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Use of Cramer-Rao Lower Bound for Performance Evaluation of Different Monolithic Crystal PET Detector Designs

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Abstract

We have previously reported on continuous miniature crystal element (cMiCE) PET detectors that provide depth of interaction (DOI) positioning capability. A key component of the design is the use of a statistics-based positioning (SBP) method for 3D event positioning. The Cramer-Rao lower bound (CRLB) expresses limits on the estimate variances for a set of deterministic parameters. We examine the CRLB as a useful metric to evaluate the performance of our SBP algorithm and to quickly compare the best possible resolution when investigating new detector designs.

In this work, the CRLB is first reported based upon experimental results from a cMiCE detector using a $50 \times 50 \times 15$ -mm³ LYSO crystal readout by a 64-channel PMT (Hamamatsu H8500) on the exit surface of the crystal. The X/Y resolution is relatively close to the CRLB, while the DOI resolution is more than double the CRLB even after correcting for beam diameter and finite X (i.e., reference DOI position) resolution of the detector. The positioning performance of the cMiCE detector with the same design was also evaluated through simulation. Similar with the experimental results, the difference between the CRLB and measured spatial resolution is bigger in DOI direction than in X/Y direction.

Another simulation study was conducted to investigate what causes the difference between the measured spatial resolution and the CRLB. The cMiCE detector with novel sensor-on-entrance-surface (SES) design was modeled as a $49.2 \times 49.2 \times 15$ -mm³ LYSO crystal readout by a 12×12 array of 3.8×3.8 -mm² silicon photomultiplier (SiPM) elements with 4.1-mm center-to-center spacing on the entrance surface of the crystal. The results show that there are two main causes to account for the differences between the spatial resolution and the CRLB. First, Compton scatter in the crystal degrades the spatial resolution. The DOI resolution is degraded more than the X/Y resolution since small angle scatter is preferred. Second, our maximum likelihood (ML) clustering algorithm also has limitations when developing 3D look up tables during detector calibration.

Index Terms

Cramer-Rao lower bound (CRLB); Continuous miniature crystal element (cMiCE) PET detector; Statistics-based positioning (SBP); silicon photomultiplier (SiPM)

I. Introduction

Our group has previously reported on high resolution, continuous miniature crystal element (cMiCE) small animal PET detectors [1]–[4]. Comparing with discrete crystal PET detectors, cMiCE has a number of advantages that includes low cost, high packing fraction, continuous sampling and intrinsic depth of interaction (DOI) decoding capability. Accurate spatial positioning is a challenging task for monolithic crystal PET detectors. A key component of our design is the use of a 3D statistics based positioning (SBP) algorithm. The SBP algorithm requires detector light response function calibration followed by maximum likelihood (ML) based event positioning [1], [2]. In addition to our work there are a number of other laboratories investigating high resolution, monolithic crystal PET detector designs [5]–[8]. Besides the ML estimation method [1], [5], the neural network method [6] and the nearest neighbor method [8] are the other two commonly used positioning algorithms.

The Cramer-Rao lower bound (CRLB) expresses a theoretical lower bound on the variance of estimators for a deterministic parameter [9]–[11]. For our SBP algorithm, the CRLB can be used to investigate the best possible spatial resolution from the maximum likelihood (ML) estimator given the detector light response function. Since the CRLB only depends on the shape of the detector light response function, it could be used to evaluate the performance of our SBP algorithm. In addition, the CRLB can be used to serve as a quick guide when investigating new detector geometries.

The aims of this work are to evaluate the positioning performance of the SBP algorithm based on experimental data and to investigate what causes the difference between the measured spatial resolution and the CRLB through simulation.

II. Detector Design and Methods

A. Experimental setup

Figure 1 illustrates the cMiCE detector module used in our experiments [3]. A $50 \times 50 \times 15$ -mm³ LYSO crystal is coupled to Hamamatsu H8500 PMT on the exit surface. In order to achieve optimum positioning performance, the entrance surface of the crystal was painted white while the sides of the crystal were painted black to reduce reflections [12]. Normally incident 511-keV photon fluxes with 0.6-mm FWHM on the entrance surface were used to generate calibration data to build look up tables (LUTs) and to generate test data for X/Y resolution characterization. 45° incident beams with 0.85-mm FWHM on the entrance surface were used to test the DOI resolution. The difference between the estimated X position and entry X position were used as the reference DOI position when calculating the DOI resolution.

The test events were positioned using all 64 channels or a subset of channels (e.g., 21 or 37 out of 64 channels) determined by the maximum signal channel. The layout is shown in figure 2. When the centroid of the light response function approaches the edge of the crystal, we truncate these patterns of photodetectors and the number of channels chosen to acquire can be reduced. Using a subset of channels could speed up the event positioning process. How it affects the positioning resolution depends on the data statistics. For detector geometries where some photodetectors receive very little light, it could potentially improve the intrinsic spatial resolution by removing the channels dominated by noise.

B. Simulation setup

Simulation tools that we previously integrated [13] were modified to investigate the cMiCE detector performance [14]. GEANT [15] was used to track the gamma ray interactions (both photoelectric and Compton scatter) within the crystal. The non-proportionality of LYSO was

modeled according to the tables reported by Rooney [16], [17]. DETECT2000 [18], [19] was used to determine the probability that a light photon generated at a specific position in the crystal is detected by a specific photodetector channel. The SiPM characteristics were modeled based upon the device performance from FBK-irst. A comprehensive model presented in [20] was used to simulate the nonlinear response of SiPM. Table I summarizes the SiPM characteristic parameters used for this work. The SiPM array was modeled as a 12×12 array of 3.8×3.8 -mm² elements with 4.1-mm center-to-center spacing based upon currently available SiPMs [21]. Each SiPM element consists of 3080 microcells [21]. The photon detection efficiency (PDE) is 16% [22]. The 0.6 MHz/mm² dark count rate represents the dark count rate at 10°C [22]. Assuming the breakdown voltage variation between different channels is 0.3 V in FWHM [22], the corresponding PDE variation is 12% in FWHM [23] and the corresponding gain variation is 15% in FWHM [24]. The crosstalk probability and the after pulsing probability are 3% and 5% [25]. We assume the temperature remains constant during detector calibration and test data collection.

The positioning performance of the cMiCE detector module with the same configuration as in figure 1 was evaluated through simulation. Quantum efficiency (QE) of 22.5% was used to match the experimental setup. The X/Y/DOI resolution was characterized for normally incident test beams with 0.6-mm FWHM. True DOI positions were used to calculate DOI resolution. The aim is to compare the positioning performance of simulation study and experimental study.

Figure 3 shows the cMiCE detector module with novel sensor-on-entrance-surface (SES) design used in simulation [26], [27]. A 144-channel silicon photomultiplier (SiPM) array was placed on the entrance surface of a $49.2 \times 49.2 \times 15$ -mm³ LYSO crystal. The exit surface of the crystal was modeled as white paint with 0.98 reflection coefficient. The sides of the crystal were modeled as black paint with 0.10 reflection coefficient. Placing photodetectors on the entrance surface could improve the X/Y/DOI spatial resolution performance compared to placing photodetectors on the exit surface [26], [27]. This is because for the SES design the majority of the events occur in the front section of the crystal, where the light response function changes more rapidly and the derivative of the light response function effectively places a lower bound on intrinsic spatial resolution. Since PMTs are bulky and cause significant attenuation when placed on the entrance surface of the crystal, we use silicon photomultipliers (SiPM) as photodetectors for the SES design.

Normally incident beams with 0.6-mm FWHM were used for detector calibration. Since true DOI position is known for simulation data. The normally incident beams could be used to test both X/Y resolution and DOI resolution. In order to be consistent with experimental setup, 45° incident beams with 0.85-mm FWHM on the entrance surface were also used to test the DOI resolution. To calculate the DOI positioning error, the estimated DOI position was compared with both true DOI position and the difference between the estimated X position and the X entry position. This can tell us how much error is introduced by using the difference between the estimated X position and the X entry position as the reference DOI position.

C. Statistics-based positioning (SBP) algorithm

A statistics based positioning (SBP) algorithm is used to improve the detector positioning characteristics compared to standard or modified Anger positioning schemes [1]. For our SBP algorithm, the distributions of output signals $M = M_{i=1, \dots, n}$ for scintillation position $\theta = (x, y, z)$ are assumed to be independent, Gaussian distributions with mean, $\mu_{i=1, \dots, n}(\theta)$ and standard deviation $\sigma_{i=1, \dots, n}(\theta)$. The likelihood function for making any single observation $m = m_{i=1, \dots, n}$ from distribution M given position θ is:

$$L[m|\vec{\theta}] = \prod_{i=1}^n \frac{1}{\sigma_i(\vec{\theta}) \sqrt{2\pi}} \exp\left(-\frac{(m_i - \mu_i(\vec{\theta}))^2}{2\sigma_i^2(\vec{\theta})}\right) \quad (1)$$

The maximum likelihood estimator of $\vec{\theta}$ is given by:

$$\hat{\vec{\theta}} = \arg \min_{\vec{\theta}} \left[\sum_{i=1}^n \frac{(m_i - \mu_i(\vec{\theta}))^2}{2\sigma_i^2(\vec{\theta})} + \ln(\sigma_i(\vec{\theta})) \right] \quad (2)$$

To allow 3D positioning, a ML clustering method is used to extract DOI information during the light response function calibration of the detector module [2]. Two 3D look-up tables (LUTs) corresponding to the mean and standard deviation of the light response functions are created during calibration. We typically collected 20,000 events per (X,Y) position prior to filtering. After filtering, 5000–8000 events remained for each (X,Y) position. 700–1200 events were used to reliably generate the mean and standard deviation for each (X,Y,DOI) position. Fewer events remained after filtering at the corners of the crystal than near the center.

Figure 4 shows the flow chart of our ML clustering algorithm for DOI decoding [26]. The initial separation is based upon solid angle considerations. For interactions occurring close to the photodetectors more light is collected by the photodetector channel right below the interaction. Then the mean and standard deviation for each photodetector are generated for every spatial position and for each DOI group. The likelihood functions are calculated for each event being assigned to each DOI group. The regrouping by maximizing the likelihood functions after initial separation improves the DOI decoding performance. After a stable separation is reached, approximately the same number of events are assigned to each DOI group. This means the heights of the different DOI groups are different. 7-depth LUTs with 1.013-mm X/Y bins are generated from the separated data. Interpolation is done afterwards to generate LUTs with 0.254-mm X/Y bins. Finally, 15-depth LUTs are generated by applying a third-order polynomial fit to the 7-depth LUTs.

D. Data filtering

For best SBP positioning performance, the LUTs should be built from single photoelectric interaction events. However for 511-keV photons, most of the first interactions in LYSO crystals (i.e., about 61%) are Compton scatter. Therefore most photons will have interacted multiple times before they are photoelectrically absorbed. We developed a four-step technique to preferentially select single interaction photoelectric events for building LUTs.

In the first step, we set a 20% energy window around the photopeak to select events that deposit 511 keV in the crystal. This energy window was applied to both the calibration data and the test data.

Second, we used an ‘Anger contour mask’ to filter out events that have Compton scattered in the crystal before being photoelectrically absorbed. Examples of an ‘Anger contour mask’ are illustrated in figures 5(a,b). Events within the photopeak energy window are positioned using Anger positioning [28]. A contour mask, a certain percentage of the maximum pixel value, is then applied to the positioning histogram. Events falling outside the contour mask are thrown away since they are most likely multi-interaction events. The rationale for implementing the ‘Anger contour filter’ is that events that have had multiple interactions in the crystal will not be positioned at the point for first interaction and also that most single

interaction events will be positioned within our ‘Anger contour mask’. For this work, a 20% Anger contour mask was applied to the calibration data, which gives the optimum filtering performance based on simulation [29].

Third, 3D LUTs are built using the calibration data within the photopeak energy window with Anger contour filter applied. Then the calibration data within the photopeak energy window are positioned using the SBP algorithm.

Finally, a ‘SBP contour filter’ is applied to the calibration data within the photopeak energy window to further filter out multi-interaction events, as shown in figures 5(c,d). This SBP contour filter is based upon the same concept as the Anger contour filter, except that the positioning is done with our SBP algorithm instead of the Anger positioning algorithm. As seen in figure 5, the SBP contour mask performs better than the Anger contour mask especially at the edges of the crystal where Anger positioning is biased while the SBP algorithm is not. The Anger contour mask and the SBP contour mask are not applied to the test data. Therefore the test results include the effects of Compton scatter on positioning performance.

E. Cramer-Rao lower bound (CRLB)

The CRLB sets the lower bound on the variance of estimators for a deterministic parameter. For our SBP algorithm, the position $\vec{\theta}$ is an unknown deterministic parameter to be estimated from measurement m , distributed according to M . The lower bound for the variance of the estimated spatial position $\vec{\theta}$ could be calculated using Fisher information.

The Fisher information matrix for $\vec{\theta} = (x, y, z)$ is a 3×3 matrix

$$I(\vec{\theta}) = \begin{bmatrix} I_{xx} & I_{xy} & I_{xz} \\ I_{xy} & I_{yy} & I_{yz} \\ I_{xz} & I_{yz} & I_{zz} \end{bmatrix} \quad (3)$$

The matrix element $(I(\vec{\theta}))_{p,q}$ is defined as

$$\begin{aligned} (I(\vec{\theta}))_{p,q} &= -E \left[\frac{\partial^2}{\partial \theta_p \partial \theta_q} \ln(L(m|\vec{\theta})) \right] \\ &= \sum_{i=1}^n \left[\frac{1}{\sigma_i^2} \left(\frac{\partial \mu_i}{\partial \theta_p} \frac{\partial \mu_i}{\partial \theta_q} + 2 \frac{\partial \sigma_i}{\partial \theta_p} \frac{\partial \sigma_i}{\partial \theta_q} \right) \right] \end{aligned} \quad (4)$$

The variance of the spatial position is then bounded as

$$\begin{aligned} \text{var}(\hat{x}) &\geq \frac{1}{\det(I(\vec{\theta}))} (I_{yy}I_{zz} - I_{yz}^2) \\ \text{var}(\hat{y}) &\geq \frac{1}{\det(I(\vec{\theta}))} (I_{xx}I_{zz} - I_{xz}^2) \\ \text{var}(\hat{z}) &\geq \frac{1}{\det(I(\vec{\theta}))} (I_{xx}I_{yy} - I_{xy}^2) \end{aligned} \quad (5)$$

where $\det(I(\vec{\theta}))$ is the determinant of the matrix.

As seen from equation (4), the CRLB is determined by the standard deviation of the light response functions and how the standard deviation and mean of the light response functions changes with respect to spatial position.

III. Results

A. Experimental results for conventional cMiCE detector

Our SBP algorithm assumes that the output signals from different channels are independent. The correlation between different channels was tested. Figure 6 shows some examples of channel dependency. The scatter plots display the correlation between channels with maximum signals for filtered events happening at one calibration position assigned to one DOI group. The absolute value of the correlation coefficient for all calibration positions and all DOI groups is 0.11 ± 0.07 for channels within the 21-channel mask. As seen, there is a slight correlation between channels; however, it is not very significant.

Another assumption for our SBP algorithm is that the light response function follows a Gaussian distribution. Figure 7 shows examples of the light response function with a Gaussian fit. As seen in figure 7(a), the light response function follows a Gaussian distribution well for all seven depths for peak channel (channel 20). The root mean square errors (RMSE) for the Gaussian fit are small. Figure 7(b) shows the light response function for the sixth depth for channel 22, which is 2 channels away from the peak channel. The light response function still follows a Gaussian distribution. The RMSE is still only 5.40. Figure 7(c) shows the light response function for channel 15, which is 3.16 channels away from peak channel. The light response function begins to deviate from a Gaussian distribution. The RMSE is 10.64.

Figure 8 shows the X/Y spatial resolution performance for test events covering half of the crystal with 2.026-mm spacing in X/Y to within 2.7 mm of the crystal edge. A 37-channel mask was applied for SBP positioning and CRLB calculation. Figure 8(a) shows the 2D FWHM contour plots that illustrate the X/Y resolution. To plot out the contour curves, 2D histograms of X/Y positioning results at different fixed test positions were calculated. The FWHM contour curves were plotted at 50% of the peak values of the histograms for each test position. The top row corresponds to the edge of the crystal, while the bottom row corresponds to the center of the crystal. The red dots in the center of the contour plots represent the incident positions of the test beams. As seen, there is almost no bias for (X,Y) positioning. Figures 8(b,c) show the comparison for the measured X/Y resolution and X/Y CRLB for row AB respectively. The degradation of X resolution at the crystal edges is due to the lack of information in that region. The detector light response function is truncated close to the edges of the crystal. The positioning performance within 2.7 mm of the crystal edge is not characterized due to poor positioning performance. The SBP resolution in X is better than CRLB for the two test positions close to the crystal's edges because the test events positioned to within 2 mm of the crystal's edge are masked off and not included in the positioning profile.

Table II summarizes the average X/Y/DOI resolution and the CRLB using all 64 channels for positioning and also when using a subset of channels (e.g., 37 and 21) for positioning. The spatial resolution was characterized by measuring the FWHM directly at each test beam position (X,Y). The CRLB was calculated from the LUTs at each (X,Y,DOI) position. To be consistent with the spatial resolution, the CRLB for each (X,Y) position was generated from the CRLB for each (X,Y,DOI) position. Assuming that the positioning error profiles for each (X,Y,DOI) position follow a Gaussian distribution and the same number of events are assigned to each DOI, the positioning error profile for each (X,Y) could be generated by combining the positioning error profiles for different DOI positions. Then the CRLB for each (X,Y) position could be measured directly. The overall spatial resolution and the CRLB across the whole crystal was characterized by calculating the mean and the standard deviation over all (X,Y) positions. The standard deviation represents the uniformity of the spatial resolution and CRLB across the crystal. As seen, the X/Y resolution is relatively

close to the CRLB. The X/Y resolution and the CRLB become better when more channels are included for positioning. However, the DOI resolution is more than double the CRLB even after correcting for the beam diameter and finite X spatial resolution.

B. Simulation results for conventional cMiCE detector

Figure 9 illustrates the 2D FWHM contour plots with 1.52-mm spacing in X/Y to within 1.52 mm of the crystal edge for normally incident test beam with 0.6-mm FWHM. All 64 channels were used for positioning and CRLB calculation.

Table III summarizes the averaged spatial resolution performance for normally incident test beams and the CRLB using LUTs built using our ML clustering algorithm. The CRLB and the spatial resolution from the simulation study are better than the experimental results for the same conventional cMiCE detector configuration. However, similar with experimental data, the difference between the spatial resolution and the CRLB is larger for DOI than for the X/Y spatial resolution.

C. Simulation results for SES cMiCE detector

Figure 10 illustrates the 2D contour plots with 1.025-mm spacing in X/Y to within 2.05 mm of the crystal edge for normally incident test beam with 0.6-mm FWHM. All 144 channels were used for positioning and CRLB calculation.

Table IV summarizes the spatial resolution performance for normally incident test beams and the CRLB using LUTs built using our ML clustering algorithm. In addition, spatial resolution performance was determined for test data with and without Compton scatter. The CRLB and the spatial resolution from the simulation study are better than the experimental results. However, similar with experimental data, the difference between the spatial resolution and the CRLB is larger for DOI than for the X/Y spatial resolution. Excluding Compton scatter from the test data improves the X/Y resolution by 8% and the DOI resolution by 16%, respectively.

Figure 11 shows the histograms for X and DOI positioning errors for normally incident beam at one test position. As seen, the histograms do not follow Gaussian distributions, especially when Compton scatter is included in the test events. The Compton scatter not only broadens the FWHM resolution but also leads to a more pronounced tail. As expected, the Compton scatter events are positioned to the DOI group further from the photodetectors.

In order to study the DOI decoding performance of our ML clustering algorithm, true DOI positions are used for building 15-depth LUTs. The same SBP contour mask was applied to the calibration data. Table V lists the spatial resolution performance for normally incident beams and the CRLB for test data with and without Compton scatter. As seen, for test events with Compton scatter, the DOI resolution improves by 22% compared to the DOI resolution using LUTs built with our ML clustering algorithm (Table IV), while the X/Y resolution improves by 5%. When excluding Compton scatter and using true DOI positions for building LUTs, both X/Y resolution and DOI resolution are very close to the CRLB. Interestingly, the CRLB using the true DOI positions is worse than the CRLB using our ML clustering algorithm.

Figure 12 shows the representative depth separation results using our ML clustering algorithm and using true DOI positions. The two figures are similar, which means our ML clustering algorithm works well for depth separation. However, the ML clustering algorithm tends to group the events with the same amount of light collected by a certain photodetector channel to one DOI group.

In order to study the error induced by using the difference between the estimated X position and entry X position as the reference DOI position, 45° incident test beams were also used to characterize DOI resolution in simulation. The overall DOI resolution covering a central area of the crystal is 1.41 $\pm$ 0.11 when using the true DOI position as the reference DOI position, while it is 1.83 $\pm$ 0.14 mm when using the difference between the estimated X position and entry X position as the reference DOI position.

IV. Discussion

The use of CRLB is computationally attractive for analyzing the limiting performance of the detector. However, critical understanding on the limitation of the CRLB is needed in order to use it correctly [30], [31]. For the CRLB to accurately predict the lowest attainable detector resolution, it is required that (1) the detector light response function is free of systematic error, (2) ML or weighted least-square (WLS) estimators is used and (3) the inverse problem follows the linear Gaussian model. These requirements are not strictly met for the application in this paper.

The absolute value of the correlation coefficient is 0.11 $\pm$ 0.07 for PMT channels within a 21-channel mask, which means there is slight correlation between different channels. Several reasons could account for the correlation. First, the number of light photons generated in the LYSO crystal is not fixed even for fixed energy deposited. Second, the calibration beam for each (X,Y) position and each DOI group includes events happening in a range of (X,Y,Z) positions. Third, there are still remaining Compton scatters in the calibration data.

We did not calibrate the conversion gain of our photodetectors, so we are unable to determine the absolute number of photoelectrons on each PMT channel for experimental data. The simulation study for conventional cMiCE detector shows that 37 PMT channels generate more than 5 photoelectrons on average. As seen from figure 7, the experimental detector light response function well follows a Gaussian distribution for PMT channels with relatively big signals, e.g., channels within the 21-channel mask. However, for low-amplitude signals, the detector response function is asymmetric and may be better represented by a scaled Poisson blurred by electronic and amplification noise.

Therefore, our independent Gaussian model for detector light response function has systematic error. For 21-channel positioning, the systematic error is small and mainly comes from the channel dependency. For 64-channel positioning, the systematic error is bigger and comes from both channel dependency and non-Gaussian distribution of light response function for channels with small signals.

After the LUTs were built, the test events were positioned based upon ML estimator. However, restraints were applied at the edges of the crystal. As shown in figure 8, this leads to artificially good X resolution when close to the edge of the crystal.

As shown by figure 11, the X and DOI positioning error profiles do not follow Gaussian distribution, especially when there are Compton scatter events in the test data. Therefore, the inverse problem does not follow linear Gaussian model strictly.

Due to the limitations discussed above, the CRLB does not represent the spatial resolution of the detector. Characterizing the spatial resolution directly by positioning test beams is still required to report accurate intrinsic resolution of the detector. However, the CRLB is a useful metric to quickly compare the detector positioning performance when investigating different detector designs.

Compared to the experimental spatial resolution (Table II), the positioning performance from simulation data for the same cMiCE detector configuration is better. However, the difference between the CRLB and the measured resolution is similar. Therefore, the simulation study could be used to investigate the positioning performance of the cMiCE detector.

Based upon simulation study, the positioning performance of the SES detector is better than the conventional detector. The difference is caused by several reasons. First, based upon the simulation study in our group [26], [27], the X/Y resolution could be improved by 25% and the DOI resolution could be improved by 20% when comparing SES design and conventional design. Second, reducing photodetector size from $6.08 \times 6.08 \text{ mm}^2$ to $4.10 \times 4.1 \text{ mm}^2$ could improve the X/Y and DOI resolution by 24% and 17% respectively because of finer sampling of the light response function [27]. While going to more finely pixilated sampling may further improve intrinsic spatial resolution, we are not planning to use photodetectors smaller than $3 \times 3 \text{ mm}^2$ due to the large number of channels required for data acquisition. Third, the 0.16 PDE of SiPM is lower than the 0.225 QE of PMT, which degrades the positioning performance of SES detector. Therefore, the performance of the SES detector could be further improved if SiPM with higher PDE is used.

As seen from Tables II–IV, for test events with Compton scatter, the spatial resolution in X/Y is relatively close to the CRLB. The difference is 15–25%. However, the spatial resolution in DOI is more than double the CRLB for experimental data and more than 1.5 times the CRLB for simulation data. The difference between DOI resolution and CRLB is greater for experimental results than simulation results because the difference between the estimated X position and entry X position was used as a surrogate for DOI position. This caused 23% error for DOI resolution shown by simulation data. The two main reasons that could account for the difference between the spatial resolution and the CRLB both in X/Y and in DOI are Compton scatter in the crystal and our ML clustering algorithm.

Through simulation study, the spatial resolution for test events excluding Compton scatter was evaluated to investigate how Compton scatter affects positioning performance. As seen from Table IV, the X/Y and DOI resolution are improved by 8% and 16% respectively when excluding Compton scatter from the test data. Compton scatter affects the DOI resolution more than the X/Y resolution, since small angle scatter is preferred. Reducing Compton scatter in the test data by applying likelihood filtering [32] [33] could further improve the spatial resolution with some sacrifice in sensitivity.

Since the true DOI positions were known for simulation data, the LUTs were built with true DOI positions to study the DOI decoding performance of our ML clustering algorithm. For test events with Compton scatter, the X/Y and DOI resolution are improved by 5% and 22% when using LUTs built with true DOI positions (Table V) compared to the spatial resolution using LUTs built with our ML clustering algorithm (Table IV). This implies that our ML clustering algorithm has limitations. Calibrating the detector using beams incident from the sides of the crystal could improve the DOI resolution. However, it is impractical for a $50 \times 50 \times 15\text{-mm}^3$ crystal. As seen from Table IV, the spatial resolution for test data without Compton scatter is very close to the CRLB when using the true DOI positions to build the LUTs.

Another interesting point is that the CRLB was degraded when building LUTs with true DOI positions although the spatial resolution was improved, as shown in Table IV and Table V. One reason to account for this could be that the ML clustering tends to group the events with the same amount of light collected by a certain photodetector channel to one DOI

group, as shown in figure 11. This underestimates the variance in the LUT and led to an artificially good CRLB when using ML clustering algorithm for depth separation.

As seen from Table III and Table IV, both the spatial resolution and the CRLB are better for the SES detector than the conventional detector based upon simulation study. The CRLB could be used as a quickly computed surrogate metric to coarsely rank order the detector spatial resolution performance when investigating different detector designs.

V. Conclusion

In conclusion, the measured X/Y resolution is close to the calculated CRLB, while the calculated CRLB in DOI is over optimistic. The main reason for this is that calibration beams with fixed X/Y positions are used when building the LUTs, while the DOI positions are estimated using a ML clustering algorithm. Compton scatter also affects the DOI resolution more than X/Y resolution because small angle scatter is preferred. Finally, while there are discrepancies between the spatial resolution and the CRLB, we think that the CRLB can be used to rank order the spatial resolution performance of different detector geometries and could serve as a guide when investigating new detector geometries.

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References

1. Joung J, Miyaoka RS, Lewellen TK. cMiCE: a high resolution animal PET using continuous LSO with a statistics based positioning scheme. *Nucl Instrum Methods Phys Res A*. 2002; 489:584–598.
2. Ling T, Lewellen TK, Miyaoka RS. Depth of interaction decoding of a continuous crystal detector module. *Phys Med Biol*. 2007; 52:2213–2228. [PubMed: 17404465]
3. Miyaoka RS, Li X, Lockhart C, Lewellen TK. New continuous miniature crystal element (cMiCE) detector geometries. *IEEE Nucl Sci Symp Conf Rec*. 2009:3639–3642.
4. Miyaoka RS, Li X, Hunter WCJ, Pierce L, McDougald W, Kinahan PE, Lewellen TK. A prototype continuous miniature crystal element (cMiCE) scanner. *IEEE Nucl Sci Symp Conf Rec*. 2010:M14–193.
5. Hunter WCJ, Barrett HH, Furenlid LR. Calibration method of ML estimation of 3D interaction position in a thick gamma-ray detector. *IEEE Trans Nucl Sci*. 2009; 56(1):189–196. [PubMed: 20191099]
6. Bruyndonckx P, Lemaitre C, Schaart D, Maas M, van der Laan DJ, Krieguer M, Devroede O, Tavernier S. Towards a continuous crystal APD-based PET detector design. *Nucl Instrum Methods Phys Res A*. 2007; 571:182–186.
7. Foudray AMK, Habte F, Levin CS, Olcott PD. Positioning annihilation photon interactions in a thin LSO crystal sheet with a position-sensitive avalanche photodiode. *IEEE Trans Nucl Sci*. 2006; 53(5):2549–2556.
8. Maas MC, Schaart DR, van der Laan DJ, Bruyndonckx P, Lemaitre C, Beekman FJ, van Eijk CWE. Monolithic scintillator PET detectors with intrinsic depth-of-interaction correction. *Phys Med Biol*. 2009; 54:1893–1908. [PubMed: 19265203]
9. Joung J, Miyaoka RS, Lewellen TK. Implementation of ML based positioning algorithms for scintillation cameras. *IEEE Trans Nucl Sci*. 2000; 47(3):1104–11.
10. Milster TD, Selberg JA, Barrett HH, Landesman AL, Seacat RH III. Digital position estimation for the modular scintillation camera. *IEEE Trans Nucl Sci*. 1985; 32(1):748–52.
11. Rogers WL, Clinthorne NH, Shao L, Koral KF. Experimental evaluation of a modular scintillation camera for SPECT. *IEEE Trans Nucl Sci*. 1989; 36(1):1122–26.

12. Hunter, WCJ. PhD thesis, Section 7.5.2. University of Arizona; 2007. Modeling stochastic processes in gamma-ray imaging detectors and evaluation of a multi-anode PMT scintillation camera for use with maximum-likelihood estimation methods.
13. Ling, T. PhD thesis, Section 3.1. University of Washington; 2007. High resolution gamma detector for small-animal positron emission tomography.
14. Li X, Lockhart C, Lewellen TK, Miyaoka RS. Study of PET detector performance with varying SiPM parameters and readout schemes. To appear in IEEE Trans Nucl Sci. 2011; 58(3)
15. Agostinelli S, et al. GEANT4-a simulation toolkit. Nucl Instrum Methods Phys Res A. 2003; 506:250–303.
16. Rooney BD, Valentine ND. Scintillator light yield nonproportionality: Calculating photon response using measured electron response. IEEE Trans Nucl Sci. 1997; 44(3):509–516.
17. Valentine JD, Rooney BD, Li J. The light yield nonproportionality component of scintillator energy resolution. IEEE Trans Nucl Sci. 1998; 45(3):512–517.
18. Tsang G, Moisan C, Rogers JG. "A simulation to model position encoding multicrystal PET detectors,". IEEE Trans Nucl Sci. 1995; 42(6):2236–2243.
19. Knoll GF, Knoll TF, Henderson TM. "Light Collection in Scintillation Detector Composites for Neutron Detection,". IEEE Trans Nucl Sci. 1988; 35(1):872–875.
20. van Dam HT, Seifert S, Vinke R, Dendooven P, Lohner H, Beekman FJ, Schaart DR. A comprehensive model of the response of silicon photomultipliers. IEEE Trans Nucl Sci. 2010; 57(4):2254–2266.
21. Zorzi N, Melchiorri M, Piazza A, Piemonte C, Tarolli A. Development of large-area silicon photomultiplier detectors for PET applications at FBK. Nucl Instrum Methods Phys Res A. Article in press.
22. Piemonte, C. SiPM technology at FBK. 12th Topical Seminar on Innovative Particle and Radiation Detectors Conference Record; Siena. 2010.
23. Piemonte C, Boscardin M, Dalla Betta GF, Melchiorri M, Zorzi Z. Recent developments of SiPMs produced at FBK-irst. IEEE Nucl Sci Symp Conf Rec. 2007:2089–2092.
24. Guerra AD, Belcari N, Bisogni MG, LLosà G, Marcatili S, Ambrosi G, Corsi F, Marzocca C, Betta GD, Piemonte C. Advantages and pitfalls of the silicon photomultiplier (SiPM) as photodetector for the next generation of PET scanners. Nucl Instrum Methods Phys Res A. 2010; 617:223–226.
25. Piemonte C, Battiston R, Boscardin M, Dalla Betta G-F, Del Guerra A, Dinu N, Pozza A, Zorzi N. Characterization of the first prototypes of silicon photomultiplier fabricated at ITC-irst. IEEE Trans Nucl Sci. 2017; 54(1):236–244.
26. Li X, Lockhart C, Lewellen TK, Miyaoka RS. A high resolution, monolithic crystal, PET/MRI detector with DOI positioning capability. Proc Conf IEEE Eng Med Biol Soc. 2008:2287–2290.
27. Miyaoka RS, Li X, Lockhart C, Lewellen TK. Comparison of detector intrinsic spatial resolution characteristics for sensor on the entrance surface and conventional readout designs. IEEE Trans Nucl Sci. 2010; 57(3):990–997. [PubMed: 21614135]
28. Karp JS, Surti S, Daube-Witherspoon ME, Freifelder R, Cardi CA, Adam L-E, Bilger K, Muehllehner G. Performance of a brain PET camera based on Anger-logic gadolinium oxyorthosilicate detectors. J Nucl Med. 2003; 44:1340–1349. [PubMed: 12902426]
29. Ling, T. PhD thesis, Section 4.2.2. University of Washington; 2007. High resolution gamma detector for small-animal positron emission tomography.
30. Hero U, Usman M, Hero AO, Fessler JA. Uniform CR bound: implementation issues and applications. IEEE Nucl Sci Symp Conf Rec. 1994:1443–1447.
31. Chiao PC, Rogers WL, Clinthorne NH, Fessler JA, Hero AO. Model-based estimation for dynamic cardiac studies using ECT. IEEE Trans Med Imaging. 1994; 13(2):217–226. [PubMed: 18218498]
32. Hunter, WCJ. PhD thesis, Section 7.5.3. University of Arizona; 2007. Modeling stochastic processes in gamma-ray imaging detectors and evaluation of a multi-anode PMT scintillation camera for use with maximum-likelihood estimation methods.
33. Chen, Y. PhD thesis. University of Arizona; 2006. System calibration and image reconstruction for a new small-animal SPECT system.

Fig. 1. CMiCE detector module with conventional design used in experiment and simulation. DOI decoding is done based on the correlation between DOI and the light distribution among different PMT channels.

Fig. 2.

A mask around the central maximum channel is used to determine which channels to use for positioning. # means channel with maximum signal. * represents neighboring channels used for positioning. (a) 21 channel mask, the largest distance between neighboring channels and peak channel is 2.24 channels; (b) 37 channel mask, the largest distance between neighboring channels and peak channel is 3.16 channels.

Fig. 3.

CMiCE detector module with SES design used in simulation. Placing photodetectors on the entrance surface could improve the spatial resolution since most interactions occur in the front section of the crystal.

Fig. 4.

Flow chart for building 3D LUTs using maximum likelihood (ML) clustering algorithm. The DOI decoding is based upon the correlation between the light response function and DOI positions.

Fig. 5. Scatter plot of 20% 'contour mask' applied to calibration events for experimental data. The estimated (X,Y) positions using Anger algorithm are continuous. The estimated (X,Y) positions using SBP algorithm are discrete with 0.254-mm bin size. The black * corresponds to the center position of the incident beam at the entrance surface. (a) 'Anger contour mask' for the calibration position close to the center of the crystal; (b) 'Anger contour mask' for the calibration position at the corner of the crystal; (c) 'SBP contour mask' for the same center calibration position with (a); (d) 'SBP contour mask' for the same corner calibration position with (b).

Fig. 6.

Examples of channel correlation. (a) channel 20 (peak channel) vs. channel 21, correlation coefficient = 0.23; (b) channel 20 vs. channel 28, correlation coefficient = 0.14; (c) channel 20 vs. channel 29, correlation coefficient = 0.17; (d) channel 28 vs. channel 29, correlation coefficient = 0.15.

Fig. 7. Histograms of amount of light collected by representative PMT channels for one (X,Y) calibration position. ML clustering algorithm is used for depth separation. (a) Peak channel (channel 20) for all seven DOI groups. The RMSE for a Gaussian fit for groups 1 through 7 are: 2.70, 2.47, 2.68, 4.93, 3.42, 3.47, 5.32. (b) Channel 22 for group 6: The RMSE for a Gaussian fit is 5.40. (c) Channel 15 for group 4: The RMSE for a Gaussian fit is 10.64.

Fig. 8. X/Y resolution and CRLB for experimental data with a 37-channel mask: (a) FWHM contour plots for SBP positioning; (b) X resolution and CRLB for row AB; (c) Y resolution and CRLB for row AB.

Fig. 9. FWHM contour plots for SBP positioning for conventional cMiCE detector using simulation data.

Fig. 10. FWHM contour plots for SBP positioning for conventional cMiCE detector using simulation data. LUTs are built using ML clustering algorithm.

(a)

(b)

Fig. 11.

Representative X/DOI positioning error for simulation data. LUTs are built using ML clustering algorithm based upon calibration data after applying SBP contour mask. (a) X direction; (b) Z (DOI) direction.

Fig. 12. Histograms of amount of light collected by the peak channel for one calibration position for simulation data. (a) ML clustering algorithm is used for depth separation; (b) True DOI positions are used for depth separation.

Table I

SiPM performance parameters

Pixel size	$3.8 \times 3.8 \text{ mm}^2$
Number of microcells per SiPM channel	3080
Photon detection efficiency (PDE)	16%
Dark count rate	0.6 MHz/mm ²
PDE variation between different channels	12% FWHM
Gain variation between different channels	25% FWHM
Crosstalk probability	3%
After pulsing probability	5%

TABLE II

Experimental: Spatial resolution and CRLB using LUTs built with ML clustering algorithm for test data with Compton scatter.

Number of channels		64	37	21
X (mm)	Resolution	1.55+/-0.29	1.59+/-0.30	1.63+/-0.31
	CRLB	1.21+/-0.27	1.23+/-0.28	1.30+/-0.27
Y (mm)	Resolution	1.50+/-0.29	1.55+/-0.29	1.62+/-0.30
	CRLB	1.22+/-0.34	1.27+/-0.38	1.35+/-0.38
Z (mm)	Resolution	3.69+/-0.41	3.65+/-0.37	3.99+/-0.30
	Corrected resolution	3.29+/-0.45	3.25+/-0.41	3.59+/-0.33
	CRLB	1.46+/-0.11	1.58+/-0.13	1.68+/-0.09

TABLE III

Simulation, Conventional cMiCE detector: Spatial resolution and CRLB using LUTs built with ML clustering algorithm for test data with Compton scatter.

	Resolution	CRLB
X/Y (mm)	1.20+/-0.13	1.02+/-0.12
DOI (mm)	2.02+/-0.15	1.33+/-0.11

TABLE IV

Simulation, SES cMiCE detector: Spatial resolution and CRLB using LUTs built with ML clustering algorithm for test data with and without Compton scatter.

	Resolution (All events)	Resolution (PE events)	CRLB
X/Y (mm)	0.91+/-0.07	0.84+/-0.07	0.73+/-0.08
DOI (mm)	1.52+/-0.21	1.27+/-0.19	0.88+/-0.12

TABLE V

Simulation, SES cMiCE detector: Spatial resolution and CRLB using LUTs built with true DOI positions for test data with and without Compton scatter.

	Resolution (All events)	Resolution (PE events)	CRLB
X/Y (mm)	0.86+/-0.08	0.80+/-0.08	0.76+/-0.09
DOI (mm)	1.19+/-0.07	1.05+/-0.05	1.06+/-0.10