Final Report
Project Title: Low Profile Detector for Breast Specific Gamma Imaging
CRADA JSA 2014S001

Abstract: Jefferson Lab (JLab), Dilon Technologies (Dilon) and Hampton University (HU) entered into a research CRADA project titled: "Low Profile Detector for Breast Specific Gamma Imaging." Dr. Benjamin Welch, Director of Research and Development/Engineering was the Principal Investigator for the detector project for Dilon. Dr. Nicholas Kenny was the Principal Investigator for the project for HU. The Jefferson Lab partner on this project was the Radiation Detector and Imaging Group in the Physics Division, led by Dr. Drew Weisenberger who was the coordinator of the project execution and acted as the chief contact with Dilon and HU. The responsibility of Jefferson Lab was the development and construction of detector instrumentation.

Summary

The ultimate goal of this research was to develop a low profile gamma camera that could be used for breast cancer detection. Additionally, the project further developed and expanded JLab's detector and imaging expertise particularly in the area of gamma-ray imaging for cancer detection. In particular JLab gained experience applying the latest silicon photomultiplier (SiPM) detector technology to non-nuclear physics applications. HU provided capabilities and equipment to form the basis of continued breast cancer research with possibilities for future sponsored research support. This project provided an opportunity for HU researchers and students to facilitate the development of an improved cancer imaging modality that could improve patient care. It was envisioned that the techniques and skills developed in working on this project could form the basis of a longer term technology development or clinical implementation project, providing prototype data for future proposals and leading consequently to additional funding support. The project allowed Dilon to make use of technical expertise and resources in Jefferson Lab and HU to facilitate the development of a SiPM based gamma camera which could improve the ability to detect breast cancer tumors. The collaboration accomplished the task of designing a large area gamma camera based on SiPM and to building and test subsystem prototypes. It was also planned to attempt to assemble a complete prototype mounted to a scintillator array provided by Dilon. This proved difficult and not achievable in the period of performance. The difficulty of achieving a reliable mounting of SiPMs to the prototype printed circuit boards using JLab in-house resources lead to delays with the ultimate choice of enlisting a vendor. Members of the collaboration are continuing to seek further funds to develop the SiPM technology for this application based on the accomplishments of this CRADA.

Silicon Photomultipliers

The Jefferson Lab detector group has been developing and testing nuclear physics detectors based on a new technology called silicon photomultiplier (SiPMs) based on silicon chip technology. Advances in high-gain silicon-based photodetector technology have resulted in the beginning of an evolution away from vacuum electronics in high energy and nuclear physics detectors. One example of this is the BCAL detector in the Hall D experiment at Thomas Jefferson National Accelerator Facility (Jefferson Lab), which uses 4000 of these devices to detect gamma radiation resulting from particle collisions. The performance and cost of this SiPM technology has allowed it to replace conventional photomultiplier tubes that have been historically the basis of these large detector systems. Additionally, the Jefferson Lab Radiation Detector and Imaging Group built in collaboration with the University of Virginia a SiPM based small hand held gamma camera (see Figure 1) [1].

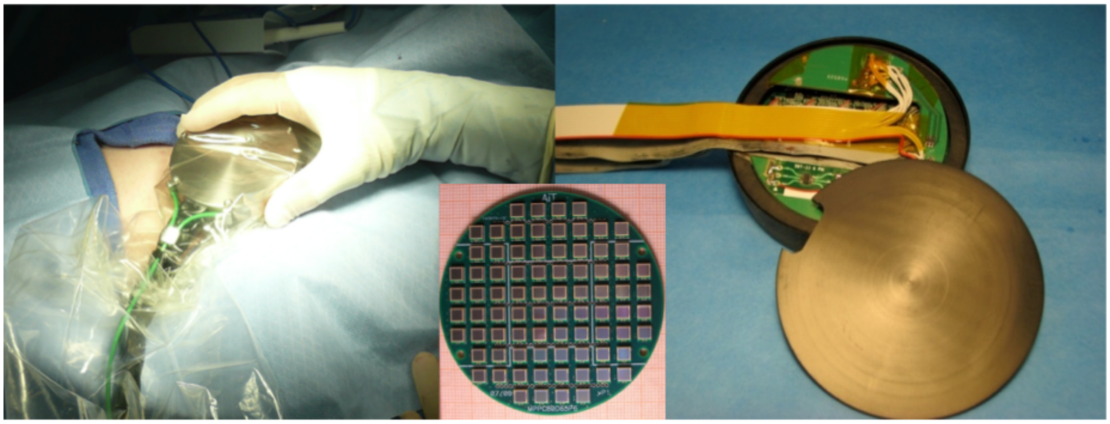

Figure 1. SiPM based small hand held gamma camera build by Jefferson Lab undergoing clinical trials at the University of Virginia.

Breast-Specific Gamma Imaging

Breast cancer is one of the leading causes of death for women in the United States. Early detection is the one of the best ways of combating the increased incidence. While x-ray mammography has long been accepted as the most effective method to detect breast cancer prior to outward signs and symptoms, it has unacceptable false negative rate for patients with radio-dense breast tissue. The sensitivity of detecting cancer via screening mammography decreases from 88% in the predominately fatty breast to 62% in the dense breast. Patients with dense breasts represent the general population of premenopausal women as well as those with fibrocystic tissue disease; cancer in younger women tends to be more virulent and grow faster. Another concern is that the positive predictive value of x-ray mammography is quite low. An alternative and complementary technology that has been under development and has been implemented commercially is formerly known as scintimammography but is now referred to as breast-specific gamma imaging (BSGI) or molecular breast imaging (MBI).

BSGI uses a dedicated gamma camera system to image the distribution of the injected radiopharmaceutical 99mTc-sestamibi in the breast. The gamma camera is based on a NaI(Tl) crystal scintillator array which is optically coupled to a set of position sensitive photomultiplier tubes (PSPMTs). When the 99mTc- decays it emits a 140 keV gamma-ray which is detected by the gamma camera through the generation of scintillation light (photons) in the NaI(Tl) crystal scintillator. The scintillation photons are them detected by the PSPMTs which convert it to an electrical signal which is used to form an image. This 99mTc agent concentrates in breast tumors by mechanisms related to electronegative cellular and mitochondrial membrane potentials and has been extensively investigated for breast cancer detection. Unlike mammography, BSGI images are minimally affected by breast density because of the higher energy photons of 99mTc. In a recent study that included patients who had inconclusive mammographic and ultrasound studies and no palpable findings, BSGI resulted in excellent overall sensitivity (96.4%), moderate specificity (59.5%), and the sensitivity for detecting sub-centimeter lesions, a criticism of gamma imaging of the breast, was 88.9%.

Research and Development Plan

The Jefferson Lab Radiation Detector and Imaging Group has developed position sensitive photomultiplier tube (PSPMT) based detector technology that enabled the building of BSGI detectors that has been licensed by a small high tech company called Dilon Technologies (see Figure 1). Dilon Technologies (www.dilon.com) located in Newport News VA has sold over a 200 BSGI gamma cameras (Dilon 6800 Gamma Camera) worldwide. The SiPMs could allow the building of 2 cm thinner and lighter BSGI detector heads. JLab was to design and build prototypes that could lead to a 15 cm x 20 cm SiPM based detector. Dilon made available detector housing and a scintillator array and assisted with the design to insure clinical relevance.

Figure 2: (Left) Dilon 6800 Gamma Camera based PSPMTs. (Right) NaI(Tl) crystal scintillator array next to PMPMT based detector module.

Development Process

Design of the readout electronics for a SiPM-based imager replaces the conventional PMT-based Dilon imager leverages recent developments in SiPM readout design and data acquisition systems. The objective is to provide both a system that is nominally compatible with the existing Dilon data acquisition system as well as providing options for more efficient readout encoding. Some of the challenges that the system addressed included the mounting of the SiPM devices to achieve uniform distribution over the entire scintillator array surface, flatness to assure uniform optical coupling to the scintillator, and thermal controls that allow gain stabilization over temperature variations. The 3 mm square (sensitive area) Hamamatsu SiPM was selected for its known package conformance, ease of handling and electrical properties. Tests were conducted with arrays of the SiPM and to facilitate experimentation with a method for fixturing the SiPM during assembly. The JLab Fast Electronics Group assisted with this task.

SiPM readout electronics include provisions for supplying bias voltage, temperature sensing for bias voltage/gain control, preamplifiers and signal buffering. The existing Dilon readout is a row-column readout with 7 rows and 9 columns, requiring a resistive charge-sharing network from the existing PSPMTs. Testing of several alternate arrangements were also executed. A block diagram of the SiPM array is shown in Figure 3. At the top are the multiple output bias voltage supplies, and at the left is the analog multiplexer and converter that measures temperatures at 48 points from within the array of SiPMs. To the right and below the array in the diagram row and column sum circuitry is shown which also provides the charge converting transimpedance amplifiers. The resulting pulse signals from row and column are further processed in pulse shaping, signal conditioning circuitry and then combined in a buffered resistive divider network.

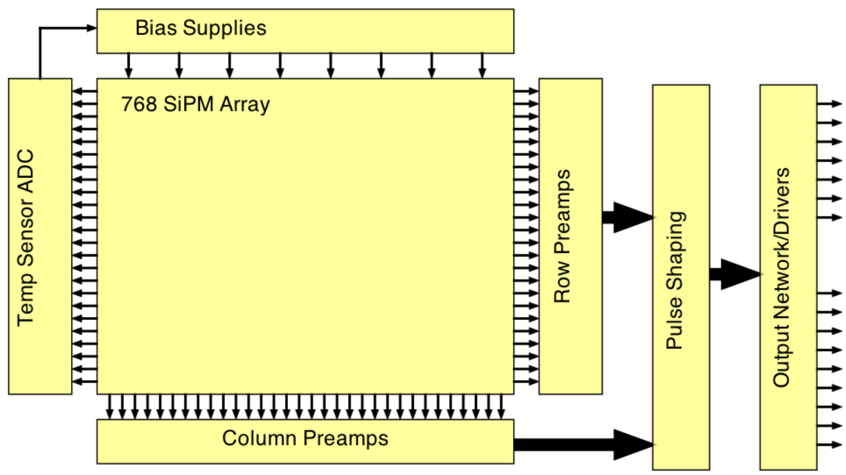

Figure 3. Block diagram of data acquisition front-end circuitry

The circuit geometry conceptual design has also benefited from previous experience with the SiPM devices. A stacked multi-level printed circuit board (PCB) design allows for thermal separation and a low noise arrangement with minimum lead length minimizes noise. Prototyping of multiple readout arrangements is facilitated by the three layer design. As mentioned above the design has 768 SiPMs mounted to the uppermost PCB layer, arranged on twelve individual PCBs of 64 devices each. This modular geometry was found to be convenient to allow assembly and test of smaller segments and is dimensionally similar to the 5 cm x 5 cm Hamamatsu H8500 position sensitive photomultiplier tube which we have prior experience. The SiPM layer modules contain the most critical signal-fidelity components, including protection resistors, thermistors, decoupling capacitors and the row and column summing resistors, but all components on the SiPM layer are passive, keeping the thermal loading to a minimum. The SiPM allows a much thinner design for the detector and can be configured for a very low power consumption, low noise and stable performance. The SiPM has a better photon detection efficiency and lower cost than the photomultiplier devices it replaces.

Passive Temperature Bias Compensation

The SiPM gain has a temperature dependence that arises because of the change in operating point voltage with temperature. There are several ways to manage this compensation to eliminate gain drift with temperature. In systems with small numbers of SiPMs a simple technique is the use of a microcontroller that adjusts bias voltage in response to a temperature sensor. But in systems where a large number of devices require compensation the approaches using such microprocessor control may not be practical. A passive bias compensation technique was incorporated in the design. For this technique, each SiPM is wired with a temperature sensitive voltage divider tuned to the specific operating voltage of the SiPM element. The design of the bias supply network allows a number of SiPMs to share a common bias supply and compensate for temperature variations over a 20 °C range.

Modular Design

The overall dimension of the initial design target is 15.3 x 20.4 cm, and the concept is to use 12 modules of 5.1 x 5.1 cm. This size module matches that size of a frequently-utilized position sensitive photomultiplier (PSPMT). Using that common size means there are several other projects and detectors that could utilize the same designs.

Position Encoding Readout Methods

With a large array of photodetectors implies a large number of individual signals, impractical for each to have its own data acquisition readout. The common practices are to form row/column readouts (which would reduce the number of data acquisition channels to 56) or to reduce the outputs further by using Anger encoding. In our application the net count rate is relatively low the Anger readout can reduce the total number of data acquisition channels to 4, but our design also envisions an 8-output arrangement. This is an intermediate compression which trades off between overall count rate and reduced numbers of data acquisition channels.

Electronic Sparsification

The Anger readout as implemented by the ?? method (ref Popov patent) relies on weighted sums of columns or row sums to generate the centroid signals. The noise contribution to the weighted sums adds in quadrature from each input. The event typically involves a small number of columns or rows with signal above the noise, while the others have no signal and thus only noise. Noise contribution from the non-participating rows degrades the weighted sum. The problem grows with the number of rows and becomes significant with large arrays and small signals.

Various approaches have been taken to reduce the noise contribution to the centroid calculation. If the data are collected from each row independently in a multichannel data acquisition system a threshold can be applied digitally to suppress the noise from non-participating channels. Another approach has been proposed and tested to suppress the non-participating channels electronically.

Using a Complex Programmable Logic Device

A complex programmable logic device (CPLD) is a small programmable logic device or computer chip similar field programmable gate array (FPGA) but with less ability to perform complex logic tasks but an inexpensive solution for straightforward logic circuit tasks. The main building block of the CPLD is a macrocell, which contains logic implementing disjunctive normal form expressions and more specialized logic operations. In this approach, gated amplifiers are controlled by logic signals derived from discriminator outputs at each channel. Individual channel noise is lower, so low level signals are easier to accurately detect. Outputs from the individual channels gate the final stage amplifiers and thus only participating channels contribute to the weighted sums.

To implement this technique, both fast and slow signal amplifiers are used. A fast sum of all channels triggers a time window and the delayed individual channels are picked off as inputs to discriminators. The logic outputs from those discriminators flow to a CPLD logic device where a "contiguous neighbors" computation is made that will include the group of all contiguous active channels with an additional channel on each "end" of the group. Outputs from the CPLD logic enable the appropriate gated amplifiers which feed the weighted sum amplifiers.

Crucial to the success of the circuit is sufficiently fast gated amplifiers as well was the choice of fast discriminators in the design. Delays at each discriminator include the timing "walk" which is proportional to the rise time of the arriving pulses, the propagation delay and the rise time of the discriminator output. The contiguous neighbors logic, implemented in a CPLD (Altera EPM240 MAX ii) is the other significant delay that impacts the design. The EPM240 was chosen for sufficient I/O pin count and a 4.7 ns propagation delay. Signal delays due to two stages of 3rd order low pass filters also needed to figured in.

Once timing is accounted for the next consideration is interoperability of the various power supply levels. The MAX 961 and 964 discriminators both operate at 3.0 to 5.0 V. This allows the discriminators driving the contiguous neighbor logic to be operated at 3.3 V and the CPLD to use input and output logic levels of 3.3 V. This is compatible with the ENABLE inputs of the LMH6611 gated amplifiers if those are operated from single supply +5V. The remaining element is the logic that manages timing. In this system an event may be defined as the set of signals that arrive at the row and column amplifiers. This discussion will follow the row signals but identical timing is used for the column signals.

Before an event arrives the CPLD is held in reset and the timing logic is at rest. When the fast sum rises above the fast threshold a window delay and a retrigger timer are started. After the window delay, the coincidence window time begins and the contiguous neighbor logic is enabled. When enabled, any of the outputs from row signal discriminators are latched as inputs to the contiguous neighbor logic. When the coincidence window closes further latching is disabled to assure the outputs are stable and remain unchanged during the arrival of the delayed row sum pulses. The contiguous neighbor logic presents outputs to enable the appropriate contiguous set of gated amplifiers. After the complete delayed pulse time the retrigger timer clears the latches and the logic returns to rest. The threshold level for the row and column signals is the sum of a constant term and a proportional term derived from the fast sum signal. This approach allows the threshold to be lower when the overall signal in an event is smaller. With the overall design complete the realization in hardware proceeded.

Detector Design

Assembly of these SiPM modules presented a challenge, since conventional parts placement does not provide sufficient alignment of components in three dimensions. To solve that problem a system of assembly fixtures and the use of the SIPAD solid solder system was attempted. Results were not satisfactory. We then employed the use of PCB placement vendor to mount the SiPMs..

The SiPM module signals (bias voltage, temperature sensor and SiPM output) are connected to the mid-layer motherboard through the module's mounting pins. Sockets on the mother board accept the pins which also provide the module-to-module spatial registration assuring alignment and a standoff distance. The mother board circuitry includes row and column preamplifiers and the shaping amplifiers for each row and column as well as the multichannel ADC to read out the temperature sensors.

The shaped signals then connect to the third layer output board where the output configuration is determined. Buffered resistive divider networks take the 24 rows and 32 column signals and convolve those to produce a 7 x 9 row/column output.

Each SiPM device is set to a recommended operating voltage (VOP) to obtain its standard gain. Matching these VOP within a group of SiPMs that share a common bias supply is important to assure good gain matching across the array. The distribution of VOP for the 1000 SiPM devices received from Hamamatsu is plotted in Figure 4. All 1000 devices fall within a 1.40 V range. Analysis shows that when SiPMs are taken in groups of 16 each group would have a maximum deviation of 30 mV, a value equivalent to a temperature variation of approximately 0.5°C. The 1.40 V overall span necessitates multiple bias supplies. A total of 24 bias voltages are required to keep the gain matching within 60 mV. This can be accomplished with either individual supplies or using a voltage division network and a smaller number of bias supplies. Both approaches will be evaluated for our tests.

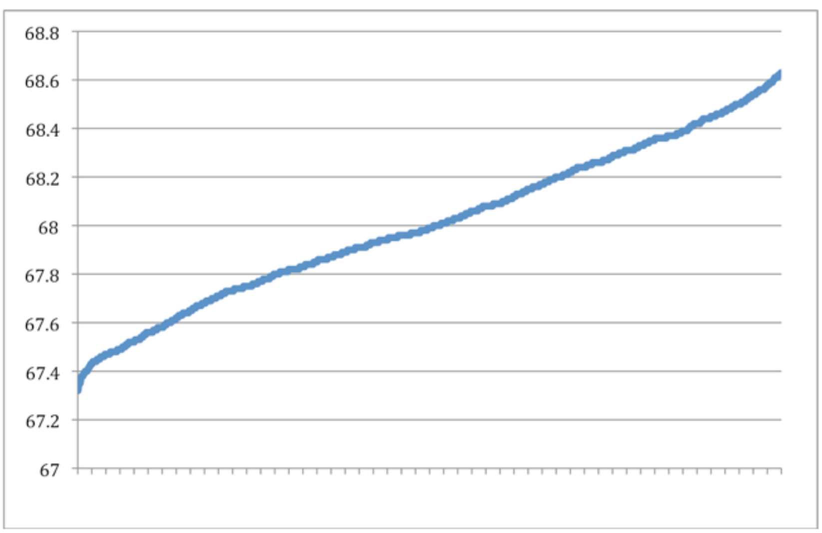

Figure 4. Manufacturer recommended VOP voltage for 1.25x106 for 1000 devices.

Results and Conclusion

JLab designed the electrical circuit to achieve a SiPM photon detector subsystem based on 728 individual surface mount reflow compatible SiPMs obtained from Hammamtsu Corporation (3x3mm MPPC: S10931-050P). Each SiPM has an active area of 9 mm^2. The design included optically coupling the SiPM based detector to the scintillating crystal array supplied by Dilon technologies. The scintillator array is composed of NaI(Tl) crystal elements with dimensions of 2.96 mm x 2.96 mm on 3.2 mm centers. The array is hermetically sealed and has a 6.50 mm thick glass window. The glass window acts as a light spreader that spreads the scintillation light so it can be detected. We had to determine the optimum spacing of the SiPMs to insure detection of enough scintillating photons so the individual crystal elements could be resolved. We wanted to use as few SiPMs as possible to remain on budget. A Monte Carlo simulation was developed and used to obtain the maximum separation. A pitch of 6.50 mm was determined to be adequate and in order to cover the area of the Dilon scintillator array a total of 768 SiPMs were required.

In order to test the appropriate electronics circuitry to read out the signals of each SiPM, two series of test circuitry were designed and used to construct prototype SiPM. The end design involved multilayer printed circuit board (PCB) on which the SiPMs and supporting electronic components are mounted. Vendors were identified to produce the PCB. The modules were used to inform the further design of the final electronics for the readout of the large number of SiPMs.modules (see Figure 3).

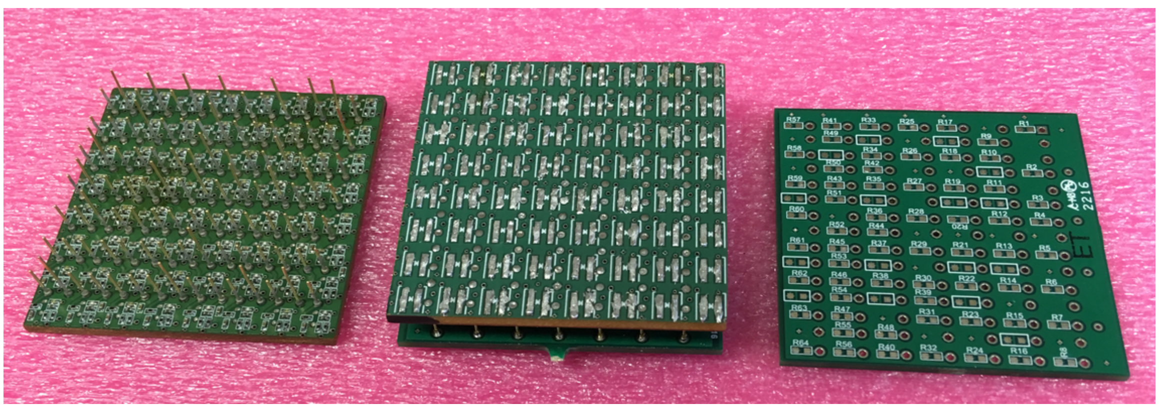

Figure 3: Samples of prototype PCB modules constructed for attempts at SiPM surface mount technology in a Jefferson Lab solder reflow oven.

Several attempts to achieve reliable mounting of SiPMs to the prototype PCBs failed and lead to delays with the ultimate choice of enlisting a vendor and populate the PCB with individual with SiPMs and insure a good optical surface for the optical coupling of the scintillator (see Figure 4).

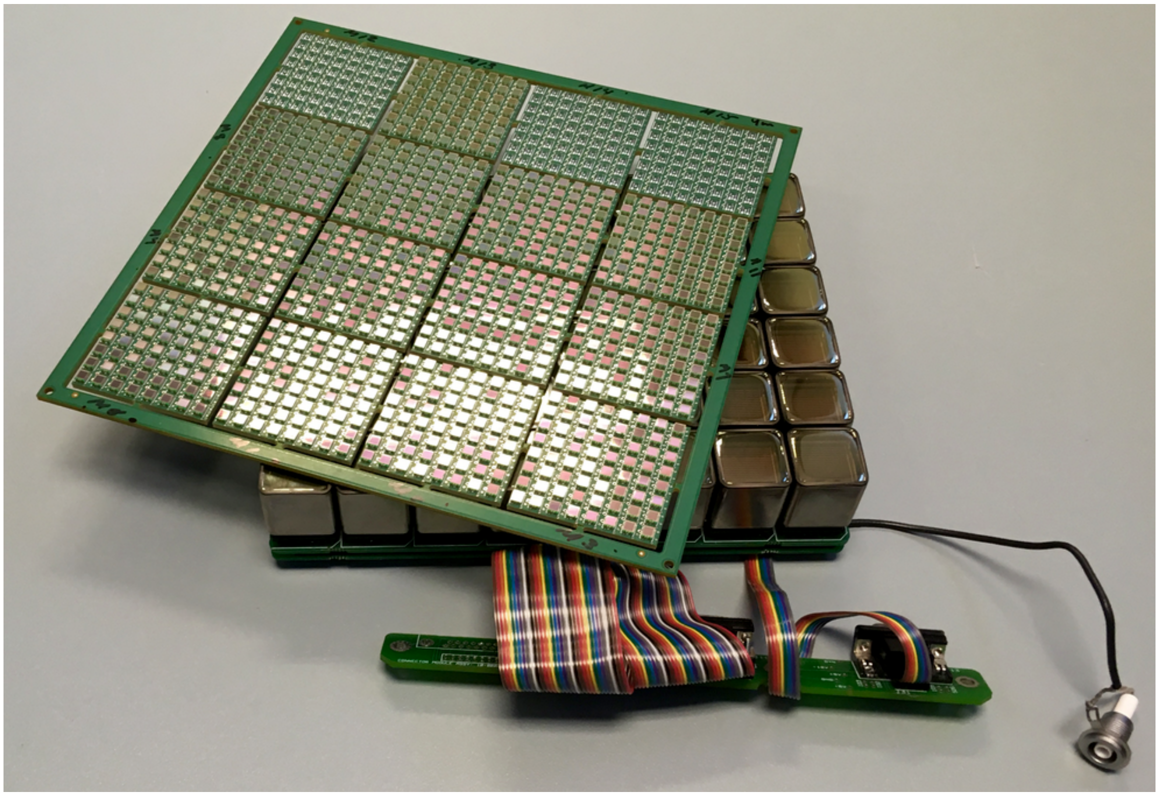

Figure 4: Successfully constructed PCB mounted SiPMs. The final SiPM detector will replace the PSPMT array shown behind the SiPM PCBs.

In summary the collaboration accomplished designing a large area gamma camera based on SiPM and to building and test subsystem prototypes. We describe the design of an imaging array designed around the silicon SiPM. The design tackles several of the usual problems with implementations using the SiPM. The photodetector elements are mounted in modular units of approximately 51 mm square, each with an 8 x 8 array of photo detectors with independent bias filtering. The initial detector utilizes a segmented NaI scintillator. A passive gain stabilization technique is employed with each photodetector element to both match gains of the SiPMs across the array and to eliminate the gain drift with temperature. Readout of the array is accomplished with an Anger-encoded resistive readout. The challenge of the noise contribution from non-participating rows and columns is addressed with a channel gating suppression method driven by fast logic implemented in a CPLD.

Members of the collaboration are continuing to seek further funds to develop the SiPM technology for this application based on the accomplishments of this CRADA.

---

[1] Popovic, K, McKisson, JE, Kross, B, Lee, S, McKisson, J, Weisenberger, AG, Proffitt, J, Stolin, A, Majewski, S, and Williams, MB, "Development and Characterization of a Round Hand-Held Silicon Photomultiplier Based Gamma Camera for Intraoperative Imaging," IEEE Trans. Nucl. Sci., vol. 61, no. 3, pp. 1084-1091, Jun. 2014.