Performance of high-resolution PET detectors based on long semi-monolithic scintillator slabs

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Abstract

Conventional positron emission tomography (PET) scanners use either highly-segmented or monolithic scintillator detectors. Depth of interaction (DOI) information is vital for high-resolution PET scanners using either segmented scintillator detectors with a large aspect ratio of crystal length to width or monolithic scintillator detectors with a large ratio of crystal thickness to spatial resolution. Semi-monolithic scintillator detectors maintain the intrinsic DOI encoding capability of monolithic detectors and meanwhile, the edge effect is much smaller. The objective of this study is to compare the performance of semi-monolithic scintillator detectors with different slab thicknesses, slab surface treatments, and reflector types. Four long semi-monolithic detectors consisting of lutetium yttrium oxyorthosilicate (LYSO) slabs of 0.96$×56×10mm3and0.81×56×10mm3,withandwithoutblackpaintatbothendandfrontsurfaceswere measure
monolithicdetectorsusingeitherbariumsulfate(BaSO4)orenhancedspecularreflector(ESR)astheinter−
slabreflectorwerecomparedforthefirsttime.Thesemi−monolithicdetectorswerereadoutby4×16siliconphotor
The detectors can be used to develop high-performance small animal and organ-specific PET scanners in the future.

Full Text

Preamble

Performance of high-resolution PET detectors based on long semi-monolithic scintillator slabs

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Conventional positron emission tomography (PET) scanners use either highly-segmented or monolithic scintillator detectors. Depth of interaction (DOI) information is vital for high-resolution PET scanners using either segmented scintillator detectors with a large aspect ratio of crystal length to width or monolithic scintillator detectors with a large ratio of crystal thickness to spatial resolution. Semi-monolithic scintillator detectors maintain the intrinsic DOI encoding capability of monolithic detectors while exhibiting much smaller edge effects. The objective of this study is to compare the performance of semi-monolithic scintillator detectors with different slab thicknesses, slab surface treatments, and reflector types.

Four long semi-monolithic detectors consisting of lutetium yttrium oxyorthosilicate (LYSO) slabs measuring $0.96 \times 56 \times 10$ mm^3 and $0.81 \times 56 \times 10$ mm^3, with and without black paint applied to both end and front surfaces, were measured. Additionally, semi-monolithic detectors using either barium sulfate ($BaSO_4$) or enhanced specular reflector (ESR) as the inter-slab reflector were compared for the first time. The semi-monolithic detectors were read out by a 4×16 silicon photomultiplier (SiPM) array with a row and column summing readout circuit, and the signals were processed using electronics developed in our lab.

Black paint treatment of the two end and front surfaces degrades the energy resolution but improves both the spatial resolution in the monolithic direction and DOI resolution, thus enhancing the overall detector performance. The detector using ESR reflector provides clearer individual slab identification in the flood histogram, with similar spatial resolution in the monolithic direction, DOI resolution, and energy resolution compared to $BaSO_4$. The squared centroid of gravity (squared COG) method improves the spatial resolution in the monolithic direction by approximately 30% compared to the conventional COG method.

The long semi-monolithic scintillator detectors optimized in this work provide clear identification of LYSO slabs of 0.96 and 0.81 mm thickness, a spatial resolution in the monolithic direction of ~1.7 ± 0.3 mm, a DOI resolution of ~2.1 ± 0.7 mm, and an energy resolution of ~17.5 ± 2.0%. These detectors can be used to develop high-performance small animal and organ-specific PET scanners in the future.

Keywords: Positron emission tomography (PET), PET detector, semi-monolithic scintillator, silicon photomultiplier (SiPM), depth of interaction (DOI)

INTRODUCTION

Positron emission tomography (PET) is a non-invasive medical imaging tool used for early detection of many major diseases such as cancer [1, 2]. Achieving high spatial resolution in a PET scanner allows for accurate measurement of biochemical processes in the organs and tissues of living subjects by reducing the partial volume effect [3], which is particularly important for small animal imaging [4–6] and clinical applications such as neuroimaging [7].

Depth of interaction (DOI) uncertainty deteriorates the spatial resolution of PET scanners, particularly for small animal and organ-specific PET scanners that use detectors with a high aspect ratio of crystal length to width [6, 8]. Due to crystal penetration, events may be incorrectly assigned to the wrong line of response when using detectors that lack DOI measurement or have poor DOI resolution. The error resulting from DOI uncertainty increases as the crystal's aspect ratio increases. In the most common cylindrical detector geometry, this DOI uncertainty error grows with both the radial offset and the ring difference. Therefore, DOI encoding in PET detectors is essential for achieving uniformly high spatial resolution.

Currently, state-of-the-art PET scanners use either pixelated or monolithic scintillator crystals read out by silicon photomultiplier (SiPM) photodetectors. Pixelated detectors can achieve high timing resolution since the scintillation photons are constrained in a smaller area, allowing the photodetector to achieve a high signal-to-noise ratio. They can also achieve superior planar position resolution by using small scintillator crystals [9, 10]. However, DOI information is not intrinsically present in pixelated detectors, and modified detector designs such as dual-ended readout or multiple-layer crystals are required to measure DOI, which increases cost and complexity [11–15]. Pixelated detectors also have lower detection efficiency due to dead space occupied by inter-crystal reflectors [5].

In monolithic scintillator detectors, DOI information is intrinsically present as it can be extracted from the scintillation photon distribution [5, 7]. Monolithic detectors offer superior efficiency and lower cost compared to pixelated detectors. However, they suffer from a large edge effect: due to loss and reflection of scintillation photons at the detector edge, fewer photons are detected and the measured planar positions are compressed for interactions occurring close to the edge, resulting in degradation of both planar and DOI resolutions. Both planar spatial resolution and DOI resolution deteriorate, and the edge effect increases as detector thickness increases [16–23].

Semi-monolithic scintillator detectors harness the advantages of both pixelated and monolithic scintillator detectors. They maintain the inherent DOI encoding capability of monolithic detectors, although the scintillation photon distribution is limited to fewer photosensors along the monolithic direction. Compared to monolithic detectors, semi-monolithic detectors have a smaller edge effect that can be further reduced by using longer scintillator slabs. Semi-monolithic scintillator PET detectors were proposed and preliminarily evaluated using detectors consisting of one or a few scintillator slabs by Chung et al. [24, 25] around 2010. Later, our group developed least-square minimization and maximum likelihood positioning algorithms [26] and optimized slab surface treatments [27, 28]. More recently, additional work has been performed on developing semi-monolithic detectors for small animal, dedicated brain, and whole-body PET scanners [30–32]. Machine learning-based positioning algorithms have also been found to improve spatial resolution in the monolithic direction and DOI resolution while reducing edge effects [32–34].

In this work, we evaluate four semi-monolithic detectors using long LYSO slab arrays with different slab surface treatments, slab thicknesses, and inter-slab reflectors. For the first time, we compare the performance of semi-monolithic detectors using two different inter-slab reflectors. We also compare the positioning resolution in the monolithic direction obtained using conventional centroid of gravity (COG) and squared COG algorithms.

MATERIALS AND METHODS

A. Detector Modules

Figure 1 [Figure 1: see original paper] shows a schematic of a detector module composed of LYSO slabs read out by a SiPM array with a lightguide in between. Table 1 provides detailed parameters of the four detector modules measured in this work. The semi-monolithic LYSO arrays were manufactured by Epic Crystal Co. (Shanghai, China). The reflector between individual slabs of detectors 1, 2, and 4 was barium sulfate ($BaSO_4$), while detector 3 used enhanced specular reflector (ESR) from 3M Company. The thickness of the $BaSO_4$ and the thickness of the ESR plus optical glue were both 0.08 mm. The optical glue is EPO-TEK 301 from EXPOXY Technology INC. (MA, USA).

For detectors 1, 3, and 4, the two end and front surfaces were unpolished and painted with a black marker pen, while the surfaces of detector 2 were unpolished and left unpainted. For all detectors, the two large surfaces of each slab and the bottom surface interfacing with the readout SiPM were polished. Each detector module was read out by a 4×16 SiPM array coupled to the bottom of the LYSO array. The SiPM array consisted of 64 single SiPM pixels (S14160-3050HS from Hamamatsu Inc., Hamamatsu, Japan). Each single SiPM has a size of 3.4×3.4 mm^2 and an active area of 3×3 mm^2, with a pitch of 3.65 mm. All measurements were performed at a SiPM bias voltage of 44.5 V. The lightguide was made of 1.5 mm thick K9 glass with a refractive index of 1.51.

To enhance slab identification, two edge grooves 0.2 mm wide and 1 mm deep were cut into the lightguide and filled with $BaSO_4$ reflector. For detectors 1–3, the grooves were 1.91 mm from both edges, while for detector 4 they were 2.05 mm from both edges. Optical grease with a refractive index of 1.41 was used between both the lightguide and scintillator slab array and between the lightguide and SiPM array.

B. Experimental Setup

The experimental setup is shown in Figure 2 [Figure 2: see original paper]. All measurements were conducted in a light-tight chamber made of plastic and covered with a black cloth, with detectors operating at 14 °C. The flood histogram was measured by placing a 0.3 mm diameter ^{22}Na point source with an activity of 165 kBq 24 mm away from one lateral face of the detector. Monolithic direction spatial, DOI, and energy resolution measurements were performed in coincidence with a reference detector consisting of a single LYSO crystal (1 $\times$ 1 $\times$ 20 mm^3) wrapped with Teflon and read out by a single Hamamatsu S14160-3050HS SiPM with a 3 $\times$ 3 mm^2 active area.

A collimated 511 keV beam was produced by placing the ^{22}Na point source between the reference detector and a 5 mm thick tungsten collimator with a 1 mm diameter hole. The 1 mm hole of the collimator, the ^{22}Na point source, and the reference detector were well aligned and placed on a motorized translational platform, while the semi-monolithic detector under test remained stationary. The translational platform could move in both the monolithic direction (y axis) and DOI direction (z axis spanning from the top of the detector to the SiPM array), irradiating the semi-monolithic scintillator detector from a series of (y, z) positions.

As shown at the top of Figure 3 [Figure 3: see original paper], detectors 1 and 4 were irradiated at 27 $\times$ 5 positions starting 2 mm from one end and 1 mm from the front with a stepping size of 2 mm in both monolithic and DOI directions. To save measurement time, detectors 2 and 3 were only irradiated at 27 y positions along the center z and 5 z positions along the middle y, as shown at the bottom of Figure 3, and only results from those positions were used to compare detector performance. The irradiation time for each position was 2200 s. The percentage of useful coincidence events to total singles events was approximately 0.02% for an energy window of 350–650 keV for both detectors.

C. Electronics and Data Acquisition

The 64 signals from the SiPM array were aggregated by a row-column summing circuit to form 4 row and 16 column signals, as shown in Figure 4 [Figure 4: see original paper]. The 4 row signals were used for slab identification (x), while the 16 column signals were used for both y and z position measurements.

The 20 signals were propagated to a preamplifier board, where all signals were first amplified by voltage feedback amplifiers (model AD8056, Analog Devices, MA, USA). A timing signal was produced by summing the 4 pre-amplified row signals and further amplified by a fast amplifier (model AD8045, Analog Devices, MA, USA). A 50 mV threshold signal was used together with the timing signal to generate 3 differential timing signal pairs by 3 high-speed comparators (model ADCMP604, Analog Devices, MA, USA) independently.

The 3 differential timing signal pairs and 20 energy signals from the test detector, along with 1 differential timing signal pair and 1 energy signal from the reference detector, were propagated by micro-coaxial cables to a singles processing unit (SPU) originally developed for our SIAT bPET scanner [35], as shown in Figure 5 [Figure 5: see original paper]. The SPU board can process 8 independent dual-ended readout detectors, each containing 8 energy channels and one differential timing signal pair. Three and one SPU electronics blocks were used to read out the test and reference detectors, respectively.

In the SPU, the energy signals from the preamplifier boards were first shaped and amplified. The waveforms were then sampled at 62.5 MHz by analog-to-digital converters (ADCs). The digital signals were processed in a field-programmable gate array (FPGA) to determine signal energies by calculating areas under the waveforms, performed by summing 18 waveform samples and subtracting the baseline (the average of 4 samples taken before the waveform's rising edge). For each electronic block, a differential timing pair was sent to a tapped delay line time-to-digital converter (TDC) to obtain the event timestamp, which also served as the starting signal for energy area calculation. Finally, from each SPU electronics block, eight energy values and a timestamp for each event were sent to the host PC via Ethernet-based User Datagram Protocol (UDP) [36–39].

Software-based data selection and coincidence processing were completed on the host PC using a coincidence timing window of 10 ns. The coincidence data containing 20 energies from the test detector and the time difference between reference and test detectors were stored as list-mode data for further analysis.

D. Data Analysis

1. Planar Position The (x) and (y) coordinates of interactions were calculated using the conventional COG algorithm as follows:

x = (cid:80)^{4} $_{1}$ j × q / (cid:80)^{4} $_{1}$ q
y = (cid:80)^{16} $_{1}$ i × q / (cid:80)^{16} $_{1}$ q

An energy window of 350–650 keV was used for all results. The irradiation beam width, estimated at ~1 mm, was not subtracted from the y and DOI resolutions.

The (y) coordinate was also calculated using a squared COG algorithm:

y = (cid:80)^{16} $_{1}$ i × q ^{2} / (cid:80)^{16} $_{1}$ q ^{2}

where i is the column number of the signals and q is the amplitude of the i-th column signal, while j is the row number and q is the amplitude of the j-th row signal.

From the calculated x, y coordinates, a flood histogram showing the 2D distribution of gamma interaction positions was plotted to demonstrate slab identification. The flood histogram was segmented to obtain a slab look-up table for assigning events to different slabs. For coincidence measurements at specific (y, z) positions, histograms of y coordinates were obtained for individual slabs using either COG or squared COG algorithms [40]. The histograms were fitted with Gaussian functions to obtain peak positions. For each (y, z) position, the peak position of the y histograms was determined as the average across all slabs.

The curve of peak positions versus true y irradiation position values for a specific z was fitted with a cubic polynomial function to obtain fitting parameters. The measured y histograms for each (y, z) position were converted from pixel values to mm using these parameters, then fitted with Gaussian functions to obtain FWHM y resolutions for all measured positions.

2. Energy Detector energy was calculated by summing the amplitudes of the 16 column signals. Energy histograms were populated for each irradiation position across all individual slabs. Gaussian fitting was performed and energy resolution calculated as the ratio of FWHM to mean.

3. DOI DOI was estimated using the inverse standard deviation of the amplitudes of the 16 column signals:

DOI = (cid:113) (cid:80)^{16} $_{1}$ (q - q̄)^{2}

where q is the normalized amplitude of the i-th column signal and q̄ is the average amplitude of the 16 column signals. DOI histograms for each y position were obtained for each slab, and Gaussian fitting was performed to obtain FWHMs and peak positions. The FWHM was converted to mm using peak positions from neighboring DOI histograms and the known DOI interval of 2 mm.

4. Timing Detector timing was measured as the timing difference between reference and test detectors. Timing spectra for each irradiation position were populated for all individual slabs using a timing window of 40 ns. Gaussian fitting was performed to obtain FWHM timing resolution.

RESULTS

A. Flood Histograms

Figure 6 [Figure 6: see original paper] shows flood histograms for the four detectors, displaying x and y positions of gamma ray interactions with grayscale values representing interaction counts. Profiles through the middle of each flood histogram are also shown. The average peak-to-valley ratios were 3.03 ± 0.96, 4.67 ± 1.29, 5.04 ± 1.44, and 2.58 ± 0.85 for detectors 1–4, respectively. All slabs were clearly resolved for detectors 1–3 using 0.96 mm thick slabs. As seen in the flood histogram, slab identification along the x coordinate was best achieved in detector 3, which used the ESR reflector.

For detector 4 using 0.81 mm thick slabs, the second and third slabs near the edges could not be clearly resolved, suggesting that the positions of the cuts in the lightguide need further optimization. Black painting of the two end and front surfaces reduced scintillation photon reflection at those surfaces, resulting in longer flood histograms in the monolithic direction that imply better y position resolution, while slab identification remained essentially unchanged.

B. Energy Resolution

Energy spectra for a middle slab of the four detectors measured at 5 DOIs are shown in Figure 7 [Figure 7: see original paper]. Detector 3, which uses the specular ESR reflector, has the lowest light output, but the photopeak amplitudes do not change with depth. The other three detectors using the diffusive $BaSO_4$ reflector have much higher light output, but the photopeak amplitude changes significantly with depth, requiring depth-dependent energy calibration.

Average energy resolutions for detectors 1 and 4 measured across 27 × 5 (y, z) positions are shown in Table 2 , achieving 17.4% and 17.6%, respectively, indicating that slab thickness had a small effect on energy resolution. Table 3 shows average energy resolutions for all four detectors measured at 27 y positions along the middle DOI: 15.8%, 14.7%, 15.8%, and 16.4% for detectors 1–4, respectively. Detector 2 (without black paint) has the best energy resolution, as the black paint absorbs some scintillation photons, degrading energy resolution in the other three detectors.

C. Spatial Resolution in the Monolithic Direction

Figure 8 [Figure 8: see original paper] shows peak position curves for COG and squared COG algorithms at different y irradiation positions measured at 3 depths for detectors 1 and 4. The curves are linear in the middle of the detectors and become non-linear at both ends due to scintillation photon reflection and truncation. Non-linearity decreases as depth increases but increases calibration challenges and degrades spatial resolution in the monolithic direction. Curves are similar for different slabs within a detector (data not shown).

Figure 9 [Figure 9: see original paper] shows y profiles for 27 different y positions and 2 DOIs from detector 1 obtained with both positioning methods. The horizontal coordinate was converted to mm using the curves in Figure 8 [Figure 8: see original paper]. For both methods, profile resolvability deteriorates toward both ends due to edge effects. To clearly illustrate the effects of positioning methods and depths on y spatial resolution, Figure 9(e) shows y profiles at DOI of 5 mm and y of 42 mm obtained using both COG and squared COG methods, while Figure 9(f) shows profiles at DOIs of 1 and 5 mm and y of 42 mm using the squared COG method.

Figure 10 [Figure 10: see original paper] shows spatial resolutions for all irradiation positions of detectors 1 and 4 using both COG and squared COG methods. For both methods, y spatial resolution improves as DOI moves toward the SiPM and degrades as y position moves toward both ends due to edge effects. Near the SiPM, variation in y spatial resolution with y position changes is observed due to gaps between SiPM pixels and inactive areas at pixel edges. The squared COG method demonstrates better y spatial resolution than COG. As shown in Table 2, y spatial resolutions averaged across whole detectors are 1.68 ± 0.29 mm and 1.67 ± 0.27 mm for detectors 1 and 4, respectively. Table 3 shows average y spatial resolutions measured at 5 mm depth: 1.66 ± 0.16 mm, 1.87 ± 0.31 mm, 1.71 ± 0.26 mm, and 1.67 ± 0.14 mm for detectors 1–4, respectively.

D. DOI Resolution

Figure 11 [Figure 11: see original paper] shows DOI profiles for the four detectors measured at a center y position (28 mm). DOI resolution significantly degrades as DOI moves away from the SiPM because the change in scintillation photon distribution width with DOI becomes smaller at greater distances. Figure 12 [Figure 12: see original paper] shows DOI resolutions at all irradiation positions for detectors 1 and 4. DOI resolution degrades toward both detector ends due to edge effects. Average DOI resolution results are summarized in Tables 2 and 3. DOI resolutions averaged across whole detectors are 2.14 ± 0.76 mm and 2.28 ± 0.67 mm for detectors 1 and 4, respectively. Detector 2 with unpainted front and end surfaces provides the worst DOI resolution of 3.41 ± 2.8 mm averaged across 5 DOIs along the center y. The other three detectors with black paint at those surfaces provide similar DOI resolution of ~1.9 mm averaged across 5 DOIs along the center y.

E. Timing Resolution

Figure 13 [Figure 13: see original paper] shows timing resolutions for detectors 1 and 4. Average timing resolution results for all four detectors are shown in Tables 2 and 3. Timing resolution is similar across the four detectors. The poor timing resolution results in this work stem from the unoptimized timing pick-off circuit rather than the semi-monolithic scintillator detector itself, as timing resolution <600 ps had been obtained for a small semi-monolithic detector using Nuclear Instrument Module electronics [26].

DISCUSSION AND CONCLUSIONS

In this work, we evaluated the performance of four PET detector modules consisting of semi-monolithic LYSO slabs with different surface treatments, inter-slab reflectors, and slab thicknesses using signal processing electronics developed in our lab. To our knowledge, these represent the longest (56 mm) and thinnest (0.81 mm) semi-monolithic scintillator PET detectors measured to date. This work also presents the first comparison of semi-monolithic scintillator PET detectors using ESR and $BaSO_4$ reflectors.

Through the use of a lightguide with grooves near both ends, clear slab identification was attained for three detectors using 0.96 mm thick LYSO slabs. For the detector using 0.81 mm thick LYSO slabs, the second and third slabs at the edges could not be clearly identified, indicating that groove positions in the lightguide will require future optimization.

Black paint treatment of the two end and front surfaces degrades energy resolution but improves both spatial resolution in the monolithic direction and DOI resolution. Energy resolution degraded from 14.7% to 15.8%. Spatial resolution in the monolithic direction improved from 2.65 mm to 2.15 mm for the COG method and from 1.87 mm to 1.66 mm for the squared COG method. DOI resolution improved from 3.41 mm to 1.92 mm. Overall, black paint treatment of crystal surfaces improves semi-monolithic PET detector performance.

Although the detector using ESR as the inter-slab reflector provides the lowest light output, the photopeak amplitude changes minimally with DOI, simplifying energy calibration. The ESR reflector provides clearer individual slab identification in the flood histogram with similar spatial resolution in the monolithic direction, DOI resolution, and energy resolution compared to $BaSO_4$. Overall, ESR is a superior inter-slab reflector to $BaSO_4$.

This work compared a squared COG positioning method with the traditional COG method. The squared COG method gives more weight to SiPM column signals with high amplitudes, improving spatial resolution in the monolithic direction by ~30% by reducing the effect of signals with poor signal-to-noise ratio. The squared COG method can also be easily implemented in modern PET electronics.

Currently, both pixelated and monolithic scintillator detectors are used in developing high-resolution small animal and organ-specific PET scanners. Semi-monolithic detectors present a suitable alternative, as they exhibit smaller edge effects than monolithic detectors and enable DOI measurement with single-ended readout, unlike pixelated detectors requiring dual-ended readout or more complex designs. The cost of semi-monolithic scintillators is lower than pixelated detectors but higher than monolithic detectors. Future work will employ SiPM arrays with smaller pixel gaps, further optimize crystal surface treatments, and develop machine learning-based positioning algorithms to improve resolution in both monolithic and DOI directions. Semi-monolithic scintillator detectors with thinner slabs using ESR reflectors will be evaluated, and advanced signal processing techniques will be studied to improve timing resolution and explore potential applications in time-of-flight PET scanners.

In summary, the long semi-monolithic scintillator detectors optimized in this work provide clear identification of LYSO slabs of 0.96 and 0.81 mm thickness, a spatial resolution in the monolithic direction of ~1.7 mm using the squared COG method, a DOI resolution of ~1.9 mm, and energy resolutions of ~16%. Since the irradiation beam width of ~1 mm was not subtracted from measured results, the true spatial resolution in the monolithic direction and DOI resolution are even better. Based on this achieved performance, these detectors can be used to develop high-performance small animal and organ-specific PET scanners in the future.

BIBLIOGRAPHY

[1] S.R. Cherry, T. Jones, J.S. Karp et al., Total-Body PET: Maximizing Sensitivity to Create New Opportunities for Clinical Research and Patient Care. J. Nucl. Med. 59, 3-12 (2018). doi: 10.2967/jnumed.116.184028
[2] S. Vandenberghe, P. Moskal, J.S. Karp, State of the art in total body PET. EJNMMI Phys. 7, 1-33 (2020). doi: 10.1186/s40658-020-00290-2
[3] V. Bettinardi, I. Castiglioni, E. De Bernardi et al., PET quantification: strategies for partial volume correction. Clin Transl Imaging. 2, 199-218 (2014). doi: 10.1007/s40336-014-0066-y
[4] Y. Yang, J. Zhou et al., A Prototype High-Resolution Small-Animal PET Scanner Dedicated to Mouse Brain Imaging. J. Nucl. Med. 57, 1130-1135 (2016). doi: 10.2967/jnumed.115.165886
[5] R.S. Miyaoka, A.L. Lehnert, Small animal PET: a review of what we have done and where we are going. Phys. Med. Biol. 65, 24TR04 (2020). doi: 10.1088/1361-6560/ab8f71
[6] J. Du, T. Jones, Technical opportunities and challenges in developing total-body PET scanners for mice and rats. EJNMMI Phys. 10, 2 (2023). doi: 10.1186/s40658-022-00523-6
[7] A. Verger, A. Kas, J. Darcourt et al., PET Imaging in Neuro-Oncology: An Update and Overview of a Rapidly Growing Area. Cancers. 14, 1103 (2022). doi: 10.3390/cancers14051103
[8] C. Catana, Development of Dedicated Brain PET Imaging Devices: Recent Advances and Future Perspectives. J. Nucl. Med. 60, 1044-1052 (2019). doi: 10.2967/jnumed.118.217901
[9] S. Vandenberghe, E. Mikhaylova, E. D'Hoe et al., Recent developments in time-of-flight PET. EJNMMI Phys. 3, 3 (2016). doi: 10.1186/s40658-016-0138-3
[10] J. Van Sluis, J. De Jong, J. Schaar et al., Performance Characteristics of the Digital Biograph Vision PET/CT System. J. Nucl. Med. 60, 1031-1036 (2019). doi:10.2967/jnumed.118.215418
[11] L. Eriksson, K. Wienhard, M. Eriksson et al., The ECAT HRRT: NEMA NEC evaluation of the HRRT system, the new high-resolution research tomograph. IEEE T. Nucl. Sci. 49, 2085-2088 (2002). doi: 10.1109/TNS.2002.803784
[12] N. Inadama, H. Murayama, M. Hamamoto et al., 8-Layer DOI Encoding of 3-Dimensional Crystal Array. IEEE T. Nucl. Sci. 53, 2523-2528 (2006). doi: 10.1109/TNS.2006.882795
[13] Y. Yang, P.A. Dokhale, R.W. Silverman et al., Depth of interaction resolution measurements for a high resolution PET detector using position sensitive avalanche photodiodes. Phys. Med. Biol. 51, 2131-2142 (2006). doi: 10.1088/0031-9155/51/9/001
[14] Z. Kuang, X. Wang, N. Ren et al., Design and performance of SIAT aPET: a uniform high-resolution small animal PET scanner using dual-ended readout detectors. Phys. Med. Biol. 65, 235013 (2020). doi: 10.1088/1361-6560/abbc83

[15] Z. Gu, R. Taschereau, N.T. Vu et al., Performance evaluation of HiPET, a high sensitivity and high resolution preclinical PET tomograph. Phys. Med. Biol. 65, 045009 (2020). doi: 10.1088/1361-6560/ab6b44
[16] P. Bruyndonckx, S. Leonard, S. Tavernier et al., Neural network-based position estimators for PET detectors using monolithic LSO blocks. IEEE T. Nucl. Sci. 51, 2520-2525 (2004). doi: 10.1109/TNS.2004.835782
[17] M.C. Maas, D.J. van der Laan, D.R. Schaart et al., Experimental characterization of monolithic-crystal small animal PET detectors read out by APD arrays. IEEE T. Nucl. Sci. 53, 1071-1077 (2006). doi: 10.1109/TNS.2006.873711
[18] M. Balcerzyk, G. Kontaxakis, M. Delgado et al., Initial performance evaluation of a high resolution Albira small animal positron emission tomography scanner with monolithic crystals and depth-of-interaction encoding from a user's perspective. Meas. Sci. Technol. 20, 104011 (2009). doi: 10.1088/0957-0233/20/10/104011
[19] S. Krishnamoorthy, E. Blankemeyer, P. Mollet et al., Performance evaluation of the MOLECUBES β-CUBE–a high spatial resolution and high sensitivity small animal PET scanner utilizing monolithic LYSO scintillation detectors. Phys. Med. Biol. 63, 155013 (2018). doi: 10.1088/1361-6560/aacec3
[20] W. Gsell, C. Molinos, C. Correcher et al., Characterization of a preclinical PET insert in a 7 tesla MRI scanner: beyond NEMA testing. Phys. Med. Biol. 65, 245016 (2020). doi: 10.1088/1361-6560/aba08c
[21] G. Borghi, V. Tabacchini, D.R. Schaart, Towards monolithic scintillator based TOF-PET systems: practical methods for detector calibration and operation. Phys. Med. Biol. 61, 4904-4928 (2016). doi: 10.1088/0031-9155/61/13/4904
[22] M. Stockhoff, R.V. Holen, S. Vandenberghe, Optical simulation study on the spatial resolution of a thick monolithic PET detector. Phys. Med. Biol. 64, 195003 (2019). doi: 10.1088/1361-6560/ab3b83
[23] G. Borghi, V. Tabacchini, S. Seifert et al., Experimental validation of an efficient fan-beam calibration procedure for k-nearest neighbor position estimation in monolithic scintillator detectors. IEEE T. Nucl. Sci. 62, 57-67 (2015). doi: 10.1109/TNS.2014.2375557
[24] Y.H. Chung, S.J. Lee, C.H. Baek et al., New design of a quasi-monolithic detector module with DOI capability for small animal pet. Nucl. Instrum. Meth. A. 593, 588-591 (2008). doi:10.1016/j.nima.2008.05.059
[25] Y.H. Chung, C.H. Baek, S.J. Lee et al., Preliminary experimental results of a quasi-monolithic detector with DOI capability for a small animal PET. Nucl. Instrum. Meth. A. 621, 590-594 (2010). doi: 10.1016/j.nima.2010.04.039
[26] X. Zhang, X. Wang, N. Ren et al., Performance of a SiPM based semi-monolithic scintillator PET detector. Phys. Med. Biol. 62, 7889-7904 (2017). doi: 10.1088/1361-6560/aa898a
[27] Z. Kuang, X. Wang, C. Li, et al., Performance of a high-resolution depth encoding PET detector using barium sulfate reflector. Phys. Med. Biol. 62, 5945-5958 (2017). doi: 10.1088/1361-6560/aa71f3
[28] X. Zhang, X. Wang, N. Ren et al., Performance of long rectangular

semi-monolithic scintillator PET detectors. Med. Phys. 46, 1608-1619 (2019). doi: 10.1002/mp.1343
[29] Y. Kuhl, F. Mueller, S. Naunheim et al., A finely segmented semi-monolithic detector tailored for high-resolution PET. Med. Phys. 51, 3421-3436 (2024). doi: 10.1002/mp.16928
[30] N. Cucarella, J. Barrio, E. Lamprou et al., Timing evaluation of a PET detector block based on semi-monolithic LYSO crystals. Med. Phys. 48, 8010-8023 (2021). doi: 10.1002/mp.15318
[31] C. Zhang, X. Wang, M. Sun et al., A thick semi-monolithic scintillator detector for clinical PET scanners. Phys. Med. Biol. 66, 065023 (2021). doi: 10.1088/1361-6560/abe761
[32] F. Mueller, S. Naunheim, Y. Kuhl et al., A semi-monolithic detector providing intrinsic DOI-encoding and sub-200 ps CRT TOF-capabilities for clinical PET applications. Med. Phys. 49, 7469-7488 (2022). doi: 10.1002/mp.16015
[33] M. Freire, J. Barrio, N. Cucarella et al., Position estimation using neural networks in semi-monolithic PET detectors. Phys. Med. Biol. 67, 245011 (2022). doi: 10.1088/1361-6560/aca389
[34] A. Iborra, A.J. González, A.G. Montoro et al., Ensemble of neural networks for 3D position estimation in monolithic PET detectors. Phys. Med. Biol. 64, 195010 (2019). doi: 10.1088/1361-6560/ab3b86
[35] Z. Kuang, Z. Sang, N. Ren et al., Development and performance of SIAT bPET: a high-resolution and high-sensitivity MR-compatible brain PET scanner using dual-ended readout detectors. Eur. J. Nucl. Med. Mol. I. 51, 346-357 (2024). doi: 10.1007/s00259-023-06458-z
[36] J. Lu, L. Zhao, K. Chen et al., Real-time FPGA-based digital signal processing and correction for a small animal PET. IEEE T. Nucl. Sci. 66, 1287-1295 (2019). doi: 10.1109/TNS.2019.2908220
[37] L. Zhao, C. Ma, S. Chu et al., Prototype of the Readout Electronics for WCDA in LHAASO. IEEE T. Nucl. Sci. 64, 1367-1373 (2017). doi: 10.1109/TNS.2017.2693296
[38] P. Deng, L. Zhao, J. Lu et al., Prototype design of singles processing unit for the small animal PET. J. Instrum. 13, T05007 (2018). doi: 10.1088/1748-0221/13/05/T05007
[39] K. Chen, L. Zhao, L. Zhang et al., Testing of Singles Processing Unit for a Brain PET. 2021 IEEE Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC). 1-3 (2021). doi: 10.1109/NSS/MIC44867.2021.9875447
[40] D. Schug, J. Wehner, B. Goldschmidt et al., Data processing for a high resolution preclinical PET detector based on Philips DPC digital SiPMs. IEEE T. Nucl. Sci. 62, 669-678 (2015). doi: 10.1109/TNS.2015.2420578

Note: Figure translations are in progress. See original paper for figures.