Published in final edited form as:

Phys Med Biol. 2011 January 7; 56(1): 139–153. doi:10.1088/0031-9155/56/1/009.

Tapered LSO Arrays for Small Animal PET

Yongfeng Yang¹, Sara St. James¹, Yibao Wu¹, Huini Du¹, Jinyi Qi¹, Richard Farrell²,
Purushottam A. Dokhale², Kanai S. Shah², Keith Vaigneur³, and Simon R. Cherry¹

¹ Department of Biomedical Engineering, University of California-Davis, One Shields Avenue, CA 95616, USA

² Radiation Monitoring Devices Inc., Watertown, MA 02172, USA

³ Agile Engineering, 123 Perimeter Park Rd., Ste. E, Knoxville, TN 37922, USA

Abstract

By using detectors with good depth encoding accuracy (~ 2 mm), an animal PET scanner can be built with a small ring diameter and thick crystals to simultaneously obtain high spatial resolution and high sensitivity. However, there will be large wedge-shaped gaps between detector modules in such a scanner if traditional cuboid crystal arrays are used in a polygonal arrangement. The gaps can be minimized by using tapered scintillator arrays enabling the sensitivity of the scanner to be further improved. In this work, tapered lutetium oxyorthosilicate (LSO) arrays with different crystal dimensions and different combinations of inter-crystal reflector and crystal surface treatments were manufactured and their performance was evaluated. Arrays were read out from both ends by position-sensitive avalanche photodiodes (PSAPDs). In the optimal configuration, arrays consisting of 0.5 mm LSO elements could be clearly resolved and a depth of interaction resolution of 2.6 mm was obtained for a 20-mm thick array. For this tapered array, the intrinsic spatial is degraded from 0.67 mm to 0.75 mm compared to a standard cuboidal array with similar dimensions, while the increase in efficiency is 41%. Tapered scintillator arrays offer the prospect of improvements in sensitivity and sampling for small-bore scanners, without large increases in manufacturing complexity.

Keywords

Scintillators; positron emission tomography; small animal imaging; depth of interaction

1. Introduction

Positron emission tomography (PET) is an *in vivo* imaging modality that can provide information on physiology, metabolism, drug biodistribution, protein concentrations and gene expression. Presently, it is estimated that there are over 200 dedicated small-animal PET scanners installed worldwide. PET has found widespread application in biomedical research and is now regarded as an established modality for preclinical studies (Chatziioannou, 2002; Cherry, 2004, 2006; Muehllehner and Karp, 2006; Rowland and Cherry, 2008). Although current generation small-animal PET systems are successfully applied for a range of applications, limitations in what can be visualized and quantified are readily apparent. Improving sensitivity and spatial resolution significantly would not only improve the quantification of signals that we are currently able to visualize (by reducing partial volume effects and increasing signal-to-noise) but would also open up important new applications that are beyond the reach of contemporary animal PET systems. A spatial resolution of ~ 0.5 mm is required if one wants to obtain a whole-body mouse image that has the same relative resolution as an image of a human body acquired on a 5 mm resolution clinical PET scanner (Larobina *et al.*, 2006; Lewellen 2008). Currently the spatial resolution

of most dedicated small animal PET scanners is only 1–2 mm (Tai *et al.*, 2003; Tai *et al.*, 2005; Wang *et al.*, 2006; Lecomte *et al.*, 2006; Schafers *et al.*, 2005). Meanwhile higher scanner sensitivity is also required to maintain image quality (signal-to-noise) for high spatial resolution scanners since the size of image voxel is reduced and the counts per voxel are decreased as the scanner spatial resolution improves (Yamaya *et al.*, 2009).

The most obvious pathway to simultaneously achieving high spatial resolution and high sensitivity are to use detector modules with small cross-section, but thick, detector elements that have depth-encoding capability to prevent deterioration in spatial resolution due to depth-of-interaction (DOI) effects (Lewellen 2008). Much attention in recent years has focused on detector designs with depth-encoding ability (Lerche *et al.*, 2005; Saoudi *et al.*, 1999; Tsuda *et al.*, 2004; Schmand *et al.*, 1998; Moses and Derenzo, 1994; Du *et al.*, 2009; Ling *et al.*, 2007; Burr *et al.*, 2004). Our group has pursued depth-encoding detectors that involve dual-ended readout of finely pixelated scintillator arrays with position-sensitive avalanche photodiodes (PSAPDs) (Dokhale *et al.*, 2004; Yang *et al.*, 2006; Yang *et al.*, 2008). To date we have successfully developed detectors from lutetium oxyorthosilicate (LSO) arrays with elements as small as $0.5 \times 0.5 \text{ mm}^2$ in cross section by 20 mm long, with a measured DOI resolution of $\sim 2 \text{ mm}$ (St James *et al.*, 2009). Using such detectors a dedicated mouse imaging PET scanner can be designed with a small ring diameter and long crystals to obtain high spatial resolution, good spatial resolution uniformity and high sensitivity. Fewer detectors are required for a PET scanner with a smaller ring diameter to cover the same solid angle; therefore the cost of the PET scanner, for a given sensitivity, can also potentially be reduced. However, such designs result in large gaps between detector modules if traditional cuboid detectors are used (Figure 1). The gaps can be minimized by using tapered arrays, providing a pathway to further improvements in scanner sensitivity (St James *et al.*, 2010).

In this work tapered LSO arrays with crystal sizes as small as 0.5 mm are manufactured and their performance evaluated. The goal is to determine whether crystals this small can be clearly resolved, and to examine how the visual quality of the flood histogram and quantitative measures of depth-of-interaction resolution and energy resolution change as different crystal surface treatments and inter-crystal reflectors are used. These surface treatments and reflectors can have a significant impact on detector performance (Yang *et al.*, 2006) and without great care, it is not possible to simultaneously resolve very small scintillation elements and achieve the DOI resolution necessary for high-resolution small-bore PET systems. It is notoriously difficult to model optical properties of reflectors and different surface treatments using simulation tools, thus the experimental data obtained here with a variety of configurations will also be a valuable resource for others developing high resolution depth-encoding PET detectors. The intrinsic spatial resolution and efficiency of a tapered LSO array was also compared with that of a standard geometry cuboid array to determine how significant the efficiency gain is, and to what extent this gain comes at the expense of a degradation in spatial resolution.

2. Materials and Methods

2.1 Tapered LSO array fabrication

Figure 2 shows a photograph of a tapered LSO array together with a traditional cuboid LSO array. The tapered array is only wedge-shaped in one dimension, allowing multiple detector rings to be stacked together in the axial direction. The procedure for making tapered LSO arrays is similar to that for making cuboid LSO arrays (Stickel *et al.*, 2007; Yang *et al.*, 2006) and is briefly described here. LSO bars are initially cut, and from these bars, wedged shaped slices are sectioned. These slices are then assembled with reflector bonded between them, into a tapered stack with slice numbers corresponding to the number of pixels in a

row. The tapered stack is then cut perpendicular to the slices with slice numbers corresponding to the number of pixels in a column. These new slices are then assembled, with reflector bonded between them, into the final two-dimensional array, which is then wrapped with reflector. The slices can also be polished on their lateral faces prior to assembly, if so desired. From our previous results (Yang *et al.*, 2008) and also the results that will be shown in Section 3, we observe by that the crystal separation in the flood histograms of the arrays are better in the direction of the second cut than the direction of the first cut. The main reason is that in making the second cuts, the reflector in the direction of the first cut is divided and may sustain some small amount of tearing or stretching, allowing crosstalk of light through the corners of the crystals. In these tapered arrays, the wedged direction is always cut first such that this effect occurs along the wider (and more easily resolved) dimension of the crystal.

2.2 LSO arrays

Initially, six 1st generation tapered LSO arrays with two different crystal sizes (Table 1) and three combinations of reflectors and crystal surface treatments (Table 2) were manufactured. All arrays have dimensions of roughly $7.8 \times 7.8 \text{ mm}^2$ at the small end, $7.8 \times 13 \text{ mm}^2$ at the large end and are 20 mm long. Two reflectors were tested in this work. The enhanced specular reflector (ESR) is a 65 μm thin multi-layer polymer film reflector that is 98.5% reflective over the entire visible spectrum, regardless of the angles of the incidence (3M, St. Paul, MN). Toray lumirror E60 film (Toray) is a 50 μm thin white microvoided film with excellent opacity (Toray Industries Inc., Japan). Detector arrays using either reflector have high packing fraction due to their low thickness. ESR is mainly used for LCD brightness enhancement and is also popular in PET detectors as an inter-crystal reflector. The Toray reflector is mainly used for cards and labels etc. A recent study showed that ESR is a specular reflector, while the Toray reflector cannot be described as a specular reflector, a diffuse reflector, nor a linear combination of the two, but instead demonstrates more complex reflection properties (Janecek and Moses, 2008). For arrays fabricated with ESR reflector, only one array consisting of unpolished (as cut) crystal surfaces was made, since previous results showed that polished crystal surfaces with this reflector could not provide adequate DOI resolution (Yang *et al.*, 2006). For arrays fabricated with the Toray reflector, two types of arrays were made; one with all four sides of the crystal unpolished and the other with just two of the four sides polished. The hypothesis was that in such long, narrow crystals, some polishing of the sides may be necessary to unambiguously resolve all the elements. The two ends of the arrays that are coupled to the photodetector were always polished. Each tapered array was read out by an $8 \times 8 \text{ mm}^2$ PSAPD (Shah *et al.*, 2002; Shah *et al.*, 2004) from the small end and a $14 \times 14 \text{ mm}^2$ PSAPD from the large end. For easy description of the arrays, a simple code is used to identify the surface treatment (U=unpolished, P=polished) and the reflectors used (E=ESR, T=Toray E60) as shown in Table 2.

Based on results obtained with these six arrays (see Section 3), two 2nd generation tapered LSO arrays with the smallest crystal size and with the reflectors and crystal surface treatments shown in Table 2 were fabricated to try and improve identification of the edge crystals. Specifically array PE/UE was made with the goal of improving identification of the edge crystals compared to array UE, and array PT was made to improve the overall flood histogram compared to arrays UT and UT/PT. The idea was to improve the crystal surface smoothness (by polishing) so that more light can reach the PSAPDs, thus leading to clearer separation of crystals in the flood histograms. It was anticipated that the DOI resolution would be degraded in these new arrays, the question was, by how much?

2.3 Detector measurements and data analysis

Details of the experimental setup for detector evaluation, data acquisition and formulas to calculate flood histograms, DOI and energy parameters for the dual-ended readout detectors can be found in our previous publications (Yang *et al.*, 2006; Yang *et al.*, 2008; Judenhofer *et al.*, 2005). For each array, measurements were performed in singles mode with the array irradiated by a 0.3 mm diameter ^{22}Na point source placed 4 cm from one side; and in coincidence mode, using the same source and selectively irradiating at five depths of 2, 6, 10, 14 and 18 mm from the narrow end of the array using electronic collimation. The radiation beam width on the array is estimated from the geometry to be ~ 1 mm. The detector module and PSAPD readout boards were placed in a light-tight box which was cooled by sending cold and dry air using an Air-Jet Crystal Cooler (FTS Systems, Inc, Stone Ridge, NY) over the detectors to obtain a stable temperature of $\sim 0^\circ\text{C}$. Measurements were performed after the box was cooled down to a temperature of 0°C for 30 minutes and the temperature variation during the measurement period was less than 1°C .

To analyze the data, first a preliminary flood histogram (with low energy threshold) was obtained from the list mode data with the detector in singles mode. From this, a crystal look-up table was generated. The list mode data was then reprocessed using the crystal look-up table to obtain crystal energy spectra for each crystal in an array. Both the average energy spectrum for interactions at all depths and the energy spectra obtained by selecting events at specific depths were measured. The photopeak amplitude and energy resolution of all crystals was obtained by Gaussian fitting of the energy spectra. In addition, the list mode data was re-analyzed using the crystal look-up table and crystal photopeak amplitude information obtained from the coincidence measurements made at a depth of 10 mm to create flood histograms representing events with an energy above or below 350 keV.

The depth information for these detectors is calculated from the ratio of the amplitude, E , of the two PSAPD signals

$$DOI\ ratio = \frac{E_2}{E_1 + E_2} \quad (1)$$

E_1 is the photodetector at the narrow end of the tapered array. Histograms of this DOI ratio as a function of irradiation depth were obtained for individual crystals, and for two different energy ranges. The full width at half maximum (FWHM) DOI resolution was calculated by a Gaussian fitting of the DOI ratio histograms. The FWHM DOI resolution was then converted to units of mm by a linear fit of the peak values of the DOI ratio histogram (averaged over all crystals in the array) to the known depth of irradiation, using the data obtained at depths of 2 mm and 18 mm as described previously (Yang *et al.*, 2009).

2.4 Intrinsic spatial resolution and efficiency of tapered array vs. cuboid array

The purpose of this measurement was to compare the intrinsic spatial resolution and efficiency of a tapered LSO array with a cuboid LSO array that has similar crystal sizes as the front of the tapered arrays. The experimental setup is shown in Figure 3. The 13×13 element tapered array UE was used. Crystals in the central column of the tapered array were aligned with a LSO slab detector ($20 \times 20 \times 0.5$ mm³) that was read out by a Hamamatsu M64 PMT. For the intrinsic spatial resolution measurement, a ^{22}Na point source (0.3 mm diameter) was moved along the direction of the arrow in Figure 3 with a step size of 0.076 mm. The coincidence counts between crystals in the central column and the slab detector were obtained at 38 source positions. The curve of the coincidence counts vs. source

position (intrinsic spatial resolution profile) was fitted using the following function that consists of a Gaussian term plus a constant background.

$$C(x) = a_0 e^{-\frac{(x-a_1)^2}{2a_2^2}} + a_3 \quad (2)$$

C is the number of coincidence counts measured, x is the source position and the parameters a_0 to a_3 are obtained from the fit. The FWHM of the intrinsic spatial resolution is given by $2.35 \times a_2$. The efficiency of the tapered array was measured in singles mode with the source 4 cm from the front of array as shown in Figure 3. The energy threshold was set just above the noise. The same intrinsic spatial resolution and efficiency measurements were repeated for the cuboid array. The cuboid array had 13×13 unpolished elements separated by ESR reflector, and a crystal size of $0.5 \times 0.5 \times 20 \text{ mm}^3$.

3. Results

3.1 1st generation tapered arrays

The flood histograms measured from the six 1st generation arrays measured in singles mode, and using a crystal-by-crystal energy threshold of 350 keV, are shown in Figure 4. For the 8×8 arrays, all crystals can be resolved in the flood histograms no matter what reflector and crystal surface treatments are used. Thus, optimal surface treatment and reflectors can be selected based on best DOI performance. For the 13×13 arrays however, where the crystals are only 34% of the area of the 8×8 array, the edge crystals in one direction cannot be resolved for arrays using ESR reflector. The flood histograms in the direction of the first cut (tapered direction) are visibly worse than in the direction of the second cut. This is a common finding and suggests that there is some damage or gaps in the ESR reflector when making the second cut leading to increased light crosstalk through the corner of the crystals in the first cut direction. For arrays using the Toray reflector, the flood histograms are more symmetric. The arrays with two polished sides (UT/PT) provide better flood histograms than the arrays with all four sides unpolished (UT) due to improved light collection from the polished crystal surfaces. Nonetheless, the edge crystals are barely resolved.

Figure 5 shows DOI responses (histograms of the DOI ratio for each irradiation depth, summed over all crystals) for each array measured at depths of 2, 6, 10, 14 and 18 mm. As expected, the dynamic range of the DOI ratio increases for the arrays with smaller crystal sizes. The UE arrays have the smallest dynamic range while the UT arrays have the largest dynamic range. Table 3 shows the calculated DOI resolution of the six arrays for two different energy ranges. DOI resolution is calculated as the mean value of the DOI resolution of each individual crystal. The data shown are the average DOI resolution over all 5 measured depths. The UT arrays have the best DOI resolution, thus for the 8×8 arrays, this would be the surface/reflector treatment of choice. The 13×13 UT array exhibits particularly good DOI resolution of 2 mm, however, the flood histogram (Figure 4) was not optimal as edge crystals are hard to resolve.

The DOI resolution is quite sensitive to the deposited energy. For events with energy $E < 350 \text{ keV}$, DOI resolution is about 30–50% worse than that for events with $E > 350 \text{ keV}$. The DOI resolution obtained when using all events is 10–20% worse than that using events with $E > 350 \text{ keV}$. Therefore, the energy window selected in a scanner based on such a detector design would need consider this trade-off in addition to the standard trade-off between sensitivity and scatter fraction as the energy threshold is lowered.

3.2 2nd generation tapered arrays

New 13×13 tapered arrays (Table 2) were constructed to try and improve the quality of the flood histograms, particularly with regard to clear identification of edge crystals, while retaining good DOI resolution. Flood histograms, DOI response and calculated DOI resolution for these arrays are shown in Figure 6, Figure 7 and Table 3 respectively. Compared with the prior UE array, the flood histograms of array PE/UE are much improved at the edge in the direction of the first cut. But the two edge columns of the array still cannot be clearly resolved. Compared with arrays UT and UT/PT, the flood histogram from array PT is improved with respect to crystal identification at the edges. To demonstrate the improvement of the flood histograms with the changes in crystal surface more clearly, Figure 8 shows the flood histograms measured at depths of 2, 10 and 18 mm (with respect to the narrow end of the array) for the three different arrays that use the Toray reflector. The flood histograms obtained at an irradiation depth of 2 mm are always the poorest, while those obtained at 10 mm are the best. Visual inspection clearly shows that the flood histograms improve (better crystal separation and identification) as more of the crystal sides are polished. However, the dynamic range of the DOI ratio is reduced with more polished faces (see Figures 5 and 7). The DOI resolution of the new arrays is therefore worse than the old arrays (see Table 3). For array PT, all crystals can be clearly resolved from the flood histogram at different depths and the DOI resolution for events >350 keV is 2.6 mm.

Figures 9 and 10 show the energy spectra for one edge crystal and one center crystal measured in coincidence mode for the five different irradiation depths for arrays PE/UE and PT respectively. They also show the energy spectra acquired in singles mode with no depth selection (whole crystal irradiated). For array PE/UE, the dependence of the photopeak amplitude on depth is small. A good energy resolution of 15–20% is therefore obtained for the individual crystals in this array when irradiated at all depths. For array PT/PT, the dependence of the photopeak amplitude on depth is significant. While a photopeak can be seen when the whole crystal is irradiated, there is a longer tail on the photopeak and energy resolution is difficult to determine. We have previously shown for imaging of a mouse-sized object with a small animal PET scanner, a wide open energy window is preferred to obtain a higher noise equivalent count rate (Yang *et al.*, 2004). So energy resolution is less important for detectors in a small animal PET scanner as compared with a clinical PET scanner.

Figure 11 looks in detail at the DOI responses of arrays PE/UE and PT. It shows the peak value of the DOI ratio at five different depths for a corner, edge, and center crystal, as well as the average over all crystals. The edge and center crystals have a slightly different DOI response with depth, while the center crystal is quite similar to the average response. The DOI ratio is not exactly linear change with depth of interaction, but a linear fit is a good approximation. It therefore appears likely that the simple linear detector and crystal DOI calibration method developed for regular cuboid arrays in our previous work (Yang *et al.*, 2009) can also be used for the tapered arrays. More complicated non-linear DOI calibration methods, such as the one proposed in (Shao *et al.*, 2008), will also be tested in the future.

In addition to the arrays described here, two further 13×13 arrays were tested (data not shown). One used polished faces with Toray reflector in the direction of the first cut and ESR reflector in the direction of the second cut. This had very similar performance to array PE/UE and was not pursued further. The second used Toray reflector on all faces, but two of the faces (first cut direction) were semi-polished – intermediate between polished and unpolished. This showed no significant improvement over array PT, and due to the difficulty of exactly defining the semi-polished finish was not pursued further.

3.3 Intrinsic spatial resolution and efficiency of tapered array vs. cuboid array

Figure 12 shows the intrinsic spatial resolution profiles averaged over the 13 crystals in the middle column of the arrays for both tapered and cuboid arrays. The tails on both sides of the curves are mainly contributed by detector scattering events. The FWHM resolution of the tapered and cuboid arrays are measured to be 0.75 mm and 0.67 mm respectively. The degradation in the intrinsic spatial resolution of the tapered array compared to the cuboid array is 11%. The crystal size at the front of the tapered array (0.514 mm) is about 3% bigger than crystal size of the cuboid array (0.5 mm). Therefore, a component of the degradation in resolution is due to the slight mismatch in crystal size at the front face of the arrays. It was also shown that the resolution did not depend much on energy window. For the cuboid array the intrinsic spatial resolution is 0.67 mm with no energy cut, and 0.68 mm for events with energy greater than 350 keV. The intrinsic spatial resolution of the 13 individual crystals were also obtained for both arrays. For the tapered array, the resolutions ranged from 0.71 mm to 0.80 mm. For the cuboid array, the resolutions ranged from 0.62 mm to 0.69 mm. The measured singles efficiency of the tapered array is 1.41 higher than the cuboid array. The volume of LSO material in the tapered array is 1.47 times greater than that in the cuboid array. The increase of the efficiency is quite close to the increase in the LSO material. This is reasonable given the geometry of the additional material in the tapered arrays that will significantly increase the number of photons that interact, as well as the increased likelihood of capturing Compton-scattered photons within the larger detector volume.

4. Discussion and Conclusions

Tapered scintillator arrays can be used in small animal PET scanners to reduce the gaps between detector modules so as to increase the sensitivity of the scanner. Because silicon-based photodetectors such as APDs or silicon photomultipliers can be manufactured in arbitrary shapes and sizes, dual-ended readout of such tapered arrays to provide depth-encoding information is also feasible, despite the different surface areas at the two ends of the array. Monte Carlo simulations showed that by using tapered LSO arrays the sensitivity of a scanner can be increased by 60% with only very small sacrifices in the spatial resolution (St James *et al.*, 2010). The detector-level spatial resolution and efficiency results measured experimentally in this paper are consistent with the Monte Carlo predictions.

The production challenges unique to manufacturing tapered arrays are that cutting of the crystal slices becomes more difficult, assembling of the stack requires special, more complex tooling, and if polishing of the non parallel lateral faces is desired, equipment modifications are required. There is also an impact to material yield due to the fact that each slice is unique, and any loss of a single slice results in the entire stack being rendered useless. It is estimated that the yield from this approach would be approximately 20% less than the yield from a similar sized cuboid array.

Maximizing signal-to-noise (high light output scintillators, good light collection efficiency, high quantum efficiency photodetector, low noise photodetector and electronics) is important in obtaining good DOI resolution and high-quality flood histograms. In addition, good DOI resolution requires a strong gradient in light collection efficiency with depth, however this implies a loss of scintillation light and therefore a degradation in the quality of the flood histogram.

As shown in this work, for arrays with larger crystals, the crystals are readily identified in the flood histograms and surface treatment and reflectors can be optimized for DOI performance. For 20 mm thick tapered arrays with $0.885 \times 0.885 \text{ mm}^2$ elements at the front face, the UT array gave the best DOI resolution of 2.1 mm for an energy threshold of 350

keV. For tapered arrays with smaller element sizes ($0.514 \times 0.514 \text{ mm}^2$ at the front face), optimization of the reflector and crystal surface are required to find the best compromise between the DOI resolution and the quality of the flood histogram. Although the UT array gave excellent DOI resolution (1.7 mm for events $> 350 \text{ keV}$), the flood histogram was not sufficiently good to clearly resolve all the crystals. Of the two 2nd generation arrays presented, the PT array provided the best flood histograms and a highly acceptable DOI resolution of 2.6 mm. This was a surprising result given that earlier studies on larger crystals (Yang *et al.*, 2006) had shown that very little DOI information could be obtained using highly polished crystals and ESR reflector. However, the aspect ratio in this study is so high and Toray reflector is used, that there is a sufficient gradient in light collection at the two ends for polished surfaces to provide good DOI resolution, and this also ensures relatively high light collection efficiency at all depths to provide high quality flood histograms. We therefore propose to pursue tapered PT arrays for development of a high resolution, high sensitivity animal PET scanner.

It should be noted that the evaluation of these tapered arrays was performed with readout from an $8 \times 8 \text{ mm}^2$ and a $14 \times 14 \text{ mm}^2$ PSAPD. Rectangular PSAPDs of $\sim 8 \times 13 \text{ mm}^2$ will be required at the far end if a small animal PET scanner is built with LSO arrays of the same dimension as in this paper. However, as these rectangular PSAPDs would be smaller in area, and therefore have a reduced capacitance, it is expected that the results would be even better with such PSAPDs when they become available.

Tapered arrays use more scintillator material as compared with cuboid arrays of the same front face size. This extra material also could be used to construct arrays with longer crystals or to slightly extend the axial length of the scanner. A detailed Monte Carlo simulation is required to compare the sensitivity gain of different approaches, and the answer also depends on the axial field of view of the scanner relative to the axial dimension of the organ/animal of interest. Each approach has drawbacks. For example, thicker crystals will produce relatively little gain in sensitivity beyond the 20 mm depth used here, and it will become increasingly difficult to resolve the individual crystals in the flood histograms. Extension of the axial field of view requires more photodetectors and more channels of electronics and may not be the most cost-effective approach to increasing sensitivity. The tapered arrays presented here are slightly more expensive to make than cuboid arrays and also have a little more raw material waste during array fabrication.

In summary, high spatial resolution, high sensitivity tapered LSO arrays with dual-ended PSAPD readout for depth encoding were fabricated and evaluated. The effects of crystal surface treatment and reflector on flood histograms and DOI resolution were studied. With the Toray reflector and polished faces, all crystals in a tapered LSO array with crystal size of 0.5 mm at the small end can be clearly resolved and an excellent DOI resolution of 2.6 mm is still obtained. The intrinsic spatial resolution only degrades from 0.67 mm FWHM for a cuboid array to 0.75 mm FWHM for a tapered array with similar (0.5 mm) crystal size at the front surface. Thus the tapered geometry does not lead to major losses in spatial resolution despite the increasing cross-section of the crystals with depth. The increase in the efficiency for the tapered array is highly significant (41%) and is close to the increase in the volume of LSO material. This would lead to major sensitivity gains if such detectors were operated in coincidence in a scanner as previously predicted via monte-carlo simulations. We therefore conclude that 20 mm thick tapered LSO arrays with small crystals and excellent DOI encoding achieved by dual-ended readout can potentially be used in a small animal PET scanner to simultaneously achieve very high sensitivity and spatial resolution.

Acknowledgments

This work was funded by NIH grants R01 EB006109 and R01 EB00993.

References

- Burr KC, Ivan A, Castleberry DE, LeBlanc JW, Shah KS, Farrell R. Evaluation of a prototype small animal PET detector with depth-of-interaction encoding. *IEEE Transactions on Nuclear Science*. 2004; 51:1791–8.
- Chatziioannou AF. Molecular imaging of small animals with dedicated PET tomographs. *European Journal of Nuclear Medicine*. 2002; 29:98–114. [PubMed: 11807613]
- Cherry SR. In vivo molecular and genomic imaging: new challenges for imaging physics. *Phys Med Biol*. 2004; 49:R13–R48. [PubMed: 15012005]
- Cherry SR. The 2006 Henry N. Wagner lecture: Of mice and men (and positrons) - Advances in PET imaging technology. *Journal of Nuclear Medicine*. 2006; 47:1735–45. [PubMed: 17079804]
- Dokhale PA, Silverman RW, Shah KS, Grazioso R, Farrell R, Glodo J, McClish MA, Entine G, Tran VH, Cherry SR. Performance measurements of a depth-encoding PET detector module based on position-sensitive avalanche photodiode read-out. *Phys Med Biol*. 2004; 49:4293–304. [PubMed: 15509066]
- Du HN, Yang YF, Glodo J, Wu YB, Shah K, Cherry SR. Continuous depth-of-interaction encoding using phosphor-coated scintillators. *Phys Med Biol*. 2009; 54:1757–71. [PubMed: 19258685]
- Janecek M, Moses WW. Optical Reflectance Measurements for Commonly Used Reflectors. *Ieee Transactions on Nuclear Science*. 2008; 55:2432–7.
- Judenhofer MS, Pichler BJ, Cherry SR. Evaluation of high performance data acquisition boards for simultaneous sampling of fast signals from PET detectors. *Phys Med Biol*. 2005; 50:29–44. [PubMed: 15715420]
- Larobina M, Brunetti A, Salvatore M. Small animal PET: A review of commercially available imaging systems. *Current Medical Imaging Reviews*. 2006; 2:187–92.
- Lecomte R, deKemp RA, Klein R, Cadorette J, Lepage MD, Robert G, Selivanov V, Belanger F, Semmaoui H, Tetrault MA, Viscogliosi N, Bergeron M, Lemieux F, Lemonde MA, Fontaine R. LabPETtm: A second-generation APD-based digital scanner for high-resolution small animal PET imaging. *Medical Physics*. 2006; 33:2671.
- Lerche CW, Benlloch JM, Sanchez F, Pavon N, Escat B, Gimenez EN, Fernandez M, Torres I, Gimenez M, Sebastia A, Martinez J. Depth of gamma-ray interaction within continuous crystals from the width of its scintillation light-distribution. *IEEE Transactions on Nuclear Science*. 2005; 52:560–72.
- Lewellen TK. Recent developments in PET detector technology. *Phys Med Biol*. 2008; 53:R287–R317. [PubMed: 18695301]
- Ling T, Lewellen TK, Miyaoka RS. Depth of interaction decoding of a continuous crystal detector module. *Phys Med Biol*. 2007; 52:2213–28. [PubMed: 17404465]
- Moses WW, Derenzo SE. Design studies for a PET detector module using a PIN photodiode to measure depth of interaction. *IEEE Transactions on Nuclear Science*. 1994; 41:1441–5.
- Muehllehner G, Karp JS. Positron emission tomography. *Phys Med Biol*. 2006; 51:R117–R37. [PubMed: 16790899]
- Rowland DJ, Cherry SR. Small-animal preclinical nuclear medicine instrumentation and methodology. *Semin Nucl Med*. 2008; 38:209–22. [PubMed: 18396180]
- Saoudi A, Pepin CM, Dion F, Bentourkia M, Lecomte R, Andreaco M, Casey M, Nutt R, Dautet H. Investigation of depth-of-interaction by pulse shape discrimination in multicrystal detectors read out by avalanche photodiodes. *IEEE Transactions on Nuclear Science*. 1999; 46:462–7.
- Schafers KP, Reader AJ, Kriens M, Knoess C, Schober O, Schafers M. Performance evaluation of the 32-module quadHIDAC small-animal PET scanner. *Journal of Nuclear Medicine*. 2005; 46:996–1004. [PubMed: 15937311]

- Schmand M, Eriksson L, Casey ME, Andreaco MS, Melcher C, Wienhard K, Flugge G, Nutt R. Performance results of a new DOI detector block for a High Resolution PET-LSO Research Tomograph HRRT. *IEEE Transactions on Nuclear Science*. 1998; 45:3000–6.
- Shah KS, Farrell R, Grazioso R, Harmon ES, Karplus E. Position-sensitive avalanche photodiodes for gamma-ray imaging. *IEEE Transactions on Nuclear Science*. 2002; 49:1687–92.
- Shah KS, Grazioso R, Farrell R, Glodo J, McClish M, Entine G, Dokhale P, Cherry SR. Position sensitive APDs for small animal PET imaging. *IEEE Transactions on Nuclear Science*. 2004; 51:91–5.
- Shao YP, Yao RT, Ma TY. A novel method to calibrate DOI function of a PET detector with a dual-ended-scintillator readout. *Medical Physics*. 2008; 35:5829–40. [PubMed: 19175139]
- St James S, Yang YF, Bowen SL, Qi JY, Cherry SR. Simulation study of spatial resolution and sensitivity for the tapered depth of interaction PET detectors for small animal imaging. *Phys Med Biol*. 2010; 55:N63–N74. [PubMed: 20023331]
- St James S, Yang YF, Wu YB, Farrell R, Dokhale P, Shah KS, Cherry SR. Experimental characterization and system simulations of depth of interaction PET detectors using 0.5 mm and 0.7 mm LSO arrays. *Phys Med Biol*. 2009; 54:4605–19. [PubMed: 19567945]
- Stickel JR, Qi JY, Cherry SR. Fabrication and characterization of a 0.5-mm lutetium oxyorthosilicate detector array for high-resolution PET applications. *Journal of Nuclear Medicine*. 2007; 48:115–21. [PubMed: 17204707]
- Tai YC, Chatziioannou AF, Yang YF, Silverman RW, Meadors K, Siegel S, Newport DF, Stickel JR, Cherry SR. MicroPET II: design, development and initial performance of an improved microPET scanner for small-animal imaging. *Phys Med Biol*. 2003; 48:1519–37. [PubMed: 12817935]
- Tai YC, Ruangma A, Rowland D, Siegel S, Newport DF, Chow PL, Laforest R. Performance evaluation of the microPET focus: A third-generation microPET scanner dedicated to animal imaging. *Journal of Nuclear Medicine*. 2005; 46:455–63. [PubMed: 15750159]
- Tsuda T, Murayama H, Kitamura K, Yamaya T, Yoshida E, Omura T, Kawai H, Inadama N, Orita N. A four-layer depth of interaction detector block for small animal PET. *IEEE Transactions on Nuclear Science*. 2004; 51:2537–42.
- Wang YC, Seidel J, Tsui BMW, Vaquero JJ, Pomper MG. Performance evaluation of the GE healthcare eXplore VISTA dual-ring small-animal PET scanner. *Journal of Nuclear Medicine*. 2006; 47:1891–900. [PubMed: 17079824]
- Yamaya T, Yoshida E, Toramatsu C, Nishimura M, Shimada Y, Inadama N, Shibuya K, Nishikido F, Murayama H. Preliminary study on potential of the jPET-D4 human brain scanner for small animal imaging. *Annals of Nuclear Medicine*. 2009; 23:183–90. [PubMed: 19225942]
- Yang Y, Tai YC, Siegel S, Newport DF, Bai B, Li QZ, Leahy RM, Cherry SR. Optimization and performance evaluation of the microPET II scanner for in vivo small-animal imaging. *Phys Med Biol*. 2004; 49:2527–45. [PubMed: 15272672]
- Yang YF, Dokhale PA, Silverman RW, Shah KS, McClish MA, Farrell R, Entine G, Cherry SR. Depth of interaction resolution measurements for a high resolution PET detector using position sensitive avalanche photodiodes. *Phys Med Biol*. 2006; 51:2131–42. [PubMed: 16625031]
- Yang YF, Qi JY, Wu YB, St James S, Farrell R, Dokhale PA, Shah KS, Cherry SR. Depth of interaction calibration for PET detectors with dual-ended readout by PSAPDs. *Phys Med Biol*. 2009; 54:433–45. [PubMed: 19098356]
- Yang YF, Wu YB, Qi J, James ST, Du HN, Dokhale PA, Shah KS, Farrell R, Cherry SR. A prototype PET scanner with DOI-encoding detectors. *Journal of Nuclear Medicine*. 2008; 49:1132–40. [PubMed: 18552140]

Figure 1.
Small animal PET scanners built with (left) traditional cuboid crystal arrays and (right) tapered arrays.

Figure 2.
Photo of a tapered array together with a cuboid array. The reflector in these two arrays is Toray lumirror E60 film.

Figure 3.
Experimental setup for intrinsic spatial resolution measurements.

Figure 4.

Flood histograms of the 6 tapered LSO arrays measured in singles mode for events with $E > 350$ keV. The horizontal and vertical directions are the tapered and parallel directions of the arrays, respectively.

Figure 5. Summed DOI responses of all crystals for the six arrays measured at five depths of 2, 6, 10, 14 and 18 mm for events with $E > 350$ keV. Lower DOI ratios correspond to irradiation locations closer to the narrow end of the array.

Figure 6. Flood histograms of the two new 13×13 tapered LSO arrays measured in singles mode for events with $E > 350$ keV.

Figure 7. Summed DOI responses over all crystals for the two new tapered arrays measured at five depths of 2, 6, 10, 14 and 18 mm for events with $E > 350$ keV.

Figure 8. Flood histograms of tapered LSO arrays (using Toray reflector and with different crystal surfaces) measured at three depths of 2, 10 and 18 mm for events with $E > 350$ keV.

Figure 9.

Energy spectra of a center crystal and an edge crystal from array PE/UE measured at five specific depths of 2, 6, 10, 14 and 18 mm (top) and the energy spectrum obtained when the whole crystal is irradiated (bottom).

Figure 10.

Energy spectra of a center crystal and an edge crystal from array PT measured at five specific depths of 2, 6, 10, 14 and 18 mm (top) and the energy spectrum obtained when the whole crystal is irradiated (bottom).

Figure 11.

Peak values of the distribution of DOI ratio at five irradiation depths (2, 6, 10, 14 and 18 mm) for three individual crystals and the average over all crystals.

Figure 12.
Intrinsic spatial resolution profiles for the tapered and cuboid LSO arrays.

Table 1

Element numbers and crystal sizes of the LSO arrays tested; the length of both arrays is 20 mm.

Elements	Dimensions (mm ²)	
	Small end	Large end
8 × 8	0.885 × 0.885	0.885 × 1.535
13 × 13	0.514 × 0.514	0.514 × 0.914

Crystal surface and inter-crystal reflector information for the tapered LSO arrays tested. The code to identify each array that is used throughout the rest of the text also is given.

Table 2

	First cut direction		Second cut direction		Code
	Surface	Reflector	Surface	Reflector	
1 st generation arrays	unpolished	ESR	unpolished	ESR	UE
	unpolished	Toray	unpolished	Toray	UT
	unpolished	Toray	polished	Toray	UT/PT
2 nd generation arrays	polished	ESR	unpolished	ESR	PE/UE
	polished	Toray	polished	Toray	PT

Table 3

DOI resolution (in mm) averaged over all depths obtained from the DOI response of individual crystals. The reproducibility of these measurements (same array measured twice) is less than ± 0.1 mm.

Array size	code	All events	E > 350 keV	E < 350 keV
8 × 8 (0.885 × 0.885 mm front face)	UE	2.5	2.2	3.3
	UT	2.3	2.1	2.8
	UT/PT	2.5	2.3	3.1
13 × 13 0.514 × 0.514 front face	UE	2.5	2.2	2.9
	UT	2.0	1.7	2.3
	UT/PT	2.5	2.2	2.9
	PE/UE	3.1	2.6	4.0
	PT	3.0	2.6	4.0