throughput or reduced tracer costs. This could be seamlessly adjusted over time (initially, tracer cost reduction maximizes and as volume grows, additional scanning capacity is added without additional hardware costs). 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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## Declarations

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

**Conflict of interest** The authors declare no competing interests.

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