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An Accurate Timing Alignment Method with Time-to-Digital Converter Linearity Calibration for High-Resolution TOF PET

Hongdi Li [Member IEEE], Chao Wang, Shaohui An, Xingyu Lu, Yun Dong, Shitao Liu, Hossain Baghaei [Member IEEE], Yuxuan Zhang [Member IEEE], Rocio Ramirez, and Wai-Hoi Wong [Member IEEE]

H. Baghaei, Y. Zhang, R. Ramirez and W.-H. Wong are with The University of Texas MD Anderson Cancer Center, Houston, Texas, USA. H. Li, S. An, C. Wang and S. Liu were with The University of Texas MD Anderson Cancer Center, Houston, Texas, USA; they are now with UIH, Shanghai, China. X. Lu and Y. Dong are with UIH, Shanghai, China

Wai-Hoi Wong: gwong@mdanderson.org

Abstract

Accurate PET system timing alignment minimizes the coincidence time window and therefore reduces random events and improves image quality. It is also critical for time-of-flight (TOF) image reconstruction. Here, we use a thin annular cylinder (shell) phantom filled with a radioactive source and located axially and centrally in a PET camera for the timing alignment of a TOF PET system. This timing alignment method involves measuring the time differences between the selected coincidence detector pairs, calibrating the differential and integral nonlinearity of the time-to-digital converter (TDC) with the same raw data and deriving the intrinsic time biases for each detector using an iterative algorithm. The raw time bias for each detector is downloaded to the front-end electronics and the residual fine time bias can be applied during the TOF list-mode reconstruction. Our results showed that a timing alignment accuracy of better than ± 25 ps can be achieved, and a preliminary timing resolution of 473 ps (full width at half maximum) was measured in our prototype TOF PET/CT system.

Index Terms

Positron emission tomography (PET); Timing alignment; Time-of-flight (TOF); Time-to-digital converter (TDC) nonlinearity

I. Introduction

The incorporation of time-of-flight (TOF) information into image reconstruction improves positron emission tomography (PET) image quality [1–7]. Improving TOF timing resolution requires a more accurate timing alignment method than is currently available. In early PET systems, attenuation correction was performed using an orbiting source instead of a CT scan, as is being done with recent PET/CT systems. The same orbiting source can also be used for timing alignment. An orbiting source of 60 cm in diameter can produce a maximum of ± 2 ns TOF time uncertainty [8] if the position of the source is unknown. Therefore, special electronics and mechanics are needed to monitor and record the position of the orbiting source at any time so that the orbiting source may be used for TOF timing alignment

correction. Moreover, we have found that timing calibration as measured with an orbiting rod source was dependent on the count rate. When the rod is in the near orbital position to a detector, the detector displays a much higher count rate than when the source is in the distal position. The count rate with the rod in front of the detector is much higher than the normal clinical operation range, and therefore this setup causes the detector and its electronics to become saturated.

This error may be corrected in a number of ways. In our HOTPET camera [9], the orbiting source was driven by a stepping motor. To lower the count rate for one rod in the near orbital position, we divided the same amount of radiation activity into 8 rods that were evenly distributed around the entire orbit. In this situation, a software-rotatable mask in the sinogram synchronizing with the stepping motor, which was designed to predict the positron annihilation location of each coincident event, and the random events outside the mask will be rejected; hence, the timing alignment accuracy was improved. In contrast, the GE Advance PET scanner [10] uses a built-in self-shielding orbiting source for detector calibration, which is convenient for users but requires a more complex mechanical design.

C. Thompson *et al.* proposed a timing alignment method in which a central positron source for a TOF PET camera is used as the reference time for all detectors [8]. All detectors are then calibrated according to the reference signal. The calibration can be carried out simultaneously for all detectors and the time reference can be made very precisely; therefore, the calibration can be done within a short time period. However, it is not easy to adopt this technique into existing electronics that use time-marks for coincidence detection because there is no way to measure the reference signal. In this case, a spare channel driven by the *same* system clock may be required to detect the reference signal simultaneously.

We recently built an animal PET (MuPET) with a gapless photomultiplier-quadrant-sharing (PQS) detector ring [11], [12], in which a small uniform rod phantom with a diameter of less than 2 cm, located at the center of the camera, is used for time calibration. Because there is no absolute time reference in this setup, we used an iterative procedure to assign the time offset to each detector. The advantages of using a small rod for time calibration are as follows. First, this method removes unnecessary coincident events with large radial offsets that are not used by the iterative algorithm, therefore enabling a lower dose to be used and fast data acquisition. Second, fewer random and scatter events are detected owing to the small volume of the source, which reduces noise and therefore improves the timing measurement.

Timing alignment with a small rod works well in our non-TOF animal PET with a small detector ring that is 16 cm in diameter, but this is not suitable for a large human PET system. The lines-of-response (LOR) from the small rod phantom cover only the central part of the sinogram. There are no coincidence data for the LORs with large radial offsets, and thus the timing alignment for these LORs can be derived only from the LORs near the center of the sinogram, creating unavoidable errors during the process. Therefore, timing alignment errors increase for the LORs with large radial offsets.

Here we report the use of a large shell phantom with a diameter of 30 cm for the timing alignment of a TOF PET/CT system recently developed [13]. The PET camera has 504 PQS blocks consisting of 129,024 LYSO detectors ($2.35 \times 2.35 \times 15.5 \text{ mm}^3$) coupled to 576 PMTs (diameter 38 mm). These detectors form a gapless cylindrical ring of 87 cm in diameter with 27.6 cm in the axial field of view (FOV). After TOF timing alignment, a unique time bias is assigned to each detector. In addition, the time-to-digital converter (TDC) nonlinearity is carefully addressed to achieve accurate timing alignment.

II. Methods

A. Timing Alignment Procedure

Poor timing alignment could cause image artifacts. The accuracy of the intrinsic timing offset measurement for each detector pair is more critical than the time resolution itself for an artifact-free image. In a state-of-the-art whole-body TOF PET system, there are hundreds of millions of detector LORs and TOF time resolution varies from 400 to 700 ps among the detector blocks. Therefore, it is not practical to measure the time resolution directly for each LOR and implement these values during the TOF list-mode image reconstruction. Instead, an average time resolution for all of the LORs can be used with the iterative TOF reconstruction algorithm, because the TOF resolution variation is relatively forgiving when this method is used [14].

Even if an annihilation event occurs at the center of a detector pair as shown in Fig. 1, the measured coincidence time-marks may still have a large time offset of 1 to 2 ns owing to the following:

- the unique light path of each scintillation detector within a detector block;
- PMT transit time variation (inter-PMT and intra-photocathode);
- mismatched cable length;
- unbalanced signal trace length on the printed circuit boards (PCBs) or delay variation for the distribution of timing reference with a field-programmable-gate-array (FPGA);
- variation of signal amplitudes and shape of the rising edge and trigger level;
- mismatched clock phase or clock frequency for time-mark generators.

As we mentioned above, this timing alignment study was applied to two PET systems. Although the scales of the two systems are different, the electronics design is similar between the systems [11], [13], including the front-end electronics and coincidence sorters, such as the analog preprocessing circuit, FPGA-based event-position decoding board, hybrid (combined traditional AND-Gate and fast time-mark technology) FPGA-based coincidence board [15] and clock and power distribution board. The major differences between these two PET systems are the PMT types used and the number of data channels.

The purpose of timing alignment is to measure the time offsets directly or indirectly for each detector and create a lookup table to compensate for the delay differences before image reconstruction. Fig. 2 shows a flow chart of the timing alignment procedure. An annular

cylinder (shell) phantom is located at the center of the FOV and aligned by the built-in lasers. A set of list-mode raw data is then acquired with an empty time lookup table to find the time offset of each individual detector. These raw data are also used to generate the TDC nonlinearity table as described in Section II-B below. One detector collects the coincident events with a group of detectors (16×16 scintillator array) at its opposite position to the PET camera. A histogram of the events shows dual timing peaks for each LOR corresponding to the cross-sections of the two shell walls of the phantom. The center of the two timing peaks is related to the isocenter of the shell phantom. Hence, any time drift observed at the center of the dual peaks is recorded as the time offset of the detector. An iterative algorithm is applied to retrieve the time bias for each individual detector of the whole PET system.

Assuming each crystal has an individual time offset c_i , measurement with a phantom could provide a series of equations:

$$\begin{bmatrix} a_{1,1} & \cdots & a_{1,n} \\ \vdots & \ddots & \vdots \\ a_{m,1} & \cdots & a_{m,n} \end{bmatrix} \begin{bmatrix} c_1 \\ \vdots \\ c_n \end{bmatrix} = \begin{bmatrix} d_1 \\ \vdots \\ d_m \end{bmatrix}, \quad (1)$$

where d_j is the measured time difference between pixel c_i and the pixel array at its opposite location in the detector ring. The value of $a_{m,n}$ must be -1 , 0 or 1 . Because each pixel i could form a coincidence with multiple other pixels, the value of m is usually greater than n ; therefore, (1) represents an overdetermined system, offering only an approximate solution. With both m and $n \gg 1000$ for any modern PET system, an iterative algorithm is the practical approach to solve the equation system.

B. TDC Nonlinearity Self-Correction

TDC nonlinearity correction is important for accurate timing alignment in a TOF system. Without this correction, the systematic error caused by a TDC is convoluted into the LOR timing offsets, decreasing the alignment accuracy and resulting in image artifacts. For a TDC that is constructed using internal logic gate circuits inside FPGA chips, the nonlinearity may be sensitive to the environmental temperature and count rate-dependent power consumption. The TDC nonlinearity self-correction method described below can be applied to provide online real-time TDC calibration.

The proposed TDC self-calibration method uses a gamma-event trigger as the “start” signal for the TDC and the rising edge of the very next clock as the “stop” signal, as shown in Fig. 3. Because each gamma signal is a random event and has no correlation with the system clock, the gamma signal should be uniformly distributed within the coincidence time window. If all TDC bins are the same size, each bin should have statistically equal counts for a large amount of total counts. Otherwise, a larger TDC bin record indicates a larger bin size. Hence, comparison of the number of events in all TDC bins allows the TDC differential nonlinearity to be derived.

Because the intrinsic delay time of the start (trigger) or stop (clock) signals varies for different TDCs, the location of effective channels (such as the shadows from 20 to 99 in Fig.

4) for each TDC could be different. Furthermore, for the differential nonlinearity to be measured accurately a few channels on both edges of the effective region affected by the timing jitter (resolution) should be excluded; only the channels with values greater than half of the maximum count (the solid horizontal line in Fig. 4) should be counted.

For the TDC integral nonlinearity measurement, we defined a time reference (shown as the vertical dashed line in Fig. 4), which divides the total counts by half. In fact, this reference point corresponds to the time of half period of the system clock ahead of the rising edge of the “stop” signal. With a reference time point and the differential nonlinearity graph shown at the top of Fig. 5, we created the integral nonlinearity curve. This graph, shown at the bottom of Fig. 5, provides the time offset correction for each measured TDC channel.

C. Experimental Setup

We first used a small rod uniform cylindrical phantom for the MuPET/CT system, which is a small animal PET system [11]. Because the TOF feature is not important for a small FOV PET camera, the MuPET system uses low-cost round PMTs (diameter 19 mm) in the system. However, the electronics in this system have the capability to carry out the timing performance measurement as a TOF system. Even a non-TOF PET system can benefit from better timing alignment through minimization of the coincidence time-window, which reduces the number of random events and improves image quality.

As we mentioned in the Introduction, when a small rod phantom is used, coincidences occur only between crystal pairs that are at opposite positions across the diameter of the detector ring. For the crystal pairs whose LORs have large radial offsets, the timing difference can be derived only indirectly by iterative algorithms, which introduce errors during the numerical computation. Using a large phantom allows data to be measured in a larger fan beam range. This large range provides more constraints in the iteration process, therefore improving the convergence and reducing the remnant errors. However, if the diameter of the rod is simply increased into a big solid cylinder phantom, there are several problems. First, if the big phantom is filled with the same amount of radioactive source as the small rod phantom, the radiation concentration of the big phantom is much lower than that of the rod phantom; hence, the count rate for each LOR is much lower for the big phantom. Second, for each LOR, the activity is distributed along the chord that the LOR passes through the phantom. The measured TOF distribution is the timing resolution convolved with the profile of the chord. Therefore, the big phantom has a much wider TOF distribution along the LOR than the small rod phantom. Given the same amount of total events, the statistics of the TOF distribution with the big phantom are much poorer. The statistical noise, along with the wider spread, makes it difficult to find the center of the TOF distribution with high accuracy. Finally, the big phantom has much higher attenuation and generates more scattering and random events to the signals compared with the small phantom, which introduces much more noise that affects the TOF measurements.

To overcome the shortcomings of the big phantom mentioned above, we instead used a shell phantom that had the same diameter as the big uniform cylinder. The shell phantom provided the same fan beam range as the big phantom while avoiding all the drawbacks. It functioned the same way as the orbiting source, but no driven mechanics were needed,

which simplified the timing alignment procedure and reduced the overall cost. The shell phantom produced two narrow peaks in the TOF distribution plot. Each peak had a similar width to that of the small rod phantom, so that the thickness of the shell source was the same as the rod diameter.

The dimension of the shell phantom is not critical. In principle, the phantom should function better as the diameter increases and the wall thickness decreases. However, some practical issues limit the dimensions of the shell phantom. First, PET phantoms are usually made of acrylic material. If the diameter of the shell is too big, it is hard to maintain mechanical tolerance owing to the material strength properties. Second, it is difficult to mount the shell phantom into the FOV of the PET scanner if the phantom is too big. Finally, if the wall thickness is too thin, it is difficult to fill the shell. According to our experience with filling the standard NEMA IEC phantom, the Hoffman brain phantom and other PET phantoms, we chose a 30-cm diameter for the shell phantom, which is close to the NEMA IEC phantom dimensions and suitably to be supported by a regular patient bed. The wall thickness of the shell phantom was 5 mm, which was thinner than the small rod phantom but still provided enough space for filling while avoiding excessive attenuation and scattering.

We investigated the timing alignment accuracy with a rod uniform phantom that was 2.5 cm in diameter and a shell phantom that was 30 cm in diameter, as illustrated in Fig. 6, using a whole-body TOF PET system [13].

III. Results

A. Using a Shell Phantom Improved Timing Alignment Accuracy

For the timing calibration study, we put a phantom filled with a radioactive source at the center of the MuPET camera, with each detector in coincidence with its opposite 16×16 detector array. The average TOF timing offsets of all assigned LORs were folded into the intrinsic timing bias for the selected detector pixel. An iterative algorithm was applied to each detector pixel until it approached its converged timing bias value.

The timing offset measurement for all 30,420 crystals in the MuPET system is shown in Fig. 7, in which the scale ranges from -20 to 16 ns. This timing alignment with the rod phantom achieved an average 650-ps (FWHM) resolution, which is adequate for a non-TOF animal system.

To determine how much timing uncertainty this timing alignment method contributed, we repeated the procedure with the whole-body clinical TOF PET system. The timing alignment accuracy was determined by investigating the time offsets after correction with the self-generated time bias table from the same data set. Both the small rod uniform phantom and the shell phantom were used for the same system. The shell phantom yielded two TOF peaks for each LOR and the time bias was assigned to the center between the two peaks.

Fig. 8 shows the time offset for all crystals after correction with the self-generated time bias table, and the results indicated that the shell phantom achieved a much better time alignment than the small rod uniform phantom. After calibration with the small rod uniform phantom, we observed an offset range of -300 to 260 ps, and the average error was about ± 100 ps for

the systematic timing error. Such error is acceptable for a TOF system, where the error could be further corrected with the shell phantom. As shown in our test, a timing alignment accuracy of better than ± 25 ps was achieved (the range of the plot for the time-offset by the shell phantom is shown in Fig. 8). After the timing correction, an average timing resolution of 473 ps (FWHM) was measured for the prototype TOF PET/CT system.

TDC Nonlinearity Self-Correction Improved the Uniformity of the TOF Sinogram

TDC nonlinearity correction is important for accurate timing alignment in a TOF PET system. Without this correction, the TOF time center of each LOR may have a bias that generates image artifacts in the TOF-based image reconstruction. In this scenario, the TOF center of an LOR is shifted and assigned to a different TOF sinogram, which can create problems for the TOF scatter and random corrections. Fig. 9 shows the sinogram for one TOF bin without the TDC nonlinearity correction (left) and the improved uniformity after applying the nonlinearity correction (right). The uniformity of the TOF sinogram improved significantly after the TDC nonlinearity correction was applied. The data were acquired by the whole-body TOF PET system using a shell phantom binned into TOF sinograms with a 94-ps bin size without detector normalization.

IV. Conclusions

We have proposed a new timing alignment method for a clinical TOF PET system, in which a large shell phantom is used and a TDC nonlinearity self-correction is applied without the need for additional electronics. Compared with the small rod uniform phantom, the shell phantom improved the timing alignment accuracy by minimizing the effects of scatters, attenuation and random coincidences, by reducing the source size variation with a thin activity wall that folded in the timing jitter, and by measuring the LOR time bias with a larger fan beam and with dual TOF peaks to provide more self-constrained measurements. Our results showed that a timing alignment accuracy of better than ± 25 ps was achieved, and a timing resolution of 473 ps (FWHM) was measured in our prototype TOF PET/CT system.

Acknowledgments

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Fig. 1.

A coincidence time-mark generated by a TDC in a PET camera.

Fig. 2.
A flow chart of the timing alignment process.

Fig. 3.

A TDC is used to measure the time-mark in a PET system.

Fig. 4.
Effective TDC channels for nonlinearity self-correction.

Fig. 5. Self-calibrated TDC differential nonlinearity (top) and integral nonlinearity (bottom).

Fig. 6. Timing alignment setups using a small rod uniform phantom (left) and a shell phantom (right). The dimensions of the phantoms and the detector rings are not drawn to scale.

Fig. 7.

Crystal-based time bias in our animal PET (MuPET) system calibrated using a small rod uniform phantom. This system achieved a 650-ps timing resolution (FWHM).

Fig. 8.

Timing alignment accuracy was improved by using a shell phantom. To evaluate the timing alignment accuracy, the time-offsets were created by the self-generated bias table with the same data set. One result was aligned using a small rod uniform phantom and the other using a shell phantom, as labeled in the plots.

Fig. 9.

After TDC nonlinearity self-correction, coincidence events are assigned to the TOF sinogram correctly, hence improving its uniformity.