Cartesion Prime:
A Well-Balanced Digital PET/CT Scanner

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Introduction

The rising societal and economic impact of cancer, heart, and neurodegenerative disease has provided the impetus for research in precision medicine. One of the pillars of precision medicine is Positron Emission Tomography (PET) because it provides information on underlying molecular pathways and receptor expression by measuring the distribution of radiotracers *in vivo*. PET assists in diagnosis, staging, treatment selection and response assessment, plus radiation therapy planning. With the advent of theranostics and the rapid development of new radiolabeled therapeutic molecules and imaging biomarkers, PET is not only in the forefront of the standard of care today, but also the evolution of precision medicine.

Over the last decade, tremendous advancements in new instrumentation, data processing technologies, and new tracers have accommodated the aforementioned evolving role of PET and have resulted in great improvements in image quality, quantification, workflow, and patient comfort. One of the latest technical developments is the evolution of digital PET systems using Silicon Photo-Multiplier (SiPM) technology.

Canon is proud to introduce Cartesion Prime, a new premium digital PET/CT scanner enabling healthcare providers to facilitate to personalized care. Founded on innovative SiPM design, one-to-one coupling, 100% of crystal coverage, large axial field of view (FOV), fast time-of-flight (TOF) resolution, and air cooling technologies, Cartesion Prime provides excellent image quality and accurate quantification. Cartesion Prime provides optimized dose, scan times and throughput, as well as streamlined workflow, while balancing performance with investment.

Cartesion Prime PET Detector Design

Principles of PET Detector Design

Before a PET scan, tracers labeled with positron-emitting isotopes are injected into the patient. A positron produced by a radioactive nucleus travels a short distance, then annihilates with an electron. The

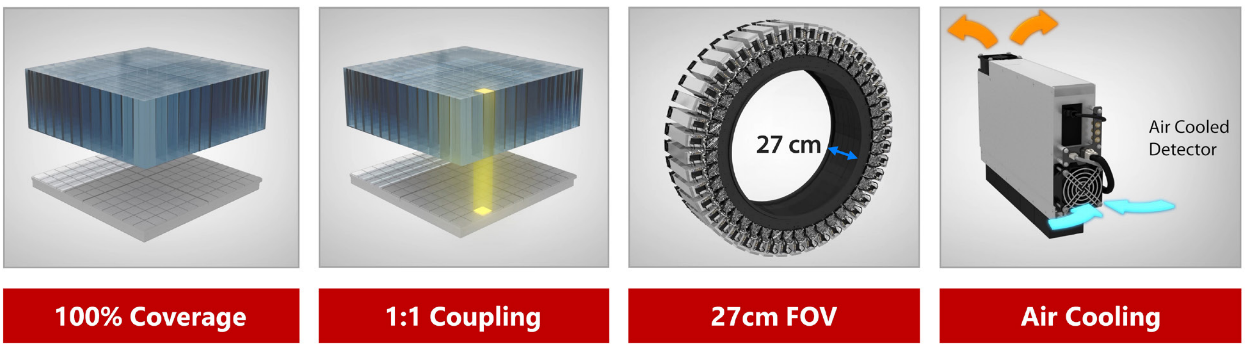

Figure 1 Balanced Detector Design

annihilation generates two back-to-back 511 keV photons inside the patient's body. These high-energy photons have to be detected and paired in coincidences to eventually determine the origin of the activity in the body. The PET detector comprises: a) scintillators that are used to stop the high-energy photon and convert its energy to low energy light photons, b) a light sensor that is used to generate an electric signal from these low energy photons, and c) an application-specific integrated circuit (ASIC) that processes the electric signal to estimate the position, energy, and arrival time of the event.

Lutetium-based scintillators such as LSO and LYSO are the choice of modern TOF PET scanners.[1] These scintillators have short decay time and can be used for TOF PET. On the other hand, they have high stopping power and very good light output so the efficiency of the detector is not compromised.

Most traditional PET scanners were designed using a photon multiplier tube (PMT) as a scintillation light sensor. Inside PMT, electrons are liberated on the photo-cathode by scintillation photons through photoelectric effect, and accelerated by a strong electric field. The electron flux is increased when the electrons collide with electrodes in the PMT, which is further accelerated to collide with succeeding electrodes, causing a large amplification of electron flux released from the anode of the tube. The final electron flux is proportional to the initial amount of electrons liberated from the photo-cathode, and the amplification factor is called the gain of the PMT. Figure 2(A) illustrates a traditional PET detector design using this approach. The size of PMT is much larger than the pixel size of the scintillator. Usually the scintillation light is shared among several neighboring PMTs and the scintillator crystal, where energy is deposited by the incoming high-energy photon is determined based on the ratios of these PMT signals, referred to as Anger logic.

Recently, SiPM has been developed to replace PMT as the scintillation light sensor.[2,3] SiPM is a solid-state photon counting device consisting of many avalanche photodiode (APD) microcells operating in Geiger mode. Figure 2(B) shows a conceptual design of a SiPM-based PET detector. The advantages of SiPM compared to PMT include better energy resolution, better spatial resolution, excellent timing resolution, and better edge crystal performance. It is also compact and operates with lower and safer voltage.

Well-balanced Detector Design

The Cartesion Prime PET detector was designed to achieve better image quality, improve throughput, optimize dose, and reduce total cost of ownership. Figure 3 shows the detector design. Each SiPM is coupled to a Lutetium-based scintillator. A 3 x 6 crystal-SiPM array is attached to a readout ASIC. A detector module contains eight such arrays placed in a 4 x 2 configuration totaling 12 x 12 channels. Finally five modules are assembled in the axial direction forming a detector unit. This detector design has the following features: 27 cm long axial FOV, one-to-one crystal-SiPM coupling, 100% coverage of scintillator area, and air-cooling.

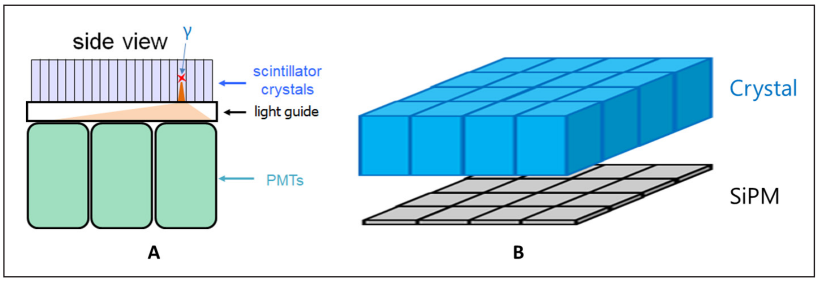

Figure 2 Conceptual PET detector using scintillator and PMT (A) or SiPM (B).

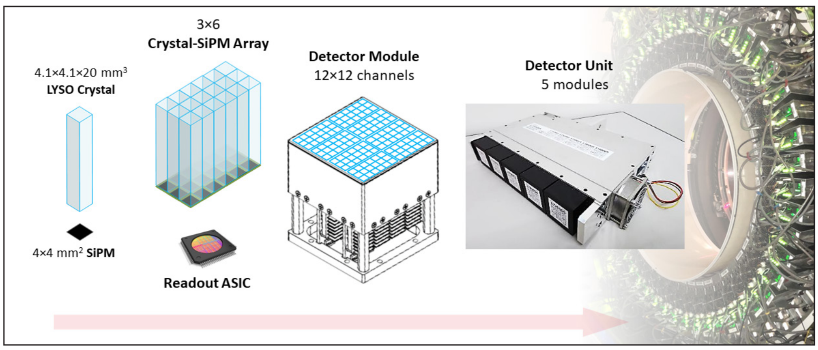

Figure 3 Cartesion Prime detector design.

Long Axial FOV

Traditional PET system designs have axial FOV ranging from approximately 16 to 22 cm.[4] While this is sufficient for imaging specific organs, such as brain or heart, it is not optimal for the majority of the PET scans, which cover from the base of skull to mid-thigh of the patient. Current generation PET detector designs extend the axial FOV with some of the recently developed total-body PET scanners using detectors with very long axial FOV (up to 2m), which are capable of covering the patient from the top of the head to the bottom of the feet.[5] However, the cost is very high and not practical for routine clinical uses.

Cartesion Prime has a long axial FOV of 27 cm, which is 23% to 69% longer than the traditional designs. By extending the axial FOV from 22 cm to 27 cm, the sensitivity of the system is increased by 51%, which enables operators to improve workflow and optimize the dose to the patient without compromising image quality.

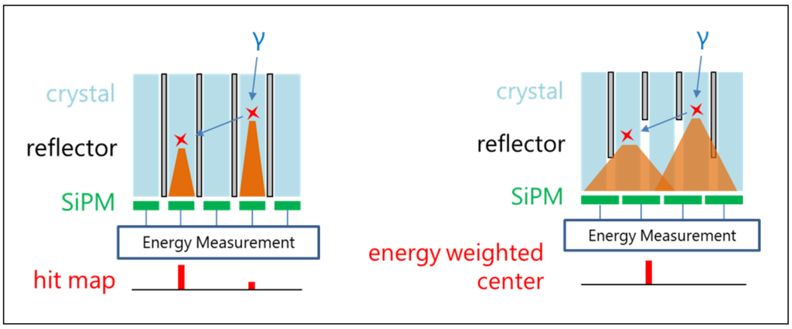

Figure 4 Two SiPM detector designs. Left: One-to-one coupling. Right: Light sharing.

Lutetium-based Scintillator

The size of the scintillator crystal is an important parameter of the system design. Smaller pixels improve spatial resolution, at the expense of reduced sensitivity. The thickness of the crystals also affects scanner performance. Thicker crystals have higher sensitivity, but the spatial resolution and timing resolution deteriorates. With Cartesion Prime, Canon chose a 4.1 x 4.1 x 20 mm^3 Lutetium-based scintillator crystal design, which balances the various requirements and optimizes the performance of the detector.

One-to-one Coupling

In Cartesion Prime, each scintillator crystal is connected directly to a SiPM cell. This one-to-one coupling design is shown in Figure 4 and compared to the light sharing design, where the SiPM is bigger than the crystal pixel and the scintillation light is received by several SiPMs. One-to-one coupling allows each scintillation photon to be detected and processed by a single SiPM cell. There are several advantages to this design. First of all, one-to-one coupling allows time to be measured from a single isolated SiPM/crystal channel with lower noise and higher output bandwidth, which translates to better timing resolution. Second, one-to-one coupling can eliminate the decoder error caused by using Anger logic when the 511 keV photon deposits all of its energy in a single crystal. Finally, one-to-one coupling design improves performance at a higher count rate.[6]

100% Coverage

In Cartesion Prime, the SiPM covers the entire scintillator area. This 100% coverage design ensures the highest photo-detection efficiency and improves the sensitivity and timing resolution of the scanner.

Compton Event Recovery

Nearly 40% of the 511 keV photons that hit the detector deposit energy in several scintillator crystals through Compton scattering. Because the energy of Compton events are biased by crosstalk, Cartesion Prime uses a multi-hit energy correction method that improves energy resolution. Canon also developed an inverse energy weighted position algorithm to improve spatial resolution of Compton events.

Timing Measurement

It has been proven that TOF information can be used to improve image quality. On Cartesion Prime, the detector was designed for optimal TOF performance, including the 20 mm thick Lutetium-based scintillator, one-to-one coupling between scintillator crystal and SiPM, plus 100% coverage of the scintillator area using SiPM. In addition, a fast time-over-threshold method is used for energy measurement. High speed comparators and high-resolution TDCs are used for timing measurement. As a result, Cartesion Prime achieves excellent typical timing resolution of 263 ps.

Air Cooling

One unique feature of Cartesion Prime is that the scanner is cooled using air. Compared to the traditional water-cooling PET/CT scanners, this design significantly reduces the complexity and cost of scanner siting, chiller requirements, maintenance and total cost of ownership.

This is made possible by several system design choices. First, the detector module is designed using highly-efficient, low-energy electronics. Second, the SiPM has a lower temperature dependency and operates in a wider temperature range compared to previous SiPM technologies. Third, a temperature compensation circuit is used to minimize the effect of temperature fluctuation on detector performance. Finally, the detector housing and scanner gantry is carefully designed using computational fluid dynamics to optimally distribute the airflow inside the gantry to reduce hotspots.

Detector Calibration

Periodic detector calibration is crucial to ensure the optimal performance of the scanner. Cartesion Prime utilizes several innovative methods to simplify the workflow and reduce processing time, while improving the calibration results.

To achieve the excellent timing resolution on Cartesion Prime, it is important to have an accurate, fast, and convenient timing calibration method. Canon has developed a novel timing calibration method using a

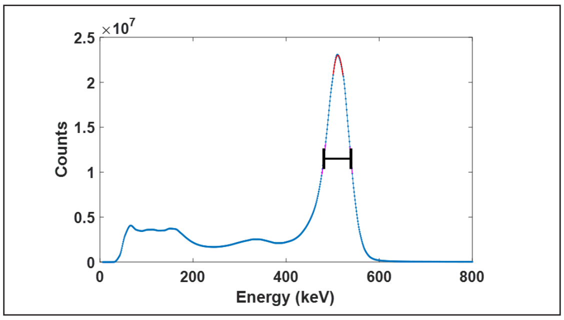

Figure 5 Cartesion Prime system energy resolution measured using a ^{68}Ge line source.

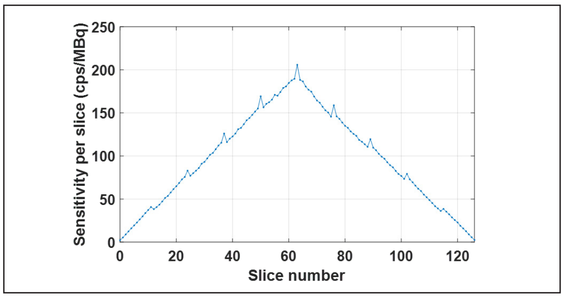

Figure 6 Axial sensitivity profile with line source at scanner iso-center.

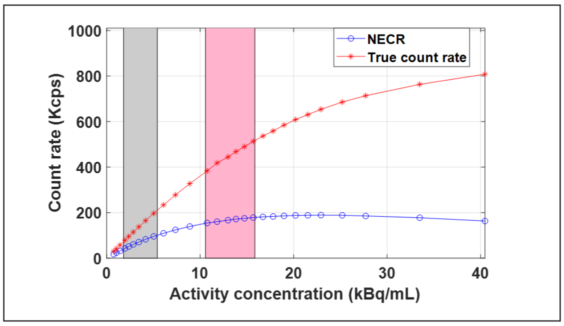

Figure 7 NECR and true count rate curves. Gray area: FDG whole body scan range (5-15 mCi injection, 60 minutes uptake). Pink area: ^{82}Rb cardiac scan range (20-30 mCi injection, start scan immediately).

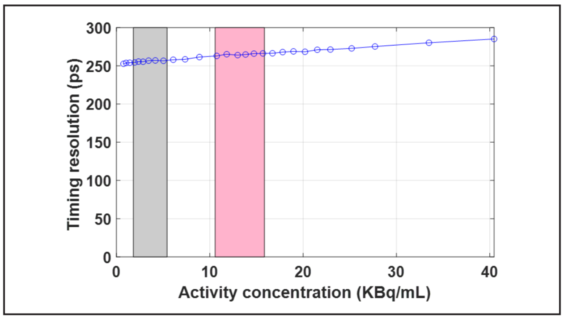

Figure 8 Timing resolution measured using NEMA count rate phantom. Gray area: FDG whole body scan region (5-15 mCi injection, 60 minutes uptake). Pink area: 82Rb cardiac scan range (20-30 mCi injection, start scan immediately).

centered ^{68}Ge line source and Lutetium background, which can be done in a few minutes and achieves excellent timing resolution (263 ps typical).[7]

Crystal efficiency normalization is an important part of scanner calibration. Usually a large uniform cylindrical phantom or a rotating line source is used for normalization. On Cartesion Prime however, a new approach using a stationary line source was developed.[8] This method is more convenient, especially for long axial FOV scanners like Cartesion Prime.

Scanner Performance

Phantom Measurements

Energy Resolution

The energy performance was measured by placing a 2.4 mCi ^{68}Ge line source at the center of the scanner FOV.[9] The energy resolution was characterized from the coincidence energy histogram after correcting for random events as shown in Figure 5. The measured energy resolution was 11.4% FWHM.

NEMA Testing

NEMA testing has been performed and reported previously.[9] Here we briefly summarize the results.

The sensitivity was measured using ^{18}F-FDG line source inside five metal sleeves according to NEMA NU 2-2018 standard. The timing resolution, the noise equivalent count rate (NECR), and the scatter fraction versus activity concentration curve were measured according to NEMA NU 2-2018 standard across clinically relevant count rates. Image quality was characterized by filling the NEMA image quality phantom with a sphere to background ratio of 4:1 and scan for 4 minutes. Standard clinical reconstruction (TOF-OSEM) and correction setting was used. Regions of interest were drawn according to NEMA NU 2-2018 standard.

The measured sensitivity was 13.5 kcps/MBq when line source was at the scanner iso-center and 10 cm when off center. Figure 6 shows the axial sensitivity profile when the line source was placed at the scanner iso-center. Peak NECR was 189.2 kcps which was achieved at 22.9 kBq/ml. Figure 7 shows the NECR and true count rate curves. The measured true count rate was still increasing at 40.5 kBq/ml.

Figure 8 shows the timing resolution measured across different count rates. The timing resolution ranged from 258 ps at average effective radioactivity concentration of 5.3 kBq/mL to 271 ps at peak NECR. At 5.3 kBq/mL average effective radioactivity concentration, the scatter fraction is 35.7%. Figure 9 shows a transaxial slice of the NEMA image quality phantom and measured contrast recovery coefficients and background variabilities of the spheres with different diameters. The contrast recovery coefficient ranged from 46.6% for the 10 mm diameter sphere to 84.6% for the 37 mm diameter sphere. The background variability ranged from 5.7% to 2.4%.

Scanner Performance Stability

The timing resolution and energy resolution of a Cartesion Prime scanner were measured over a 5-month period. The results are shown in Figure 10. The range of measurement was 263 ps to 268 ps for timing resolution and 11.4% to 11.7% for energy resolution.

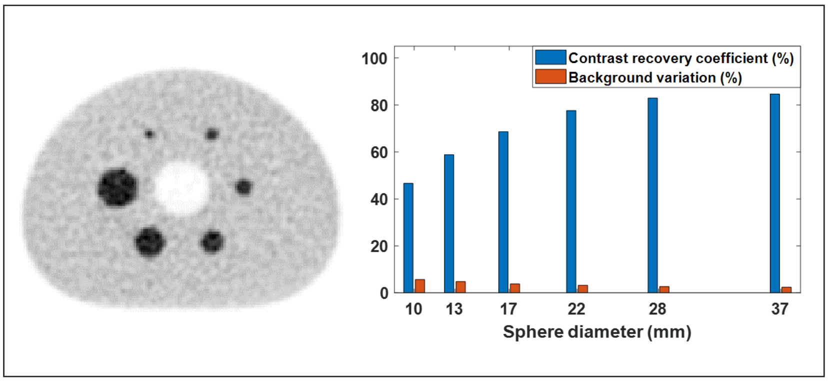

Figure 9 Left: Transaxial slice through the NEMA image quality phantom with a sphere to background ratio of 4:1. Right: Contrast recovery coefficient and background variability for all hot spheres.

TOF Gain and Effective Sensitivity

It can be shown that using TOF information in image reconstruction can significantly improve the signal-to-noise ratio (SNR) of the image. Therefore, TOF can be used to reduce counts (through less injected dose or shorter scan time) needed to maintain image quality compared to non-TOF.[10,11] TOF technology can possibly reduce radiation dose, PET scan time, and overall table time for improved workflow and patient satisfaction during PET procedures. The dose (or time) reduction factor, also known as the TOF gain, can be estimated using the following equation[10,12]:

$$\frac{SNR_{TOF}^{2}}{SNR_{Non-TOF}^{2}} = \frac{2D}{c\Delta t}$$

where D is the diameter of the subject being imaged and Δt is the timing resolution. Figure 11 shows the TOF gain of several objects size—timing resolution combinations. Cartesion Prime has a typical timing resolution of 263 ps, so the typical TOF gain is 5.1 for 20 cm diameter subjects and 12.7 for 50 cm diameter subjects.

The product of NEMA sensitivity and TOF gain is called TOF effective sensitivity. Improved TOF gain results in improved effective sensitivity for the same sensitivity with a larger benefit demonstrated in imaging of larger patients.

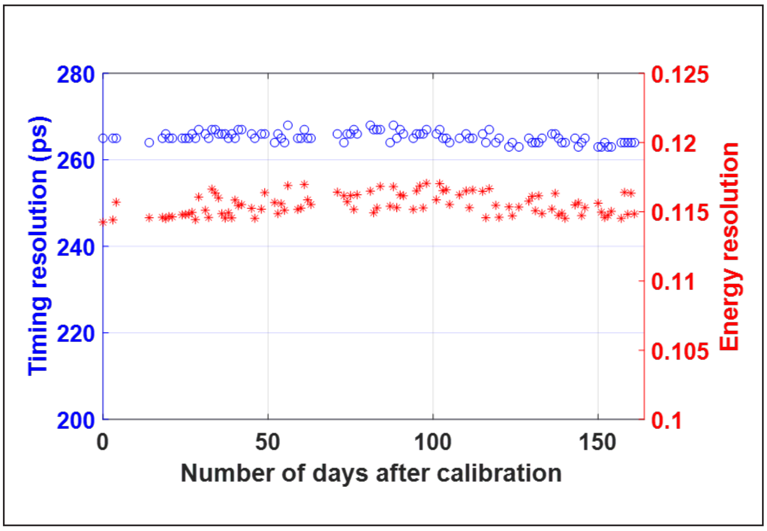

Figure 10 Timing resolution and energy resolution of a Cartesion Prime scanner over 5 months.

Patient Studies

Brain Scan

Figure 12 shows brain ^{18}F-FDG scans of a patient. The patient was injected with 285 MBq (7.7 mCi) of ^{18}F-FDG and waited for 48 minutes before scanned on a Cartesion Prime PET/CT for 7.5 minutes. The image was reconstructed using a 3D TOF listmode OSEM method using 5 iterations and 12 subsets, followed by a Gaussian filter with 4 mm FWHM.

Whole Body Scan

Figure 13 shows the whole body ^{18}F-FDG scans of a patient (BMI 24.3) with metastatic squamous cell carcinoma of the left upper lobe. The patient was injected with 289 MBq (7.8 mCi) of ^{18}F-FDG and waited for 56 minutes before scanned on a Cartesion Prime PET/CT for 7 beds with 2 minutes per bed and 50% bed overlap. Image was reconstructed using 3 iterations and 12 subsets, followed by a Gaussian filter with 6 mm FWHM.

Variable Bed Time (VBT) Whole Body Scan

Figure 14 shows the ^{18}F-FDG scans of a patient (5'10" tall, BMI 24.3) scanned from the top of the head to the toes. The patient was injected with 274 MBq (7.4 mCi) of ^{18}F-FDG and waited for 67 minutes before scanned on a Cartesion Prime PET/CT. This scan was done using the variable bed time feature, with 5 beds at 2 minutes each and 6 beds at 90 seconds each. The bed overlap was kept at 50%. The total scan time was 19 minutes. Image was reconstructed using 3 iterations and 12 subsets, followed by a Gaussian filter with 6 mm FWHM.

Low Dose ¹⁸F-FDG Scan

One of the benefits of Cartesion Prime is the potential to reduce injected dose.* Here we show two examples. The first patient is shown in Figure 15. This patient (BMI 20.7) was injected with 198 MBq (5.4 mCi) of ^{18}F-FDG and waited for 60 minutes before being scanned on a Cartesion Prime PET/CT. The acquisition protocol included 7 bed positions with 90 seconds per bed and 50% bed overlap. The liver shows homogeneous uptake. Normal FDG uptake is shown in the left ventricular muscle.

Figure 16 shows a follicular lymphoma patient (BMI 22.2) injected with 254 MBq (6.9 mCi) of ^{18}F-FDG scanned on a Cartesion Prime PET/CT with 90 seconds per bed for 7 bed positions. The tumor is clearly delineated in the image. Also note the physiological uptake of ^{18}F-FDG in the spinal cord is clearly seen in the sagittal image. These

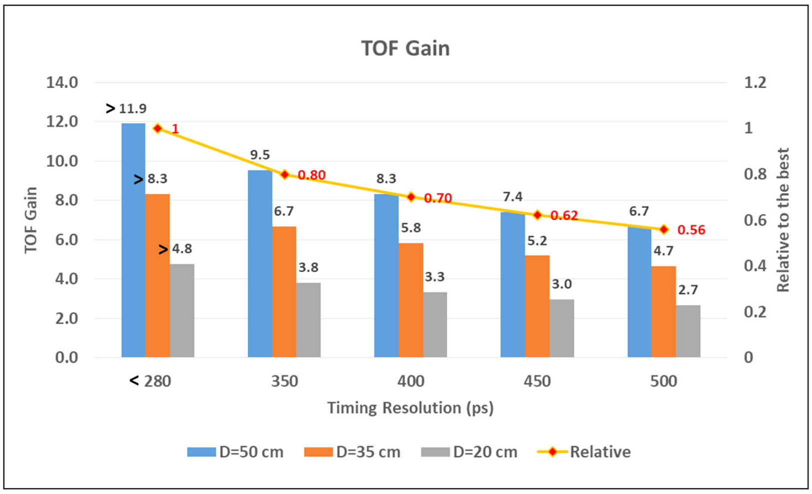

Figure 11 Example of TOF gain for several subject size and timing resolution combination.

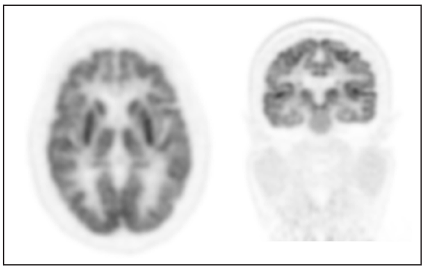

Figure 12 Axial and coronal images of ^{18}F-FDG brain scans of a patient with memory loss and lower extremity weakness.

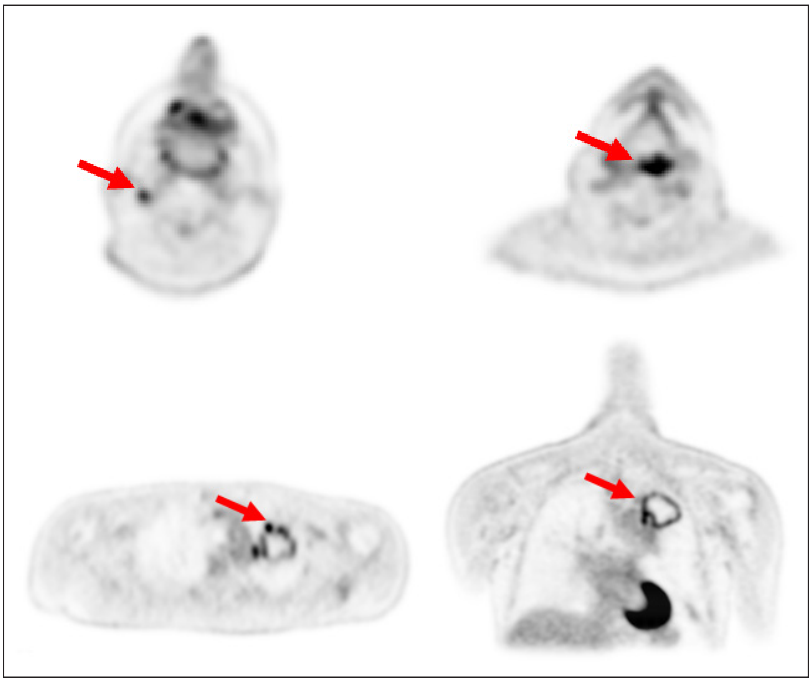

Figure 13 Images of ^{18}F-FDG whole body scans of a patient. Top left: Axial image shows a FDG avid right cervical node. Top right: Axial image shows focal FDG uptake in the left base of the tongue. Bottom left: Axial image shows necrotic primary lung mass. Bottom right: Coronal image shows necrotic primary lung mass.

Figure 14 ^{18}F-FDG image of a patient scanned from the top of the head to the toes in 19 minutes.

**Injected dose is prescribed by the drug manufacturer. Any decision to alter a prescribed dose is a medical decision that must be made by a physician who has deemed this medically necessary.*

two examples demonstrated the capability of Cartesion Prime to generate high quality ^{18}F-FDG PET images of adult patients using a dose as low as 200 MBq (5.4 mCi).

Reduced Scan Time Per Bed

We also explored the possibility of reducing scan time per bed. A breast cancer patient (BMI 25.3) was injected with 307 MBq (8.3 mCi) of ^{18}F-FDG and waited for 65 minutes before being scanned on a Cartesion Prime PET/CT. The acquisition protocol included 5 bed positions with 2 minutes per bed and 50% bed overlap. Two more datasets were generated by randomly sampling the list mode file to extract a fraction of counts equivalent to 60 seconds and 90 seconds per bed respectively. All three datasets were reconstructed using 3 iterations and 12 subsets, followed by a Gaussian filter with 6 mm FWHM. Figure 17 compares the images reconstructed from all three datasets. The 60 sec/bed image shows a slight increase in noise. The images were reviewed by two experienced physicians and all three images were deemed adequate for diagnosis purposes.

Conclusions

Canon Medical's digital PET/CT technologies are designed to navigate the path to personalized care. Combining years of product development with the latest digital PET innovations, Canon has created Cartesion Prime PET/CT, a system that delivers exceptional image quality at high speed with accurate quantification and low dose. We have achieved this by exploiting the abilities of digital PET to achieve high photon detection efficiency, increased sensitivity, timing resolution, and compact packaging to provide:

- ✓ SiPM photosensors
- ✓ 100% coverage
- ✓ One-to-one coupling
- ✓ 263 ps timing resolution (typical)
- ✓ 27 cm Axial FOV
- ✓ Air-cooling technology

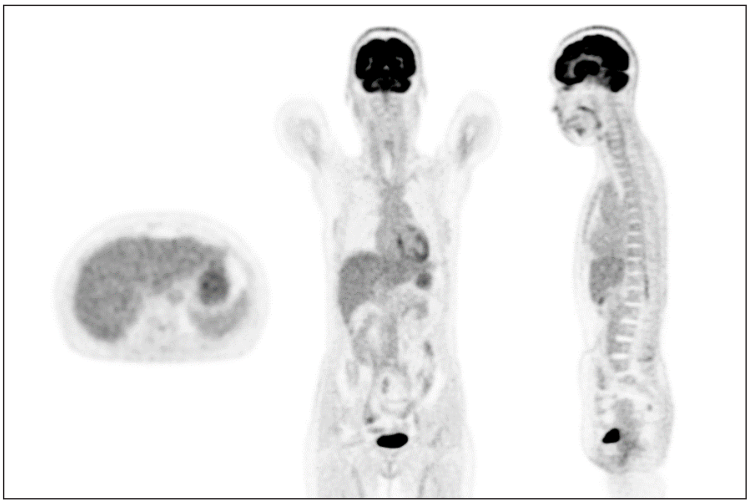

Figure 15 Image of a patient injected with 198 MBq of ^{18}F-FDG and scanned in 10.5 minutes.

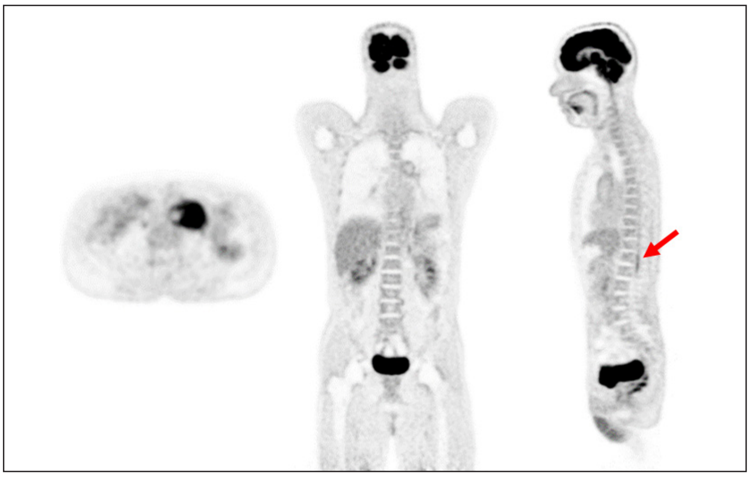

Figure 16 Image of a patient injected with 254 MBq of ^{18}F-FDG and scanned in 10.5 minutes. Arrow shows physiological spinal cord uptake.

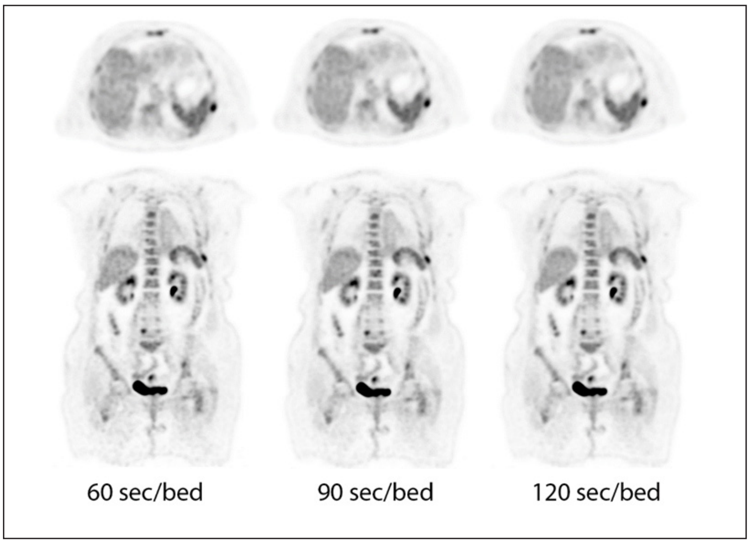

Figure 17 Images of ^{18}F-FDG whole body scans of a patient scan, reconstructed from data equivalent to 60 sec/bed, 90 sec/bed and 120 sec/bed.

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The clinical results described in this paper are the experience of the author(s).
Results may vary due to clinical setting, patient presentation and other factors.

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