GE Healthcare

Clinical Implementation of VUE Point FX™

White Paper

Introduction

This publication is part of a series of white papers aimed at communicating the importance of each component in the image chain of a PET/CT study. From data acquisition to the creation of images available for diagnostic interpretation, each component of the image chain has a critical function in the generation of high quality images. Some of the most important elements in the PET/CT image chain are: the detector scintillation crystal type and length and photomultiplier tubes (PMTs), the coincidence processor, the image reconstruction algorithm, data processing, prescription management, and patient motion correction techniques. The best image quality is delivered when all these components are well matched to the imaging situation. This paper will focus on advanced time-of-flight reconstruction with VUE Point FX.

Background

Although time-of-flight (TOF) sounds new, as it has recently been touted by all three major Positron Emission Tomography (PET) manufacturers, it was in fact developed and commercialized during the infancy of the PET modality. Scanditronix/PETT Electronics produced and sold a TOF PET scanner based on BaF_2 scintillators in the late 1980's. That scanner had a time resolution of approximately 550 pico seconds (ps).[1] The projected improvement was that the TOF information would provide increased positional certainty to each event and thereby produce a pseudo increase to the scanner photon sensitivity. The major challenge with that scanner was the low stopping power of the BaF_2 scintillator material to 511 keV positron annihilation photons. Although TOF did improve the relative signal to noise ratio (SNR) on that system, the intrinsic stopping power of BaF_2 was so low, as compared to other scintillators like Bismuth germinate (BGO), that the TOF impact was overwhelmed by the initial sensitivity loss of utilizing BaF_2. As a result TOF was abandoned in favor of BGO.[2] Since this initial BaF_2 TOF implementation, alternate scintillators have become available. Lutetium based scintillators (LBS) were first developed in 1989 and commercialized into non-TOF products in 1998. In 1999 Moses et al. demonstrated that LBS could achieve approximately 500 pico second time resolution in a bench top single crystal configuration.[3] However the translation to a whole-body scanner configuration required advances in PMT, electronics, and computing power. Over time, advances in these technologies have made TOF plausible for modern commercial systems. This has resulted in a recent resurgence of interest in TOF.

Figure 1: Commercial SP-3000 TOF system (Scanditronix/PETT Electronics, St Louis, MO) installed at the University of Washington in the mid 80s.

Basics of TOF

At a high level, time-of-flight is a technique that localizes the decay site based on the arrival time of the photons at the detector. The thing that makes this particularly complex is that we are trying to measure a distance of approximately a milimeter for a photon traveling at 300,000,000 m/sec. Figure 2 shows the positional uncertainty as a function of the time resolution. From this data it can easily be understood that localization on the order of a few mm pixel will require temporal resolution capability at or better than 10 picoseconds (ps). Temporal resolution with current LBS detector technology is likely limited to around 500 ps. At this temporal resolution the spatial uncertainty is about 15 cm. As a result, TOF does not provide precise localization. Rather, it provides some spatial likelihood to the origin of decay. This is like determining where you are based on the current time zone you are in. Given the 1 hour resolution of the time zone system, several cities, states, and countries may fall into the same time zone. Therefore positioning by this metric will help you identify the region or country you are in but not your precise location.

That said, the regional location information provided by TOF does have an impact. Traditional coincidence detection simply

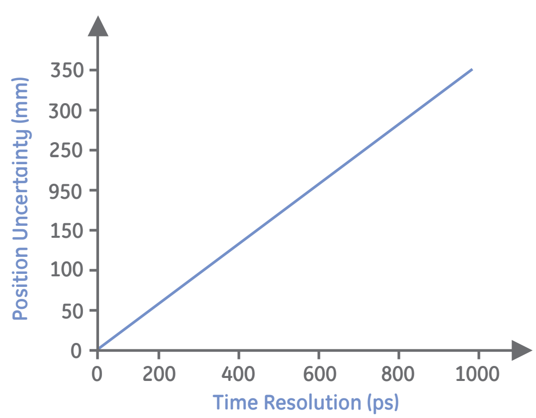

Figure 2: Spatial positioning uncertainty as a function of temporal resolution.

identifies that two 511 keV photons have been acquired "simultaneously" between two detectors. However, the reconstruction does not know where between the detectors the event occurred. Historically the filtered back projection (FBP) reconstruction algorithm had no option but to spread the measured event across the entire image line of response (LOR) between the detector pair. This puts the signal in the correct location but in essence places noise across the remaining image space that lies between the detectors. If there are two events along the same LOR, they will contribute noise to each other in this traditional FBP process. If on the other hand the detection system has the ability to approximate the arrival time of the photon pair, there is an opportunity to back project to a region probabilistically localized to the annihilation origin. Therefore the noise will also be regionally localized, and two events that are separated by a distance greater than the time resolution of the measurement will not contribute noise to each other. An example of traditional and TOF projections are shown in figure 3.

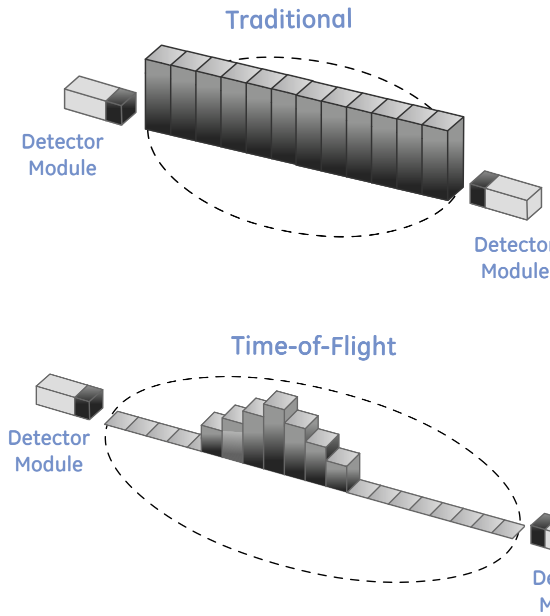

Figure 3: Traditional and TOF projection examples.

Because TOF increases the information from a single event it has been considered as a pseudo increase in system sensitivity. The impact of TOF information for the FBP process was derived and can be described with Equation 1. [4]

$$G_{TOF} = \frac{D}{1.6\left(c\left(\delta\Delta t\right)/2\right)}$$

Equation 1: TOF description

The main parameters in this equation are D, the diameter of the activity distribution, and t the temporal resolution of the detection process. Equation 1 is plotted in figure 4 to show the theoretical improvement of TOF across a range of uniform activity diameters and temporal resolutions. From this plot it can be seen that the estimate of TOF value is approximately a factor of 3 improvement for a 40 cm activity diameter and a 600 ps time resolution.

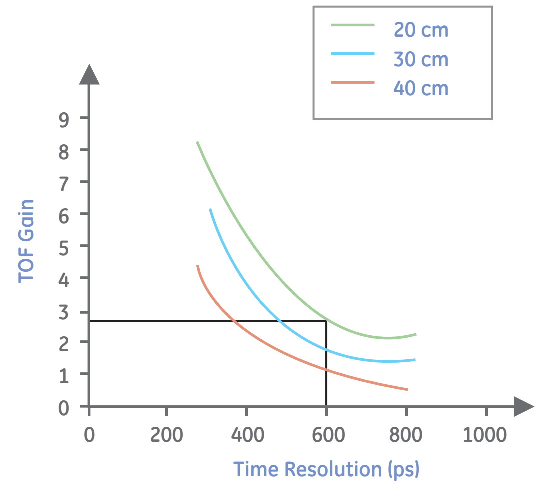

Figure 4: Plot of estimated TOF gain as a function of uniform activity diameter and timing resolutions.

Two caveats to keep in mind are as follows:

1. The D in equation 1 is the uniform activity distribution diameter not the attenuation diameter.
2. Equation 1 was derived to estimate TOF value in a FBP reconstruction, which is no longer employed in general clinical practice.

TOF - System Design Considerations

The capability to measure the difference in arrival times of the two coincident photons traveling at the speed of light requires a very bright and fast scintillator, very fast PMTs, a small block detector design and advanced electronics.

BGO has a very high stopping power, but its lower light output and longer decay time results in insufficient timing resolution for TOF reconstruction. Modern TOF capable scanners are using LBS which have high light output and fast decay times. However LBS does have an inherent reduction in stopping power as compared to BGO. In addition, LBS is a relatively expensive material and often requires design tradeoffs, such as shorter radial depth, for cost effectiveness. It is important to select a system design that maintains sensitivity. Keep in mind the experience of the SP-3000 from the late 1980s. If the initial sensitivity of the scanner it too low, the TOF gains may be overwhelmed by the initial sensitivity deficit.

Given the expense of the scintillator and PMTs, one solution to reduce cost is to utilize fewer large PMTs to decode a larger block detector. However the size (photo-sensitive area) of the detector is a very critical design consideration for high count rate capability. Figure 5 shows the resulting count pileup when a second photon strikes the detector while the detector electronics are still processing a previous event. Pileup can result in missing both events or creating errors in both the timing pick off and energy detection of the events. The probability of pileup can be directly reduced by packaging the detectors into smaller block units as shown in Figure 6. This is like adding additional ticket booths to a toll highway. However this design requires an increase in number of block units and PMT channels for the overall system design. Table 1 shows the block surface area and event processing time for the LBS systems capable of supporting TOF. The probability of pileup is directly related to the busy area. From this data it can be seen that the GE design has approximately 1/2 and 1/6 the probability of pileup as either the vendor A or B respectively, as shown in Table 1. The impact of pileup on energy, spatial, and temporal resolution was previously published as a function of countrate for a TOF system with a large area detector design.[5] The effects of pileup for that scanner are clearly identifiable in the plot of temporal resolution versus countrate shown in figure 7.

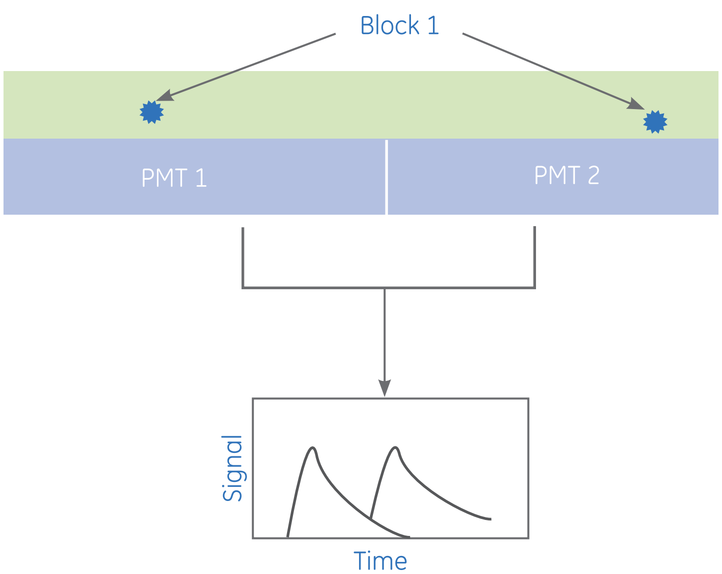

Figure 5: Pile up in single detector that covers a large surface area

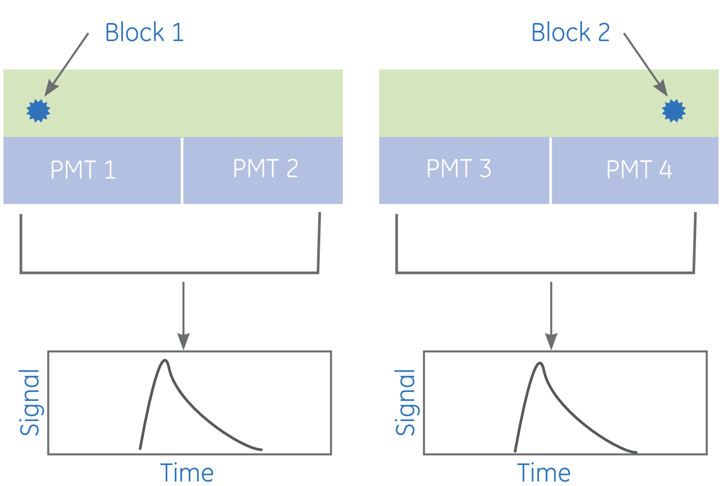

Figure 6: Reduced signal pileup with two smaller blocks that cover the same surface area as the single block shown in figure 5.

Vendor	GE	Vendor A	Vendor B
Scintillator	LBS	LBS	LBS
Area (cm^2)	14	29	162
Busy time (ns)	200	200	120
Busy area (cm^2 ns)	2800	5800	19400

Table 1: TOF compatible block configurations

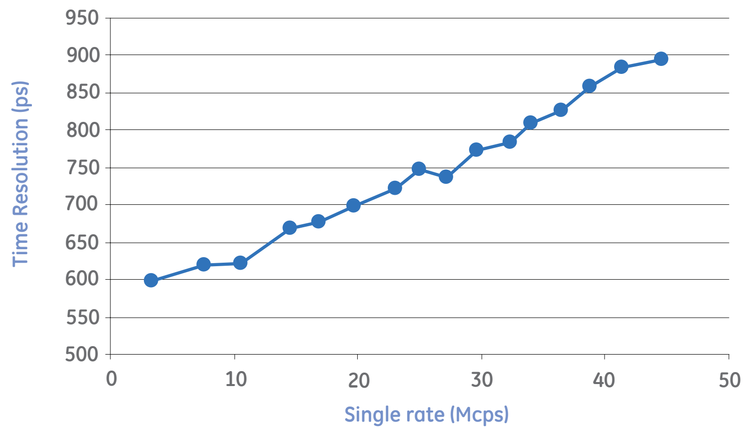

Figure 7: Temporal resolution vs countrate for a competitor's large area detector (Surti et al., JNM 2007)

PET systems have historically run analog signals from the detector blocks to a central digitization rack. This results in two effects. First there is a loss in signal fidelity through the transmission over a distance. Second, given the central location of the electronics and the ring geometry of the scanner, the signal path lengths from the detector to the digitizer differ from block to block and therefore the signal transit times vary. Both the loss in signal fidelity and the variable transit times would contribute to degradation in temporal resolution for the system. To compensate for this, the Discovery PET/CT 600 & 690 has distributed digitization electronics placed at the base of each detector unit as shown in figure 8. This results in immediate digitization without loss in signal fidelity and in uniform transit time from signal origin to digital timestamp.

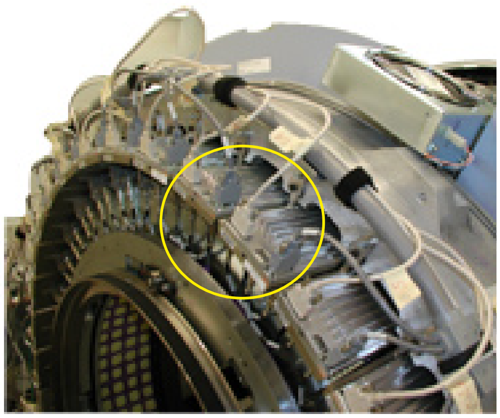

Figure 8: Distributed digitization units. Example digitizer circled in yellow.

Advanced reconstruction:

Although there are significant hardware requirements to support TOF, in the end it is really a reconstruction technique. Therefore the non-TOF reconstruction foundation is critical to maximize the TOF impact. In 2007 GE launched the VUE Point HD intelligent reconstruction algorithm that enabled reduced scan times, lower injections and increased contrast recovery. The key features of that reconstruction are as follows:

- Variance reduction with fully 3D iterative reconstruction
- Resolution enhancement with native geometry modeling
- Increased quantitative accuracy with model based 3D scatter correction
- Improved convergence through accurate Poisson noise modeling with all the corrections in the loop

Expanding the VUE Point HD algorithm for TOF (VUE Point FX) requires that timing information be applied to each correction step (normalization, randoms, deadtime, scatter, attenuation) within the iterative loop. Of these corrections the TOF impact on scatter is most notable.

The model-based scatter estimator in VUE Point HD calculates the scatter coincidence distribution predicted by the Klein-Nishina equation. It operates on every pair of coincident detectors (one for the scattered photon and one for the unscattered photon), and for every scatter point within the patient. For each combination of those parameters, the model computes the geometry of the scattered event.

Extending the scatter estimate to TOF imaging requires expansion of the geometry calculation for the coincidence event. Distance along the photons' trajectory is converted into timing difference, and the result for each element of the calculation may be assigned to a timing bin along the appropriate line of response as shown in figure 9. After all scattered coincidences have been assigned, the scatter estimate is then convolved by the timing response of the system to form the final TOF scatter estimate.

Many of the details of this method are described in US Patent 7,129,496:*Method and system for scattered coincidence estimation in a time-of-flight positron emission tomography system*, by C.W. Stearns and R.M. Manjeshwar.

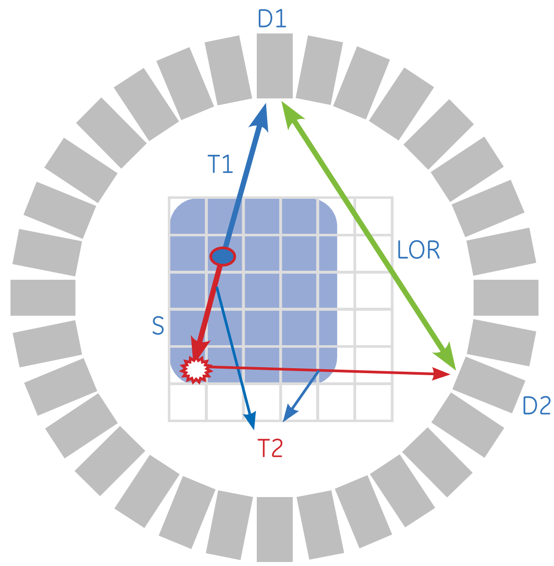

Figure 9: Conversion of flight distance into time difference for TOF scatter correction.

Sinogram datasets that contain TOF information are approximately 60 times larger than non-TOF equivalent. Combine that with the additional computational demands of the VUE Point FX algorithm and it is easy to understand the potential impact of reconstruction time on overall exam throughput. With that in mind the Discovery PET/CT 690 provides an exclusive use of the IBM BladeCenter™ architecture shown in figure 10. This platform enables the capability to reconstruct VUE Point FX data at a rate of approximately 2 minutes 30 seconds per FOV. Combine that with the prospective reconstruction manager that initiates each FOV from a multi FOV exam as soon as the data is available and you have an acquisition and reconstruction paradigm that supports VUE Point FX use for routine use in clinical exams.

Figure 10: IBM BladeCenter™ recon reconstruction engine

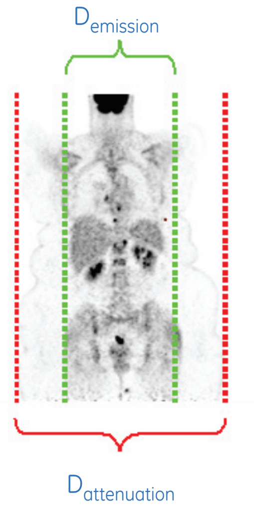

Figure 11: Common FDG bio-distribution for obese patients.

Clinical Experience

A prototype TOF PET/CT system was developed and sited in a mobile van outside Mayo Clinic, Rochester, MN in October, 2007. Under an IRB, patients who underwent normal clinical scans were consented for a second PET/CT scan in the mobile TOF unit immediately following their clinical procedure. 40 patients were acquired across a range of BMI. Non-TOF vs. TOF assessment was conducted on the self-consistent dataset acquired on the TOF unit by reconstructing with and without TOF information (VUE Point FX and VUE Point HD respectively). Four blinded physicians rated noise, lung boundary definition, overall image quality, and lesion conspicuity. The conclusions from that initial study were "Noise and overall image quality degraded as BMI increased for non-TOF and TOF while resolution and lung boundary was maintained for TOF. Generally the TOF images possessed greater contrast and delineation of activity, at the expense of slight increase in noise, which can be attributed to the different convergence rates for the TOF and non-TOF reconstructions. There was no significant increase in the conspicuity of lesions with TOF."[6]

Although there were some qualitative differences when applying TOF to the Mayo study, it was lower than originally anticipated through equation 1. As previously mentioned the first caveat to equation 1 is that it assumes a uniform activity distribution. In the Mayo experience we realized that as patients increase in BMI they often obtain a significant layer of lipid tissue surrounding normal sized organs. Since the lipid tissue has low uptake of FDG, the effective activity diameter for many obese patients is more consistent with that of a standard size patient as shown in figure 11.

To fully analyze the impact of this bio-distribution effect, a series of studies were conducted at GE's Global Research Center (GRC). Normal organ sizes and uptake distribution were simulated within a layer of lipid tissue with mild activity. Data was generated for temporal resolutions of 200, 500, 650 pico seconds and compared to non-TOF for both FBP and VUE Point FX algorithms. The image data are shown in figure 12. The difference between the FBP non-TOF and 650 ps TOF is very dramatic and seems consistent with the gains expected from equation 1. Likewise, the difference between non-TOF FBP and non-TOF VUE Point HD is very dramatic. However, the difference between the VUE Point HD (non-TOF) and 500 or 600 ps VUE Point FX reconstructions is far less significant. This speaks to the second caveat on equation 1, it appears consistent for FPB (the reconstruction method for which the equation was derived), but it doesn't seem to hold for iterative techniques. Further, it seems that iterative reconstruction done well has already achieved a significant gain toward the potential of TOF as compared to FBP. The TOF gains at 200 ps are more striking, but will require scintillator and photo sensor technology not currently commercially available.

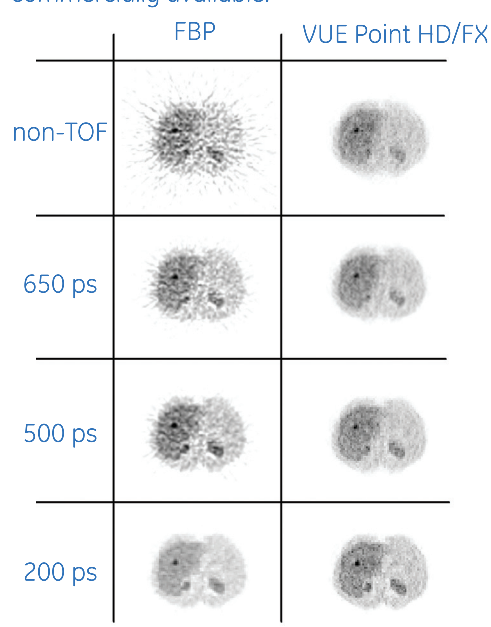

Figure 12: Obese patient simulation comparison for different time resolution and reconstruction options.

Although less than anticipated, there is an image quality impact of VUE Point FX reconstruction. GE launched the Discovery PET/CT 690 in October of 2008 and installed TOF enabled commerical systems at six global sites in December, 2008. Example images are shown in figures 13. Systematic evaluation of the clinical impact of TOF reconstruction with VUE Point FX is ongoing and will continue as the community of sites grows.

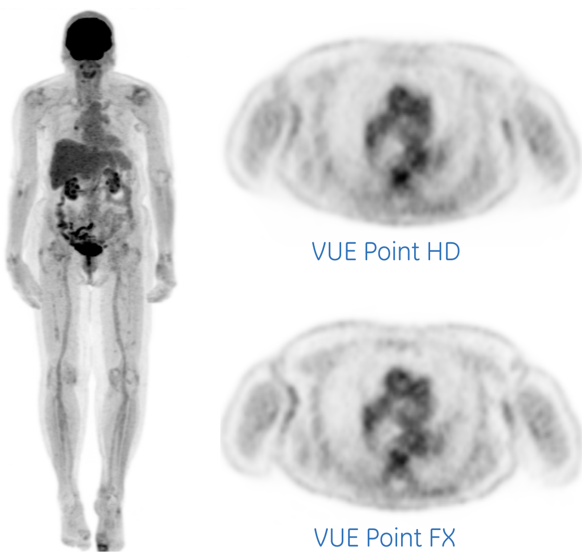

Figure 13: Clinical example from Discovery PET/CT 690.

Conclusions:

The experience with BaF2 TOF systems in the late 1980's is a key reminder that TOF in and of itself doesn't guarantee success. As with most system features, TOF requires a complete system design that does not overly sacrifice intrinsic slice sensitivity, provides adequate temporal resolution, maintains a stable temporal resolution across a range of operating conditions, applies sophisticated reconstruction techniques and provides reconstructed images in a timeframe consistent with the exam duration. Achieving these design requirements demands cutting edge technology that will not be obtained without expense.

Even with the best system design available today, the clinical impact of TOF has not been definitively demonstrated. Much of the value theory (such as equation 1) for TOF is based on outdated FBP reconstruction methodologies. In addition many large or obese patients don't exhibit a large FDG activity distribution diameter. From the recent literature there is no question that TOF provides some improvements to physics experiments and phantom measurements. There are limited data on clinical experience, but large studies that clearly establish the value have yet to be conducted. GE has developed a cutting edge TOF product and is actively engaged in the pursuit of understanding the potential clinical gains. In addition, TOF gains have to be compared to alternate avenues of improvement in clinical performance such as motion management for respiration, improved quantitative accuracy for response assessment, and workflow efficiency.

New technology is always exciting. The clinical question is whether the new technology provides an improvement in patient management and care that is commensurate to its expense. In the face of our challenging and dynamic global economic environment, GE is aggressively working to answer this critical question in the appropriate settings. As was communicated through our healthymagination program (www.healthymagination.com), our mission is to increase access, reduce cost and increase quality.

References

1) Lewellen et. al, Performance *Measurements of the SP3000/UW Time of Flight PET Emission Tomograph*, 1988 IEEE TNS

2) Lewellen, *Time of Flight PET*, 1997

3) Moses et. al, Prospect of Time of Flight PET using LSO scintillator, 1999 IEEE TNS

About GE Healthcare

GE Healthcare provides transformational medical technologies and services that are shaping a new age of patient care. Our broad expertise in medical imaging and information technologies, medical diagnostics, patient monitoring systems, drug discovery, biopharmaceutical manufacturing technologies, performance improvement and performance solutions services help our customers to deliver better care to more people around the world at a lower cost. In addition, we partner with healthcare leaders, striving to leverage the global policy change necessary to implement a successful shift to sustainable healthcare systems.

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