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Readout Strategy of an Electro-optical Coupled PET Detector for Time-of-Flight PET/MRI

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Abstract

Combining PET with MRI in a single system provides clinicians with complementary molecular and anatomical information. However, existing integrated PET/MRI systems do not have time-of-flight PET capabilities. This work describes an MRI-compatible front-end electronic system with ToF capabilities. The approach employs a fast arrival-time pickoff comparator to digitize the timing information, and a laser diode to drive a 10m fiber-optic cable to optically transmit asynchronous timing information to a photodiode receiver readout system. The comparator and this electro-optical link show a combined 11.5ps fwhm jitter in response to a fast digital pulse. When configured with LYSO scintillation crystals and Hamamatsu MPPC silicon photo-multipliers the comparator and electro-optical link achieved a 511keV coincidence time resolution of 254.7ps $\pm$ 8.0ps fwhm with 3 $\times$ 3 $\times$ 20mm crystals and 166.5 $\pm$ 2.5ps fwhm with 3 $\times$ 3 $\times$ 5mm crystals.

1. Introduction

Positron emission tomography (PET) has become a widely accepted tool for molecular imaging in the past two decades. A PET signal is produced by radiolabeled molecular contrast agents (tracers) that have been injected into the patient. The tracer accumulates in regions of the body where the biological process of interest is occurring. When a PET tracer undergoes a nuclear decay, it emits a positron. The positron in turn annihilates and produces two 511keV photons that travel in a straight line away from each other. PET detectors sense these photon pairs, and advanced mathematical algorithms use the acquired data to reconstruct a map of the PET tracer concentration.

Time-of-flight (ToF) in PET is a technological advance enabling more accurate estimation of the annihilation event locations along lines of response (LOR). ToF PET technology is based on the precise (<1ns) measurement of the time difference between the detection of the two simultaneously emitted photons resulting from annihilation of the positron emitted from each decay event of the radioactive PET tracer. This arrival time difference information enables more accurate placement of each event along LORs (see Figure 1) and thus, more accurate estimates of the 3-D distribution of the tracer using advanced tomographic image reconstruction methods. ToF can greatly improve the signal-to-noise (SNR) performance of

PET systems (Budinger *et al* 1983, Moses *et al* 2007, Levin *et al* 2008, Karp *et al* 2008). The improvement is given by the formula:

$$SNR_{increase} = \sqrt{\frac{2D}{c\Delta}} t \quad (1)$$

Where D is the diameter of the patient, Δt is the time resolution of the scanner, and c is the speed of light. For example on a 35cm diameter patient 170ps timing resolution would improve SNR by a factor of 3.7. The technique can be exploited to substantially improve lesion detection above background, lower radio-pharmaceutical dose administered, or shorten scan time. These features increase PETs accuracy as well as make it safer and more practical in the clinical management of disease.

There has been great interest in developing combined PET/MRI systems. PET/MRI has a number of anticipated benefits over PET/CT including motion correction abilities, better soft tissue contrast, and the use of additional physiological and molecular imaging techniques from the MRI (Prato *et al* 2011, Nekolla *et al* 2009, Pichler *et al* 2010). A number of PET/MRI systems have been developed, and have shown promising results (Herzog *et al* 2010, Wehrl *et al* 2009, Pichler *et al* 2006). However, the design of PET/MRI systems is challenging due to the size constraints of the MRI system and the electro-magnetic fields inside the MRI bore. Traditional PET detectors use photomultiplier tubes (PMTs) which are both bulky and sensitive to magnetic fields. Early combined PET/MRI systems coupled the PET scintillator crystals directly to fiber optic cables to transport the scintillator light outside the MRI bore where PMT's could safely operate (Shao *et al* 1997). Systems later used semiconductor light detectors such as avalanche photodiodes (Pichler *et al* 2006) or silicon photomultipliers (SiPM) (Yamamoto *et al* 2012). These detectors can function inside of an MRI bore with little mutual interference. Analog signals from the light detectors can then be transmitted out of the MRI bore by coaxial cables with or without pre-amplification. Despite these advances in detector technology, ToF has not been achieved on existing integrated PET/MRI systems.

Our group has proposed using compact vertical cavity surface emitting lasers (VCSEL) and fiber optics to read out PET SiPM signals instead of coaxial cables (Olcott *et al* 2009). The coaxial cables currently used to transmit analog timing signals are bulky and have a low bandwidth that degrades the time resolution of the PET system (Andrews 1988). A fiber optic cable has a high bandwidth to enable ToF. It also integrates extremely well with an MRI due to its low loss, electrical isolation, immunity to EM interference and cross-talk, and compact size.

The proposed timing system will convert the SiPM signal to a digital pulse inside the MRI bore with a comparator. The digital pulses can then be easily multiplexed without degrading time resolution before being transmitted by a VCSEL away from the MRI. Outside the MRI-bore the light from the fiber optic can be converted back to an electrical signal using a photodiode receiver followed by a conventional electronic data acquisition system. A schematic of this entire "electro-optical" scintillation detector processing chain is shown in Figure 2. Compared to current SiPM systems, the proposed system will have better time resolution for ToF, be more compact due to the elimination of large coaxial cables, and reduce interference to and from the MRI because of fiber optic immunity to EM interference and the absence of synchronous electronics inside the MRI bore. In this work, we present a proof of concept two channel ToF capable electro-optically coupled PET detector. With the addition of shielding, and use of MRI compatible electronics the architecture presented here could be the basis of a PET/MRI timing system.

2. Methods

A number of different methods have been implemented to achieve good timing resolution using SiPMs. These include waveform analysis (Schaart *et al* 2010), constant fraction discrimination (Fallu-Labruyere *et al* 2007) leading edge discrimination (Kim *et al* 2009), and multi-threshold discrimination (Choong 2009). For this work leading edge discrimination was chosen for its high performance and simplicity. Leading edge discrimination can be implemented with a fixed threshold comparator. While effects like baseline wander and amplitude dependent time walk are not accounted for by leading edge discrimination, the timing resolution can still be sufficient for ToF.

2.1. Simulation

The time resolution of a leading edge discrimination system was first simulated for 3mm×3mm×5mm LYSO crystals and for 3mm×3mm×20mm LYSO crystals at different thresholds to estimate the system's ToF capabilities and find reasonable comparator threshold ranges. Each photon arrival time was modeled as a sum of random variables:

$$T_{\text{photon}} = \text{Exp}(Xtal_{\text{rise}}) + \text{Exp}(Xtal_{\text{decay}}) + N(0, Elec_{\text{noise}}) + Xtal_{\text{trans}}$$

$\text{Exp}(Xtal_{\text{rise}})$ is an exponential random variable modeling the rise time of LYSO. Its rate parameter is 90ps (Seifert *et al* 2012). $\text{Exp}(Xtal_{\text{decay}})$ is an exponential random variable modeling the decay time of LYSO. Its rate parameter is 53ns (Pepin *et al* 2004). $N(0, Elec_{\text{noise}})$ is a normal random variable modeling the noise from the SiPM and readout electronics. The standard deviation of the single pixel SiPM jitter used was 100ps (Vinke *et al* 2009). The electronics jitter used had a standard deviation of 25ps. $Xtal_{\text{trans}}$ is a random variable modeling the photon transport path through the crystal to the photodetector. Each photon's path length was randomly chosen from a large number of simulated photon paths. The number of photons sensed is determined by the crystal light yield (27 photons/ keV) (Haas *et al* 2008) and detector quantum efficiency (0.3) parameters. A random number of photons were also removed to simulate the effects of finite energy resolution (10% energy resolution was assumed). The exponential and normal random variables were modeled using Matlab (MathWorks, Natick, MA) and the crystal transport was modeled using DETECT2000 (Cayouette *et al* 2002). The time resolution for an N photon threshold was given by the fwhm of the distribution of time delays of the arrival of the Nth photon over many trials.

2.2. Setup Characterization

Two channels of the experimental setup were constructed to verify the proposed system's timing resolution (see Figures 2, 3 and 4). The system's input was first amplified by a 13dB Minicircuits ZX60-4016E+ preamplifier. This was followed by an RF splitter. One output of the splitter was coupled to a Agilent 2.5GHz 20GSa/s DSO90254A oscilloscope to read pulse height for energy information, the other was coupled to an ultra-high-speed Maxim 9601 comparator to pick off arrival times of the detector pulses. This comparator signal was then used to drive a telecommunications-grade vertical cavity surface emitting laser (VCSEL) and 10m fiber-optic cable using a MAX3740A VCSEL driver. The timing resolution of this set up was first measured in response to a 500kHz square wave from a TDR scope with the comparator only and with the comparator followed by the electro-optical link. Because the laser driver circuit was designed for high frequency communication (not our low frequency PET signal), the electro-optical link (without the comparator) was also further characterized for different frequency inputs. Its jitter, baseline, and magnitude (see Figure 5) were taken in response to different frequency inputs from a square wave

synthesizer. These results were used to estimate the electro-optical link's effect on the system's timing resolution.

The SiPMs (single channel 3mm×3mm Hamamatsu devices) were also characterized by taking the magnitude of a single SiPM pixel pulse to determine the number of incident photons each comparator trigger corresponded to. When dark counts are observed on the scope discrete levels of dark counts can be seen that correspond to different numbers of individual pixels firing. The difference between these levels corresponds to the voltage magnitude of an individual pixel firing, and thus the voltage magnitude of a single photon being detected by the SiPM.

2.3. PET Detector Measurements

To test the feasibility of ToF-PET with this configuration, the coincidence timing resolution in response to a Na-22 source was measured using 3mm×3mm×5mm and 3mm×3mm×20mm LYSO crystals. The 3mm×3mm×5mm crystals were polished, and wrapped with Teflon. The 3mm×3mm×20mm crystals were polished, and wrapped with a specular reflector. The crystals were coupled to single channel 3mm×3mm Hamamatsu MPPC SiPMs biased at 71.2V for 3mm×3mm×5mm crystal measurements and 71.4V for 3mm×3mm×20mm crystal measurements. The comparator threshold voltages were swept from 4mV to 25mV. The experiments were repeated with the comparator signal bypassing the electro-optical link and going straight to the scope to determine the contribution of the electro-optical link to the overall timing resolution. Thresholds lower than 4mV lead to the detector triggering frequently on dark counts or noise. To verify that the timing distribution can in fact be used to track the source and give the benefits of ToF, measurements were made with the source at different positions between the two detectors. Energy resolution data was also calibrated on our devices by taking data with gamma emitters of varying energies (Cs-137, Co-57, Ba-133, in addition to the Na-22), and fitting the resulting amplitude to energy curve to a polynomial.

3. Results

3.1. Simulation

Simulations predict that the system's timing resolution will improve as the threshold is lowered until the Gaussian noise of the electronics is dominant. The simulation results (as well as measured results to be described later) can be seen in Figure 6. With 3mm×3mm×5mm LYSO crystals the best simulated timing resolution was 188.1 ps at a threshold of 6 photons and with 3mm×3mm×20mm crystals the best simulated timing resolution was 236.9ps at a threshold of 5 photons.

3.2. Setup Characterization

In response to a 500kHz square wave from a TDR scope the comparator and electro-optical link has a fwhm jitter of 11.5ps, while the comparator alone has a fwhm jitter of 9.9ps. In response to a square wave generator the electro-optical link's jitter, amplitude, baseline and magnitude changed as a function of input frequency for each detector as seen in Figure 7. The measurements in Figure 7 are slightly different from the TDR scope measurements due to the change in setup. The SiPM dark count measurements show the magnitude of a single photoelectron is ~1.5mV (see Figure 8).

3.3. PET Detector Measurements

The Na-22 coincidence data from our PET detectors was energy windowed with a +/- 1 fwhm window from the 511keV photopeak. The energy windowed coincident time resolutions found are summarized in Figure 6 and Table 1. The minimum timing

distributions with the electro-optical link are also displayed in Figure 9. Timing resolutions of 254.7 ± 8.0 ps fwhm at a 7mV threshold for $3 \times 3 \times 20$ mm crystals and 166.5 ± 2.5 ps fwhm at a 5mV threshold for $3 \times 3 \times 5$ mm crystals were achieved with the electro-optical link. The 7mV threshold corresponds to the 5th photon, and the 5mV threshold corresponds to the 4th. The average timing resolution over all thresholds with the electro-optical link was 18.2ps higher for 5mm long crystals and 31.2ps higher for 20mm long crystals than without the link. When the Na-22 source was moved a corresponding timing distribution movement was observed (see Figure 10). The source was moved 2.4cm between detectors, which would correspond to a 160ps shift in the time distribution mean. The 5mm long crystals showed a 155.5 ± 7.2 ps shift and the 20mm long crystals showed 163.8 ± 7.1 ps shift. The energy resolutions after calibration were 15.0% for detector 1 and 13.5% for detector 2 (see Figure 11).

4. Discussion

The timing resolutions achieved of 254.7 ± 8.0 ps for 20mm long crystals and 166.5 ± 2.5 ps for 5mm crystals are sufficient for significant SNR improvements if implemented in a clinical PET/MRI scanners. As predicted in the simulations the timing resolutions improved as the threshold was lowered until the threshold reaches the noise floor of the electronics. Figure 6 shows that the measured results showed slightly better timing resolutions and lower noise floors than predicted. This could be due to lower than expected jitter in our SiPM pixels.

Another unexpected result is the significant difference between timing resolutions of the system with and without the optical link (18.2ps and 31.2ps for 5mm and 20mm length crystals, respectively). The comparator and optical link showed a jitter of just 11.5ps. Since jitters add in quadrature, this 11.5ps fwhm should be negligible compared to the 100+ps time resolution of the scintillation detectors. However, the 11.5ps fwhm jitter was measured in response to a constant 500kHz square wave. The measured scintillation signals came at much lower rates (average of 1kHz), and at random intervals. The optical system used was from an off-the-shelf optical communications system designed for high data rates (up to 3.2Gbps). As a result, the optical link's behavior was much different at lower data rates (see Figure 7). Another complication was that each detector had a different frequency dependence. If the frequency components of the Poisson input of radioactive decay are taken into account, simulations show that with each optical-link's frequency dependent behavior we expect to see a 24.9ps degradation for 5mm crystals and a 19.9ps degradation for 20mm crystals which much more closely matches the observed difference in timing resolutions. With custom designed laser driver circuitry designed for PET systems we should be able to eliminate the difference in timing resolution with and without the link given the 11.5ps jitter for a single frequency. PET systems in the clinic often experience low and irregular data rates in practice so the consideration of the count rate on the driver circuit is a necessity.

5. Conclusions

Our experiments have shown that an off-the-shelf comparator, laser driver, and electro-optical link can achieve ToF resolution. The system's 254.7 ± 8.0 ps fwhm time resolution for $3 \times 3 \times 20$ mm crystals and 166.5 ± 2.5 ps fwhm time resolution for $3 \times 3 \times 5$ mm crystals would enable ToF performance, and associated SNR improvements to existing PET/MRI systems. It also closely matches simulated trends for optimal timing given our scintillation crystals and time pickoff scheme. However, to improve these results, more work must be done to create laser driver circuits better suited to our application. Due to the digital nature of the signal, multiple channels could be multiplexed into the same optical fiber to

reduce the number of readout channels without affecting SNR, making the construction of a larger electro-optically coupled PET/MRI system plausible.

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Figure 1. Depiction of how event positions are estimated along the LORs in (a) conventional versus (b) ToF PET system. ToF PET enables more events to be positioned closer the correct location of the true two-photon emission point.

Figure 2.
Schematic of a single channel readout of the detector system.

Figure 3.
The detector setup with bias circuitry and pre-amps shown. Inside the detector housings are LYSO crystals coupled to Hamamatsu MPPC silicon photo-multipliers, bias-Ts, and pre-amplifiers.

Figure 4. The comparator and electro-optical link circuitry. The amplified signals are sent to comparators, followed by laser drivers attached to vertical-cavity surface-emitting lasers. The optical signals are sent over 10m multimode fiber patch cables to receiver amplifiers before reaching the scope.

Figure 5. The characterization measurements (baseline, delay, jitter, and magnitude) for the electro-optical link. The output of the optical receiver was characterized in response to a square wave generator for different frequencies.

Figure 6. Simulated (blue), and measured fwhm coincidence timing resolutions of the detector system with (green) and without (red) the electro-optical link. The electro-optical link has an effect on the timing resolution, but excellent timing resolution is easily achieved on both 3mmx3mmx5mm crystals (top) and 3mmx3mmx20mm crystals (bottom).

Figure 7. Jitter, delay, baseline, and magnitude characterized for the two optical links vs frequency

Figure 8.

A persistence scope capture of dark counts shows the magnitude of single SiPM pixels. The histogram on the left corresponds to the relative number of dark counts that crossed the orange vertical line at each voltage. The quantized peaks are at the heights of different numbers of SiPM pixels firing.

Figure 9. Minimum measured 511keV energy windowed coincidence timing distributions of the electro-optical detector system with 3mm×3mm×5mm crystals at a 5mV threshold (left) and 3mm×3mm×20mm crystals at a 7mV threshold (right).

Figure 10.

Timing histograms (dots) and Gaussian fits (solid lines) showing the shift in energy windowed coincident timing distributions can be observed when the source is moved relative to the two detectors. Results are shown with 3mm×3mm×5mm crystals (left) and 3mm×3mm×20mm crystals (right). For each detector the source was moved 2.4cm. A shift of 160ps was expected. Both crystal sizes have measured shifts within one standard deviation of 160ps.

Figure 11. Polynomial curves fit to the calibration measurements of different energy gamma emitters (top) for energy linearity correction, and linearity corrected energy spectra of (bottom) of each detector.

Table 1

Summary of results

Measurement		5mm long crystal	20mm long crystal
simulation	min time res	188.1ps	236.9ps
	threshold	6 photons (9.0mV)	5 photons (7.5mV)
without optical link	min time res	158.6 +/- 4.8ps	221.6 +/- 3.8ps
	threshold	6mV	5mV
with optical link	min time res	166.5 +/- 2.5ps	254.7 +/- 8.0ps
	threshold	5mV	7mV