DOE Award Number: DE-FG02-08ER64676

Award Recipient: Robert Miyaoka, PhD

Title: A High Resolution Monolithic Crystal, DOI, MR Compatible, PET Detector

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Abstract:

The principle objective of this proposal is to develop a positron emission tomography (PET) detector with depth-of-interaction (DOI) positioning capability that will achieve state of the art spatial resolution and sensitivity performance for small animal PET imaging. When arranged in a ring or box detector geometry, the proposed detector module will support <1 mm^3 image resolution and >15% absolute detection efficiency. The detector will also be compatible with operation in a MR scanner to support simultaneous multi-modality imaging. The detector design will utilize a thick, monolithic crystal scintillator readout by a two-dimensional array of silicon photomultiplier (SiPM) devices using a novel sensor on the entrance surface (SES) design. Our hypothesis is that our single-ended readout SES design will provide an effective DOI positioning performance equivalent to more expensive dual-ended readout techniques and at a significantly lower cost. Our monolithic crystal design will also lead to a significantly lower cost system. It is our goal to design a detector with state of the art performance but at a price point that is affordable so the technology can be disseminated to many laboratories. A second hypothesis is that using SiPM arrays, the detector will be able to operate in a MR scanner without any degradation in performance to support simultaneous PET/MR imaging. Having a co-registered MR image will assist in radiotracer localization and may also be used for partial volume corrections to improve radiotracer uptake quantitation. The far reaching goal of this research is to develop technology for medical research that will lead to improvements in human health care.

Executive Summary

This project focused on the development of a positron emission detector that can provide three dimensional positioning within the detector. A novel aspect of the design was the placement of photosensors on the entrance surface of the crystal detector versus conventional placement of the back surface of the detector. Our hypothesis was that using the sensor on the entrance surface (SES) design, our detector would provide better X, Y and Z positioning localization in the detector than using conventional bad sided readout. To facilitate our design, we needed to use two-dimensional arrays of silicon photomultipler (SiPM) devices. SiPMs are an emerging technology being looked at as a possible replacement for photomultiplier tubes. SiPMs are solid state devices made using CMOS processing techniques that are very low attenuating for the photons produced in positron emission tomography. Because of their low attenuation characteristic they can be placed on the front surface of a detector without affecting the incoming flux of photons. In addition to their low attenuation characteristics, they also have electronic and amplification characteristics similar to bulkier photomultipliers the current photosensor utilized in most PET detectors. Thus this research adds to the knowledge of three-dimensional positioning detectors for PET and also how best to use SiPM technology.

One of the exciting aspects of the design is that it has the potential to improve performance without adding cost to the detector. Our preliminary investigations indicated that a 20-25% improvement in positioning resolution could be achieved by just changing the location of the readout sensors. To get similar three-dimensional positioning performance other researchers have proposed methods that double the cost of sensors and readout electronics. In regards to SiPMs, they have the potential to be very economically priced. Current device are made in low quantities; however, the basic fabrication process is similar to CMOS processing and should be very economical as production scales increase. Thus we believe the technology we are proposing should be economical enough to be a practical design alternative for future high resolution PET detector systems.

While this project is mainly focused on a new PET detector design, it can potentially have far reaching benefits to the public as PET has emerged as a very important medical imaging technology. PET is already improving health care in oncology, cardiology and neurology. Improvements to PET instrumentation can lead to even better diagnosis and also potentially broader access to the public.

Report on Accomplishment of Specific Aims

There were three specific aims proposed in this research project. They are listed below.

Specific Aim 1 – Investigate via computer simulation the intrinsic spatial resolution in X, Y and Z of a detector utilizing of a thick, monolithic crystal coupled to a 2-D array of SiPM devices.

Specific Aim 2 – Develop prototype detector electronics including FPGA implementation to support real time processing of event data.

Specific Aim 3 – Measure the performance characteristics (i.e., intrinsic 3-D spatial resolution, energy resolution, timing resolution and detection efficiency) of a detector utilizing of a thick, monolithic crystal coupled to a 2-D array of micro-pixel avalanche photodiode (MAPD) devices.

Summary:

Specific aim 1 was fully completed during the course of the project. Computer simulation was used to investigate the intrinsic spatial resolution in X, Y and Z of a detector utilizing a thick, monolithic crystal coupled to a 2-D array of SiPM devices. Simulations were used to investigate the effects of different SiPM parameters on detector readout performance (J2 and CR3, as listed below). In addition, a detailed study of the detector spatial resolution performance was conducting using the Cramer Rao lower bound (J3 and CR6). Finally, this funding helped support the development of another simulation resource tools (CR8) and also the investigation of multi-hit parameter estimation techniques to improve spatial imaging performance (CR11).

Specific aim 2 was mostly completed during the course of the project. There was effort to develop frontend detector electronics including investigations into ASIC solutions (CR5 and CR10). Further, the development of a FireWire-based data acquisition board was partially funded through this project (CR12). All of the hardware components of the board are functional; however, some of the control software still needs to be written. There was significant development of FPGA code to support real-time processing of data. This included implementation of a three-dimensional statistical-based positioning algorithm in an FPGA (J1 and CR2) and signal processing techniques including methods to correct for pulse-pileup in the FPGA (CR9).

Specific aim 3 was completed during the course of the project. We believe that the detector module can be better optimized but the initial results indicate that the SES approach improves intrinsic spatial resolution performance by 14% over conventional back-sided readout (CR15). A highlight of this work was demonstrating that 1.33 mm intrinsic spatial resolution was achievable using a 15 mm thick monolithic crystal using our SES detector design. This 1.33 mm intrinsic spatial resolution should support 1 mm image resolution. Further in addition to providing 14% better intrinsic spatial resolution than conventional readout the useful imaging area was better for the SES design than the back-sided readout method. During the course of the experimental testing we also did a study of the SiPM temperature dependence and how it affected the readout signals.

Project Summary

SES cMiCE PET detector (simulation results, specific aim 1).

The initial efforts in this project were simulation based. We had previously developed a number of simulation tools for investigating monolithic crystal decoding performance for PMT-based detectors. Comparing the intrinsic spatial resolution performance between SES and conventional readout detector modules in simulation, the SES detectors provided about 25% better spatial resolution in X and Y and about 20% better positioning performance in Z (i.e., DOI). These initial simulations encouraged us to further pursue the SES detector concept and helped lead to DOE grant funding.

While SiPM devices have similar gain to PMTs they also have more background dark current signal as part of their operation. They are also much more temperature sensitive than PMTs. Therefore we did a thorough investigation of our SES detector's decoding performance while varying SiPM parameters. The main parameters that we varied were variable gain between SiPM macro-cell channels, dark current (as a function of temperature), after pulsing of the SiPM micro-cells, cross-talk between micro-cells, photon detection efficiency (PDE), and gain shifts in SiPM due to temperature changes between calibration and data collection. While PDE has the largest impact on performance, it is a device characteristic and not that sensitive to temperature. Of the parameters that are sensitive to temperature dark count noise and gain shifts had the largest impact on performance. Based upon these results, we will develop techniques to both control and monitor the temperature of the SiPM devices. Further, we plan to cool the devices down below room temperature when operating to reduce the dark count rate, as we know that higher dark count rates will affect both event positioning and timing performance.

In addition to studying how SiPM parameters affect positioning performance, we did a detailed investigation on the effectiveness of our statistics-based positioning method and detector characterization process using the Cramer-Rao lower bound. The results of the study were that our positioning method was nearly efficient in X and Y positioning but much poorer in DOI (or Z) positioning. The main reason for the poorer DOI positioning was due to Compton scattering in the detector. A secondary reason was inaccuracies in our depth characterization of the detector and we are currently investigating methods to improve this.

Finally we did a simulation study using measured intrinsic detector response functions to investigate image-based figures of merit for small animal PET systems. We simulated two systems using conventional detector readout and one system using SES readout. For the first conventional detector system we used an 8 mm thick crystal detector (representing high spatial resolution). For the second conventional detector system we used a 15 mm thick crystal detector (representing high sensitivity). For the SES detector system we use a 15 mm thick crystal detector (representing both high detection efficiency and high spatial resolution). The results of the study were that the SES detector provided the best overall performance. It provided similar quantitative imaging performance as the 8mm thick conventional readout detector and better quantitative imaging performance than the 15 mm thick conventional detector system, as quantitative imaging performance is largely driven by spatial resolution. It also provided similar detection performance as the 15 mm thick conventional readout detector and better detection performance than the 8 mm thick conventional detector, as detection performance is driven by sensitivity.

<u>SES cMiCE PET detector electronics (data acquisition electronics, specific aim 2).</u>

We initially started out using SensL SiPM devices and their front end electronics; however, the devices had problems with cross-talk between the SiPM macro-cells due to routing of the power and output signal lines. We also did some initial investigation with a Zecotek 2-D SiPM array; however, that device also had less than optimum characteristics (i.e., >10 gain variability between SiPM macro-cells). During the progress of this grant we obtained funding to work with Philips Medical Systems to further develop the SES detector concept with the goal of building a complete scanner with SES detectors. Through our association with Philips we got access to 2-D SiPM arrays, as pictured in Figure 1, and began working with those devices. After we received the 2D-SiPM arrays we worked with a local company to develop a flex cable connector that allows us to route the SiPM signal to our electronics boards when using the SES design. An SiPM array with flex cables attached is pictured in Figure 2. In addition to the 2-D SiPM arrays we also obtained frontend detector electronics and a data acquisition system to collect signals from the 2D arrays. While the data acquisition system is rather bulky, it has much higher bandwidth than the VME acquisition system that we also have in our laboratory. Therefore we used the SiPM arrays and data acquisition system from Philips Medical Systems for the initial evaluation of our SES detector design.

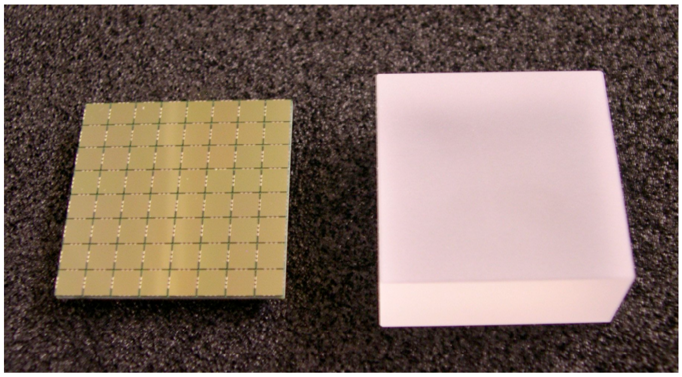

Figure 1. Photograph of an 8x8 SiPM array next to a 32.55 mm by 32.55 mm by 15 mm LYSO crystal.

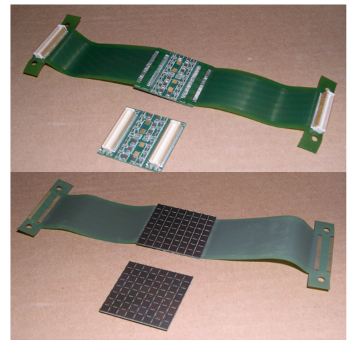

Figure 2. Pictures of 2D SiPM arrays from Philips with and without flex circuit cable assembly.

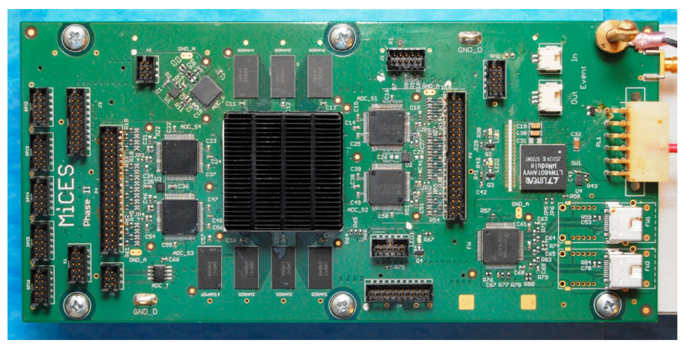

Figure 3. Photograph of UW data acquisition electronics board to support the SES cMiCE detector design.

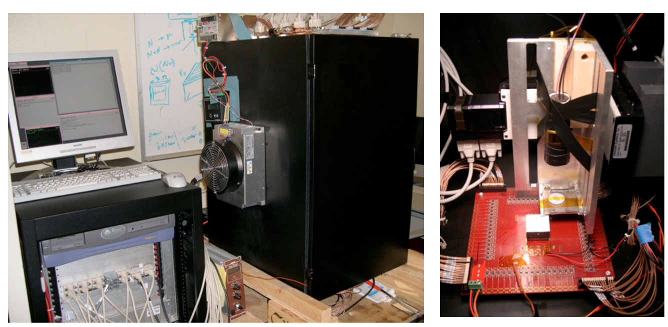

Figure 4. Picture of temperature controlled light tight box, data acquisition computer, and detector setup for SES cMiCE testing. Bottom right: SES detector assembly with tile mounted on entrance surface.

In addition to the electronics and data acquisition system described above we also continued to develop more compact data acquisition boards customized to the needs of our detector design. A photograph of the board we developed is shown in Figure 3. The board has a large FPGA on it and supports data acquisition of 65 signal channels. It can digitize up to 64 channels at 65M samples per second and one channel at 300M samples per second. It communicates to an acquisition computer via FireWire. Using the FireWire protocol allows up to 63 of these boards to be daisy chained together with adequate bandwidth to support a full imaging system. In addition to the electronics board development, there was significant development of FPGA programs to allow for local, real-time processing of events within the onboard FPGA. We implemented real-time three-dimensional statistics-based processing of our SES detector within the FPGA. To support this we also added over 440 Mbytes of RAM to the board.

We also investigated ASIC development for amplifying the SiPM signals. While ASIC development is beyond the scope of this project, some investigative work regarding the requirements for an ASIC to support an SES detector was conducted.

SES cMiCE PET Detector Module Performance Measurements (specific aim 3).

Using the experimental setup pictured in Figure 4, we have fully characterized X, Y intrinsic positioning performance for monolithic crystal PET detectors with a 32 mm by 32 mm by 15 mm LYSO crystal coupled to an 8x8 SiPM array. We measured the positioning performance for both an SES detector module and one using conventional photosensor readout. The results of the experimental testing are summarized in Figure 5 and Table 1. In Figure 5, we also show contours illustrating the full width at half maximum of the intrinsic spatial resolution positioning performance at different locations of the monolithic PET detector modules. One can visually see that the contours are smaller (i.e., have small diameters) for the SES detector. Each red dot in the contour images represents a test location. The red dots are separated by 2mm. While testing was done at 1 mm steps across the face of the detector, for visual clarity contour results are only shown with 2mm spacing. The second column of images in Figure 5 pictorially illustrates the intrinsic spatial resolution at each test location. The color bar at the top of the column shows what spatial resolution each color represents. As can be seen the SES detector has much more blue and bluish-green points that represent better positioning performance.

Table 1. Average intrinsic spatial resolution and coincidence timing resolution for SES and conventional PET detector modules.

	Avg. Position FWHM [mm]	Avg. Position Bias [mm]	Avg. Coinc.Timing FWHM (ns)
Conventional	1.54	0.251	1.13
SES	1.33	0.248	1.02

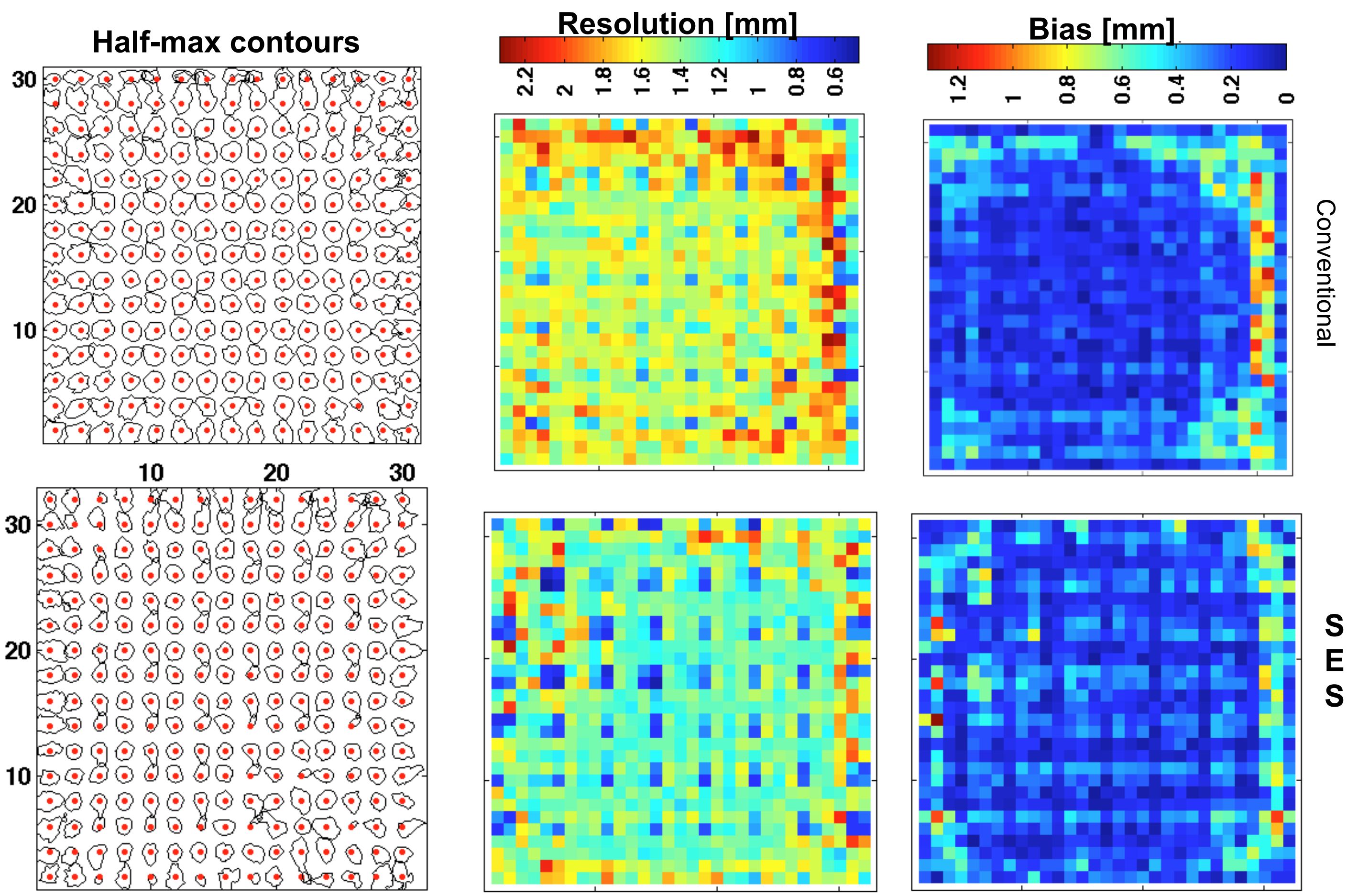

Figure 5. SBP-positioning results for Conventional (top) and SES (bottom) readouts. Shown are: (LEFT) half-max contours of the SBP-estimate distributions for event for an array of beam positions (2-mm spacing). (CENTER) Geometric average Half-max contour widths at each test position on a 1-mm grid (average FWHM) over array. (RIGHT) Ensemble bias of SBP positioning.

Likewise in the third column, images are provided to illustrate positioning bias in the detector. Average positioning bias was approximately 0.25 mm for both the SES and conventional PET detector, so both methods resulted in low positioning bias which is what we expected from the fact that we are using an unbiased positioning estimator. In summary, the SES detector provided 14% better intrinsic spatial resolution positioning performance than the conventional detector design. Again, this improved performance does not require any extra electronics processing than what is required by the conventional detector design.

One of the reasons that the positioning performance for the SES detector does not look as good in the upper left hand region of the detector is that we lost the signal from one of the SiPM channels when we attached the flex circuit connector onto the board. Also in the upper section of the map just right of center the resolution is slightly poorer. Again this is related to degraded signal fidelity due to two SiPM channels being shorted together during the attachment of the flex connector. Therefore our expectation is that the SES PET detector will perform even better than the results provided. It is worthwhile to note that we worked with a vendor to attach the flex circuits onto our SiPM arrays. The pin spacing for the connector was very tight as the SiPM board was designed to have a high density connector attached to it. We had flex cables attached to another SiPM array and from preliminary measurements it looked that the procedure was more successful; however, we were not able to characterize a SES PET detector module with the new array before this grant ended. In future work we plan to design a rigid-flex circuit solution to replace the workaround to get this preliminary data.

Final Summary

The SES cMiCE PET detector is a new design with the potential of providing very high intrinsic spatial resolution and excellent detection efficiency. An enabling technology is the development of tightly packed 2D SiPM arrays with suitable performance to achieve our design goals. During the course of this funding, we developed and characterized a prototype SES PET detector module and compared its decoding performance with a similar PET detector using conventional detector readout. We demonstrate that the SES design led to a 14% improvement in intrinsic spatial resolution performance and achieved an intrinsic spatial resolution of 1.33 mm FHWM for the SES detector. In addition, we developed a flex circuit solution to enable the SES design; and evaluated the impact that the SES design has on task based image figures of merit. Using the SES design approach, one can achieve both better quantitative imaging performance and also achieve better lesion detectability versus conventional detector designs.

Publications

- We had three peer reviewed paper accepted for publication.
  - J1. Johnson-Williams NG, Miyaoka RS, Li X, Lewellen TK, Hauck S. Design of a Real Time FPGA-based Three Dimensional Positioning Algorithm. *IEEE Trans. Nucl. Sci* vol. 58(1): pp. 26-33, February 2011.
  - J2. Li X, Lockhart C, Lewellen TK, Miyaoka RS. Study of PET Detector Performance with Varying SiPM Parameters and Readout Schemes. *IEEE Trans. Nucl. Sci* vol. 58(3): pp. 590-596, 2011.
  - J3. Li X, Hunter WCJ, Lewellen TK, Miyaoka RS. Use of Cramer-Rao Lower Bound for Performance Evaluation of Different Monolithic Crystal PET Detector Designs. *IEEE Trans. Nucl. Sci* vol. 59(1): pp. 3-12, February 2012.
- We had fifteen conference records.
  - CR1. Hunter WCJ, Miyaoka RS, MacDonald LR, Lewellen TK. Measured Temperature Dependence of Scintillation Camera Signals Read Out by Geiger–Müller Mode Avalanche Photodiodes. *2009 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Orlando, Florida. 2009 pp 2662-2665. PMID and PMCID in process.
  - CR2. Johnson-Williams NG, Miyaoka RS, Li X,Lewellen TK, Hauck S. Design of a Real Time FPGA-based Three Dimensional Positioning Algorithm. *2009 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Orlando, Florida. 2009 pp 3652-3659.
  - CR3. Li X, Lockhart C, Lewellen TK, Miyaoka RS. Impact on the Spatial Resolution Performance of a Monolithic Crystal PET Detector Due to Different Sensor Parameters. *2009 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Orlando, Florida. 2009 pp. 3102-3105.
  - CR4. Miyaoka RS, Li X, Lockhart C, Lewellen TK. New Continuous Miniature Crystal Element (cMiCE) Detector Geometries. *2009 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Orlando, Florida. 2009 pp 3639-3642. PMID1936292.
  - CR5. Shih YC, Sun FW, MacDonald LR, Otis BP, Miyaoka RS, McDougald W, Lewellen TK. An 8x8 Row-Column Summing Readout Electronics for Preclinical Positron Emission Tomography Scanners. *2009 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Orlando, Florida. 2009 pp 2976-2980. PMID and PMCID in process.
  - CR6. Li X, Hunter WCJ, Lewellen TK, Miyaoka RS. Spatial resolution performance evaluation of a monolithic crystal PET detector with Cramer-Rao lower bound (CRLB). *2010 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Knoxville, Tennessee, 2010.
  - CR7. Li X, Hunter WCJ, Lewellen TK, Miyaoka RS. Design of a trapezoidal slat crystal (TSC) PET detector for small animal PET/MR imaging. *2010 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Knoxville, Tennessee, 2010.
  - CR8. Hunter WCJ, Barrett HH, Lewellen TK, Miyaoka RS, Muzi JP, Li X, McDougald W, MacDonald LR. SCOUT: A fast Monte-Carlo modeling tool of scintillation camera output. *2010 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Knoxville, Tennessee, 2010.
  - CR9. Haselman MD, Hauck S, Lewellen TK, Miyaoka RS. FPGA-based pulse pileup correction. *2010 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Knoxville, Tennessee, 2010.
  - CR10. Dey S, Banks L, Chen SP, Xu W, Lewellen TK, Miyaoka RS, Rudell JC. A CMOS ASIC Design for SiPM Arrays. *2011 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Valencia, Spain, 2011.
  - CR11. Hunter WCJ, Barrett HH, Miyaoka RS, Lewellen TK. Multiple-hit Parameter Estimation in Monolithic Detectors. *2011 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Valencia, Spain, 2011.
  - CR12. Lewellen TK, Miyaoka RS, MacDonald LR, DeWitt D, Hauck S. Evolution of the Design of a Second Generation FireWire Based Data Acquisition System. *2011 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Valencia, Spain, 2011.

CR13. Miyaoka RS, Li X, Hunter WCJ, Lewellen TK. A Trapezoidal Slat Crystal (TSC) PET Detector. *2011 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Valencia, Spain, 2011.

CR14. Miyaoka RS, Li X, Hunter WCJ, Yuan E, Lewellen TK. Design of a Time-of-Flight PET Imaging Probe. *2011 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Valencia, Spain, 2011.

CR15. Hunter WCJ, Li X, McDougald W, Griesmer JJ, Shao L, Zahn R, Lewellen TK, Miyaoka RS. Measurement of Entrance-Surface vs. Conventional Single-Ended Readout of a Monolithic Scintillator. *2011 IEEE Nuclear Science Symposium and Medical Imaging Conference*. Valencia, Spain, 2011.