Truly **digital** PET imaging

Philips proprietary Digital Photon Counting technology

Vereos PET/CT is the first commercially available scanner to offer truly digital PET, resulting in significantly improved performance compared with an analog system.* Digital PET is made possible through a number of advances, including proprietary digital photon counting (DPC), 1:1 (pronounced “one-to-one”) coupling between the scintillator element and the light-sensing element, and faster Time-of-Flight (TOF) technology.

Philips DPC technology was developed to overcome the limitations of conventional photomultiplier technology. DPC in combination with 1:1 coupling and enhanced TOF allows the Vereos system to offer approximately double the volumetric resolution, sensitivity gain, and accuracy of a comparable analog system.*

Overcoming limitations of conventional PET

Key advances contribute to the high level of performance of Vereos digital PET/CT:

1. Digital photon counting (DPC)
2. Detector tile design
3. DPC and 1:1 coupling
4. Factors influencing performance specifications
5. Timing resolution and TOF technology
6. Point spread function (PSF) technology
7. Technology pillars supporting improved performance

Vereos PET/CT specifications

Preliminary performance data, subject to change.

Number of detectors	23,040
System spatial resolution	4.1 mm
Effective system sensitivity**	23.4 kcps/MBq
Effective peak NECR**	687 kcps @ 50 kBq/mL
Maximum trues	>800 kcps
System timing resolution	310 ps
Quantitative accuracy	± 5%

* GEMINI TF

** Effective gain defined as a ratio between patient size (20 cm diameter used in these specifications) and TOF localization accuracy.

Digital photon counting (DPC)

At the heart of the digital PET system is Philips proprietary digital photon counting (DPC) technology. This was developed in order to overcome the limitations of conventional photomultiplier technology.

During a PET scan, detectors need to be able to accurately pick up and locate the pairs of high-energy photons that are emitted when positrons, produced by the decay of the radioactive tracer that is introduced into the body before the scan, interact with electrons in the body. Scintillating crystals are used to collect these pairs of high-energy photons and convert them to visible light, which is then picked up by a light sensor, with the output being an electronic signal (ultimately used to construct the resulting image).

Different types of light sensors have been developed over the years: arrays of photomultiplier tubes (PMTs), avalanche photodiodes (APDs), analog silicon photomultipliers (SiPMs), and now – as used in the Vereos PET/CT system – DPC technology.

The older technologies have limitations. PMTs are widely used today, and were the foundation of PET imaging. However, PMT design has reached its limits in counting performance, due to the relatively large size of the device and the timing resolution.

APDs have been used in PET systems for many years, but although they have a higher sensitivity than PMTs, APDs offer lower internal gain and no TOF capability.

Analog SiPMs use single photon avalanche diode (SPAD) arrays. These are capable – as the name suggests – of detecting single photons. However, when used in conventional analog SiPMs, the pulses generated by multiple photon detections (avalanche diode breakdowns) are combined into an analog output signal that requires extensive off-chip processing to produce a photon count and time of arrival for the photon (see **Figure 1**). Also, analog noise interferes with the signal, making it even harder to exactly determine the number of photons and the time of arrival.

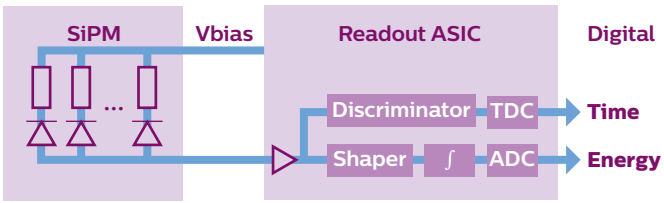

Figure 1 Processing of the analog signal in conventional analog SiPMs. Reproduced from: Frach T, Prescher G, Degenhardt C. Silicon photomultiplier technology goes fully digital. Electronic Engineering Times Europe, January 2010.

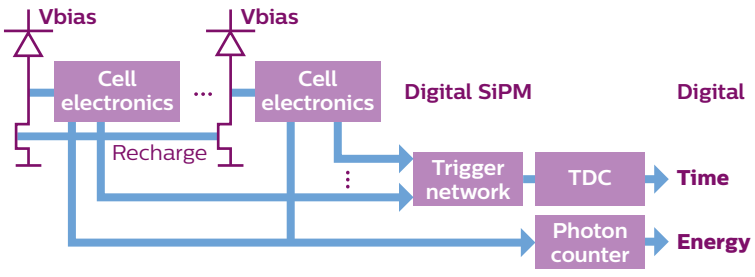

Figure 2 Digital in/digital out photon counting in digital SiPMs. Reproduced from: Frach T, Prescher G, Degenhardt C. Silicon photomultiplier technology goes fully digital. Electronic Engineering Times Europe, January 2010.

In contrast to analog SiPMs, the digital SiPMs seen in Philips DPC technology enable the detection and counting of the breakdown of individual SPADs on-chip. Light photons produced by the scintillator are counted directly by the chip, yielding a pure binary signal (0 or 1). This is achieved without the need for amplification or off-chip analog-to-digital processing of the signal (see **Figure 2**), minimizing signal noise.

Conventional CMOS (complementary metal-oxide-semiconductor) process technology is used to combine SPADs and low-voltage CMOS logic on the same silicon substrate. With both the sensor and the data processing now on a single silicon chip, photon counting in ultra-low light levels (down to single photons) is faster, more accurate, and fully scalable.

In practice, how are the DPC measurements made?

During a scan, when the first photon reaches a sensor the integrated (on-chip) photon counter increases to 1, and the integrated timer measures the arrival time of the first photon (**Figure 3**, top left). When the second and third photons hit sensors, the photon counter increases to 2 and 3 respectively (**Figure 3**, top right and bottom left). At the end of the desired length of the detection process, the values of the photon counter and timer can be read (**Figure 3**, bottom right).

Data acquisition is initiated by a trigger signal, generated when the number of photons detected in a pixel becomes higher than the configured trigger threshold.

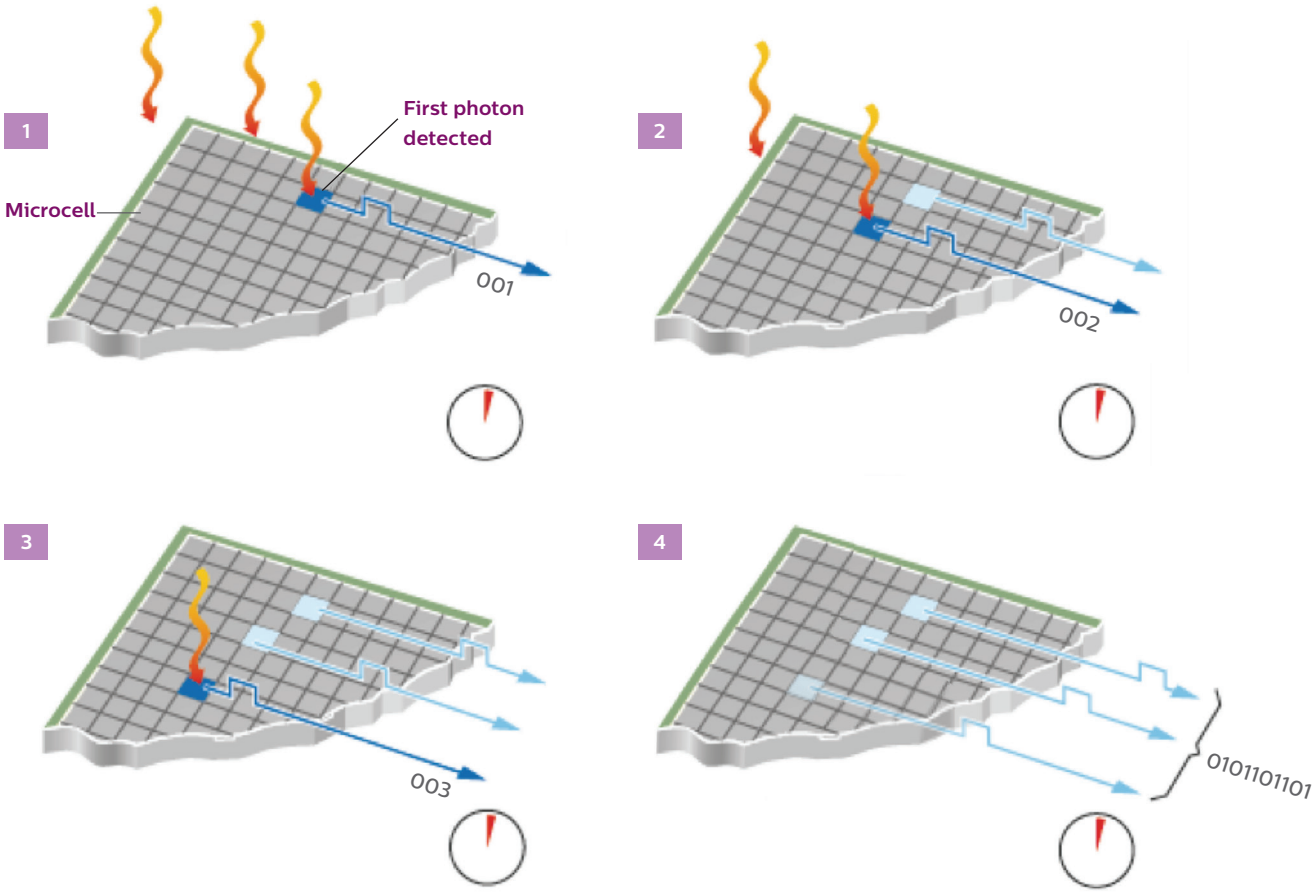

Figure 3 Digital photon counting in practice, showing the arrival and detection of individual photons, and timing measurements.

Detector tile design

The DPC technology used in the Vereos system takes the form of highly integrated arrays, or tiles, that contain more than 200,000 cells, each of which is capable of detecting a single photon.

Each tile consists of 16 independent die sensors, arranged in a 4 x 4 matrix. Each die sensor consists of four pixels, arranged in a 2 x 2 matrix. Each of these pixels contains 3,200 cells.

Each of the four pixels on a die has a photon count value. Each die contains a pair of time-to-digital converters, which generate a single timestamp for registered photon detection events.

The generation of a trigger signal – when the number of photons detected in a pixel becomes higher than the configured threshold – prompts a timestamp to be saved, and begins a validation process to detect a user-configured number of further photons within a certain time. If this validation threshold is exceeded, there is a subsequent integration period before a readout process sends data (four photon count values – one per pixel on the die – and one timestamp per event) to a readout buffer. After readout, the cells are recharged so that the die is ready for further data acquisition. Cells are also recharged immediately if the original event is not validated. **Figure 4** shows the full data acquisition sequence, and the timings involved.

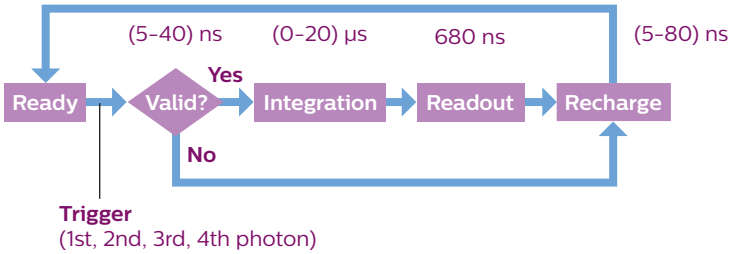

Figure 4 The data acquisition sequence within each die in a digital SiPM.

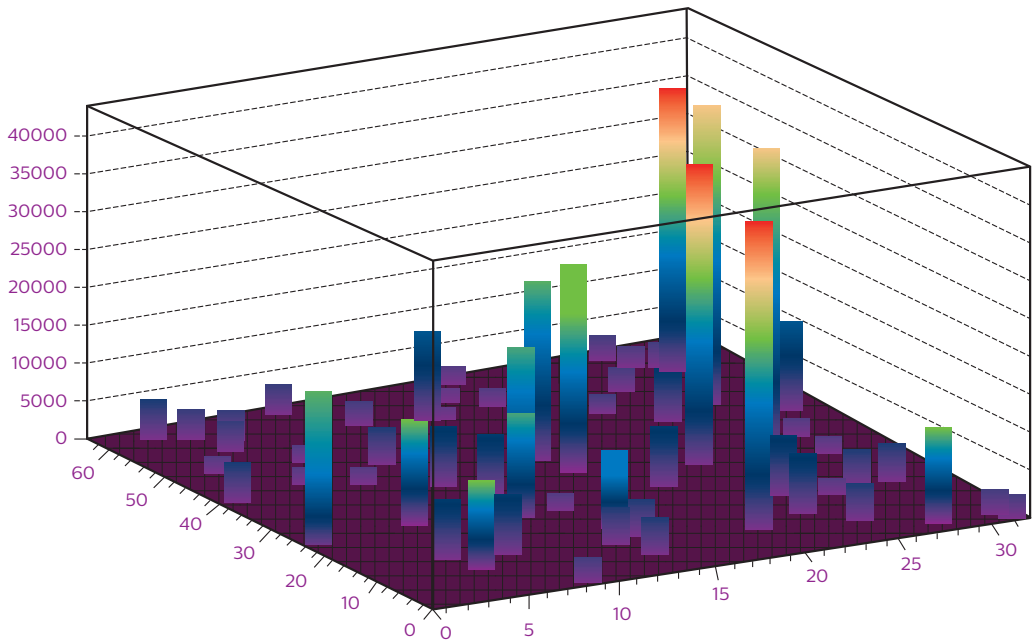

Figure 5 **Dark counts of cells in a sub-pixel, at room temperature.** Reproduced from Haemisch Y, et al. Physics Procedia 2012;37:1546-60.

The design of the DPC technology allows every cell to be individually activated or inactivated. This means that background noise – the dark count rate – can be measured and managed effectively.

By switching on and off each individual cell, in a fully dark environment, a map of dark counts can be produced automatically by the system (see **Figure 5** for an example). A cumulative logarithmic plot of dark counts (see **Figure 6**) shows that the overall dark count rate is greatly reduced by switching off the noisiest cells.

The DPC technology is also much less sensitive to temperature variations than conventional analog SiPMs. In analog SiPMs, the temperature dependence of the ionization coefficients and holes in silicon leads to a temperature-dependent drift in each sensor's breakdown voltage and a change in gain. In DPC technology, any shift in breakdown voltage must exceed the threshold voltage of the CMOS inverter before the count rate is affected since the logic gate just looks for voltage above or below the CMOS threshold, not the amount of charge.

The implications of DPC and 1:1 coupling will be discussed in the next section.

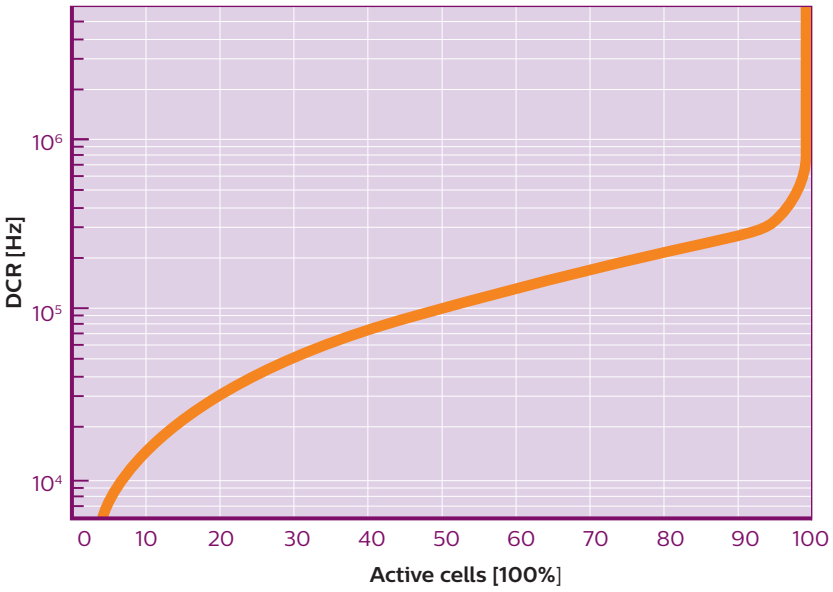

Figure 6 A cumulative logarithmic plot of dark count rate as a function of the number of active cells. Reproduced from Haemisch Y, et al. Physics Procedia 2012;37:1546-60.

DPC and 1:1 coupling

In the detectors used in the Vereos PET/CT system, each scintillator is connected to a single detector pixel. This is called 1:1 coupling (see **Figure 7**).

The 1:1 coupling of scintillator crystals to detectors, coupled with fast timing resolution, reduced pile-up effects, and TOF benefits, allows for a much higher count rate capability compared to analog* systems.

The direct 1:1 coupling also results in an improved spatial resolution. The final spatial resolution of a PET image is the result of multiple factors, some related to the annihilation events and interactions (such as non-co-linearity of annihilation photons, and the positron range), and others related to the detection system (such as the scintillation crystal size and crystal identification, or decoding). In the Vereos system, with 1:1 coupling, the contribution of the decoding is eliminated. A related improvement comes from the elimination of distortions and edge effects in the decoding. PMT-based detectors typically have worse resolution directly underneath the tubes and at the edges of the field of view. With 1:1 coupling, the crystal identification is uniform across the entire detector, resulting in a more uniform image.

Because they are pixelated, the digital detectors in Vereos also show a uniform response across their surface, and across the entire field of view. This is in contrast to analog PMT-based systems that use Anger logic for crystal identification, where the response varies across the detector and is worse directly underneath the PMTs and at the edge of the field of view. 1:1 coupling eliminates this effect in Vereos.

Users will also benefit from Vereos' high peak true rate (≥ 800 kcps), also known as the maximum true rate. This is the maximum count rate of true coincidences, which occurs at a certain level of activity, beyond which the system is paralyzed. With Vereos, researchers can perform high count rate studies, such as short-lived isotope dynamic and bolus imaging, while maintaining sensitivity – important for quantitative accuracy.

> "There is non-uniform behavior across PMT-based detector modules that impacts image quality and quantitation. With Philips digital photon counting technology, we deliver uniformity throughout."
>
> *Chi-Hua Tung, Director*
> *Advanced Molecular Imaging, Philips*

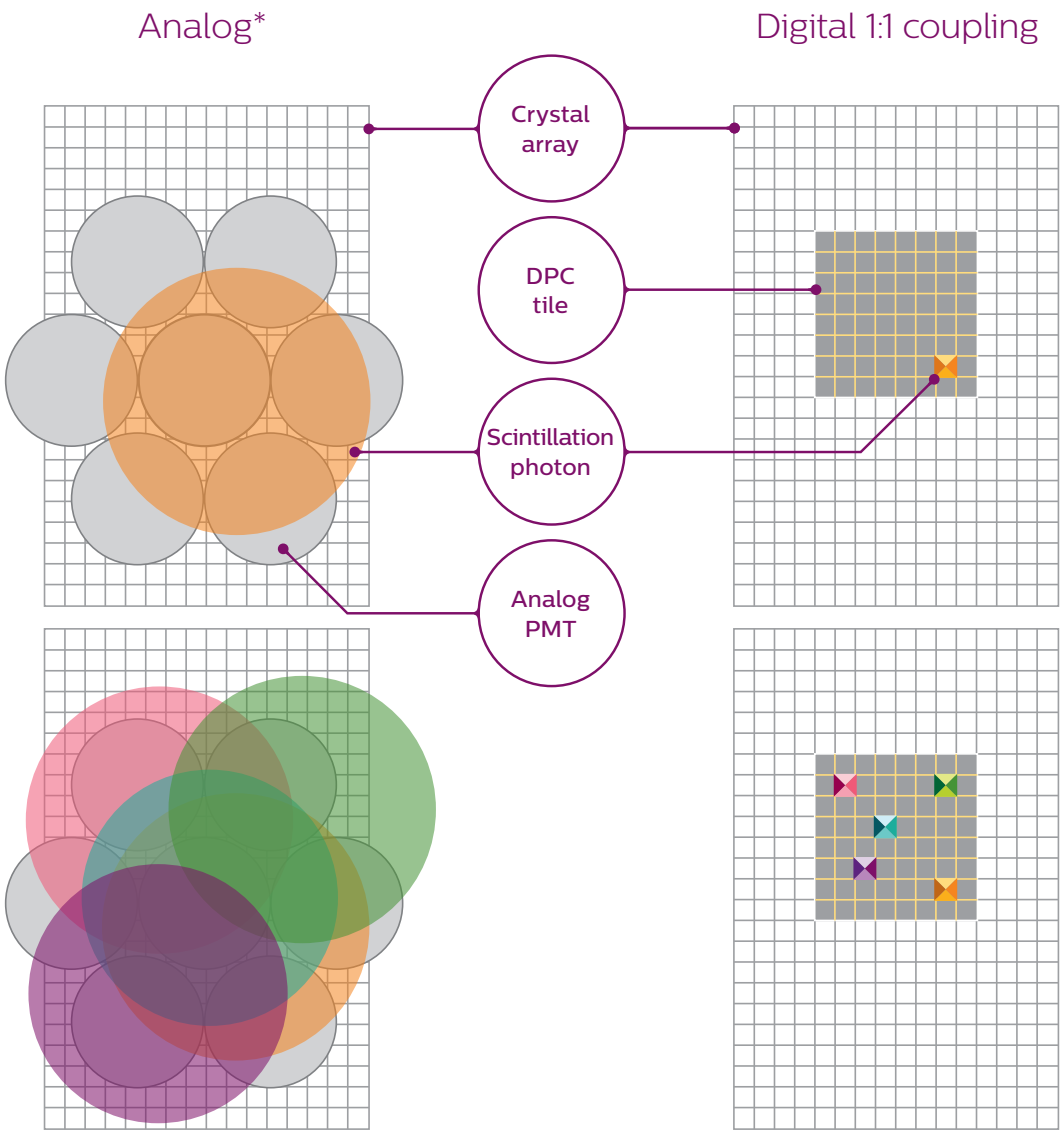

Figure 7 Comparison of analog* and digital photon counting. A PMT covers multiple crystals in the analog* system, while the digital system shows 1:1 coupling between scintillator crystals and single photon counters.

*GEMINI TF

Factors influencing performance specifications

A number of different factors influence and enhance the performance specifications of the DPC technology used in the Vereos system.

List mode-based TOF reconstruction

Vereos uses list mode TOF reconstruction. The list mode reconstruction method does not require any binning of the raw data. Event location and time of flight information are retained without degradation from binning, providing exceptional image quality and quantitation.

Energy resolution and spectrum/system dead time

The 1:1 coupling and sharp detection pulses seen with the DPC technology in Vereos effectively eliminates problems caused by coincident event pile-ups and electronic drift seen with analog systems. These problems can occur in analog* systems if there is a high level of activity and two or more events are detected almost simultaneously. In terms of resolution and the energy spectrum, pulse pile-up and drift cause good counts to be pushed out of the observed energy window, in favor of scatter counts. In terms of system dead time, the overlapping of the distributions for almost simultaneous events means a loss of sensitivity and the system will be partially dead at high count rates.

Comparison of dead time factors**

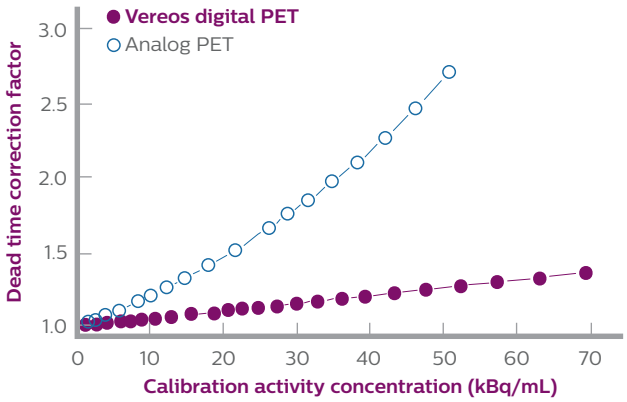

Figure 8 Comparison of dead time correction factors measured on Vereos digital PET and analog PET (Ingenuity TF).

The benefits of 1:1 coupling in terms of dead time are further illustrated by a plot of dead time factors against activity concentration for Vereos and an analog* system (see **Figure 8**). Dead time factors are defined as the inverse of the actual measured counts divided by the expected counts. As **Figure 8** indicates, at a clinical activity concentration of 10 kBq/ml which is typical of most whole body studies, Vereos has a deadtime factor of 1. In contrast, we see a higher dead-time factor of 1.17 for the analog* system. This effectively translates into an additional 17% sensitivity gain for Vereos.

Sensitivity measurement

NEMA (National Electrical Manufacturers Association) sensitivity is a measure of a system's ability to convert positron emissions to raw counts. However, this measure was developed for analog systems and does not take into account the quality of counts, such as the impact of TOF, the spatial resolution, and the degradation with high count rate (or dead time). Therefore, for superb sensitivity, obtaining good counts is more important than obtaining many mixed counts.

Digital PET offers real sensitivity gains, largely due to the application of TOF. The effective sensitivity gain is $D/\Delta x$, where D is the object diameter and Δx is position uncertainty along the line of response, equal to the speed of light (c) multiplied by time resolution divided by 2 ($\Delta t/2$).

Calculations for a range of object diameters show a TOF gain with Vereos of 3.9 for an object with a diameter of 20 cm, 5.8 for an object with a diameter of 30 cm, and 7.7 for an object with a diameter of 40 cm – objects approximately representing a brain, small body, and large body respectively [Philips, data on file].

Reconstruction and noise

The process of reconstruction involves mathematically estimating the original radioactivity distribution, based on the collected dispersed data. This brings with it penalties in terms of noise. However, Vereos' 1:1 coupling of crystals to sensors, better TOF resolution, and more uniform detector response reduce the reconstruction noise. Less noise translates into increased sensitivity.

* Ingenuity TF

** Results are based on a uniform phantom (20 cm diameter and 30 cm long); Vereos results are preliminary and may be changed

Timing resolution and TOF technology

In conventional non-TOF PET, the image reconstruction process must assume that there is a uniform probability that the annihilation event occurs at any one point along the line of response (LOR). This major limitation has been overcome by the development of TOF technology.

Vereos has a fast timing resolution of just 310 ps (currently the fastest resolution on the market). This is the minimum time interval between two photon events required for them to be recorded as separate events. In systems with fast timing resolution, TOF is able to be used to locate each annihilation event on a specific part or segment of the LOR. The difference in flight time for the two photon events is used to produce a more localized distribution of probabilities (see **Figure 9**). For Vereos, the TOF localization accuracy is 4.6 cm.

This has the effect of improving effective sensitivity and image quality, and the speed of processing. With effective sensitivity gain defined as $D/\Delta x$ (where D is the object diameter and Δx is position uncertainty along the LOR), reducing the position uncertainty through the application of TOF leads to a real sensitivity gain.

Calculated effective sensitivity gains for Vereos, due to the benefits of TOF technology, demonstrate greater gains for larger diameter objects: 3.9 for a 20 cm diameter, rising to 7.7 for a 40 cm diameter [Philips, data on file]. TOF may be particularly beneficial in larger, heavier patients, as increased levels of attenuation and scatter in these patients would typically result in poor quality PET images in the absence of TOF.[1]

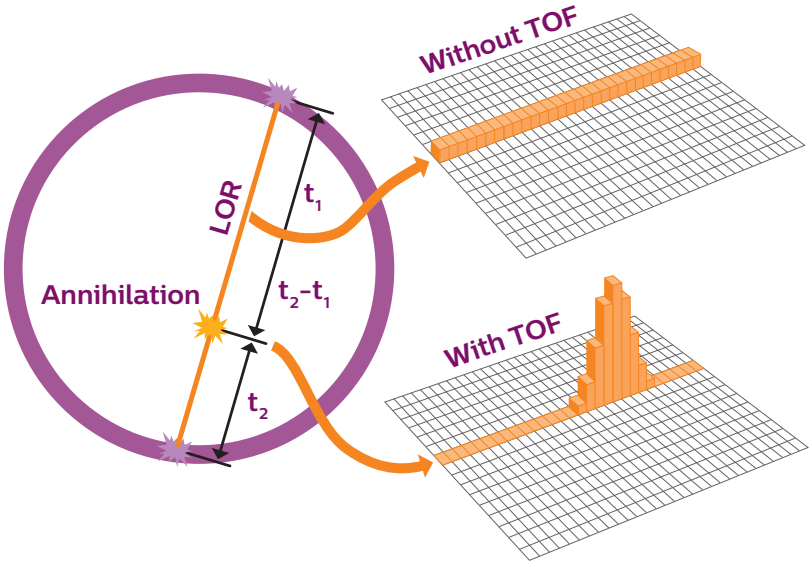

Figure 9 How TOF technology can lead to improved localization of the annihilation event along the LOR.

[1] El Fakhri G, et al. Improvement in lesion detection with whole-body oncologic time-of-flight PET. J Nucl Med. 2011;52:347-53.

Point spread function (PSF) technology

Vereos makes use of a point spread function (PSF) algorithm to correct for partial-volume effects in PET images. PET spatial resolution can be influenced by factors such as the positron range (which is radioisotope-dependent), non-co-linearity of annihilation photons, crystal/detector size, and reconstruction parameters such as voxel dimensions and the use of post-filters.

PET scanner resolution can therefore be spatially variant, resulting in blurred images if not corrected for. A system's PSF is determined by imaging point-sources at many different locations within the scanner, producing a three-dimensional PSF. Correcting for this PSF allows users to retrieve images that closely match the true object scanned (see **Figure 10**).

Experience with PSF correction in the analog Ingenuity TF PET/CT system has demonstrated good improvement in image resolution and quantification. The same method is applied in Vereos. Overall, PSF needs to be used carefully, as it can significantly influence quantitative accuracy. Users can adjust two parameters: the number of iterations and a regularization factor. Evaluations using phantoms and clinical patients suggest that 1-2 PSF iterations is sufficient to recover resolution, with more iterations leading only to increased noise in the final image. Choosing PSF regularization values similar to the resolution of the scanner (in this case 6-8 mm for clinical images) provided good resolution without excessive noise or quantification errors.

The effects of applying various values for iteration and regularization in PSF correction can be seen in the following images from a phantom study (**Figure 11**).

In addition, Vereos has the ability to reconstruct images with a voxel size of 1 mm (for clinical brain images and research-only 1 mm body images), which further minimizes pixel sampling errors and improves image quality.

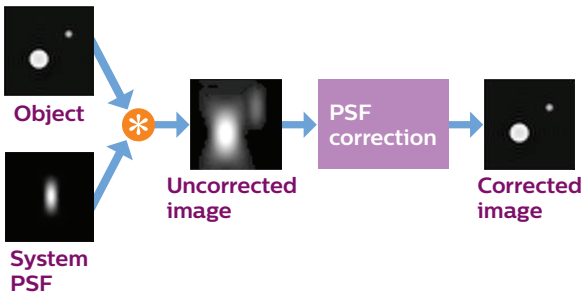

Figure 10 Correcting for a system's PSF provides superb image clarity.

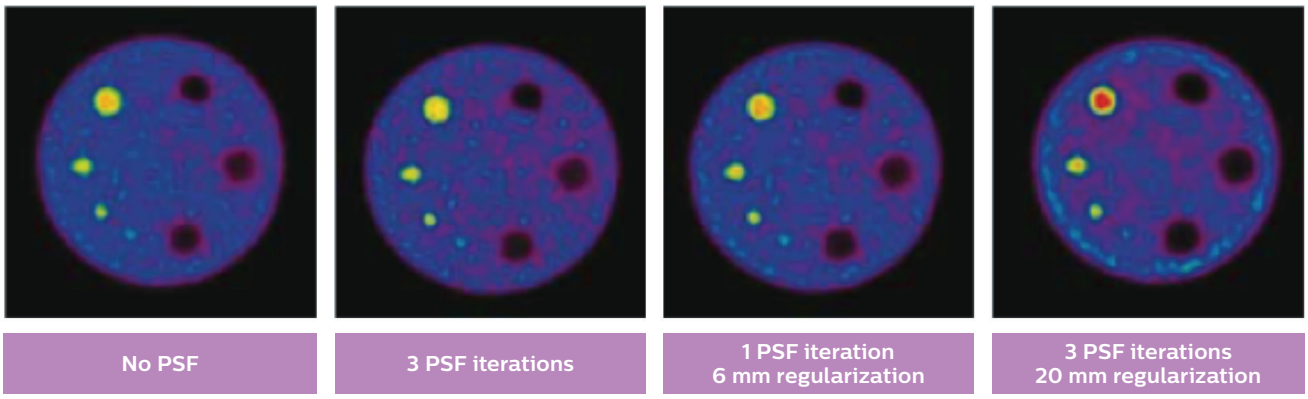

Figure 11 Transverse slices of 2 mm voxel ACR (American College of Radiology) phantom images, for various PSF iterations and levels of regularization. Reproduced from Narayanan M, Perkins A. Resolution recovery in the Ingenuity TF PET/CT. Data originally courtesy of the Hospital of the University of Pennsylvania.

Technology pillars supporting improved performance

The Vereos system has approximately double the volumetric resolution, sensitivity gain, and accuracy of a comparable analog* system. These benefits are gained through the advantages offered by DPC technology, enhanced TOF, and 1:1 coupling.

The improved volumetric resolution is largely due to 1:1 coupling. The overall resolution is typically expressed as the full width at half maximum (FWHM), which has been calculated as 69 mm^3 for Vereos. The 1:1 coupling improves overall volumetric resolution through the gains in spatial resolution seen across the entire field of view.

Most of the improved sensitivity gain seen with Vereos is attributed to the application of TOF to more accurately locate each annihilation event along the line of response (LOR). The result is less dispersed data and improved image contrast. The remaining improvement is provided by reduced dead time.

Sensitivity gains have been measured for a range of object sizes. For a typical patient body size (Δ30 cm), the Vereos system showed a sensitivity gain of 5.8, compared with a gain of 3.3 with the analog system* (both compared with non-TOF). With the additional 20% to 25% sensitivity gain due to less dead time, the overall clinical sensitivity gain is about a factor of 2. Such improvements in sensitivity produce high quality images (see **Figure 12**).

Vereos has improved quantitative accuracy of +/- 5% when compared to +/- 10% seen with the analog system.* This improvement is primarily the result of the uniform detector response enabled by 1:1 coupling and the enhanced detector efficiency normalization algorithm.

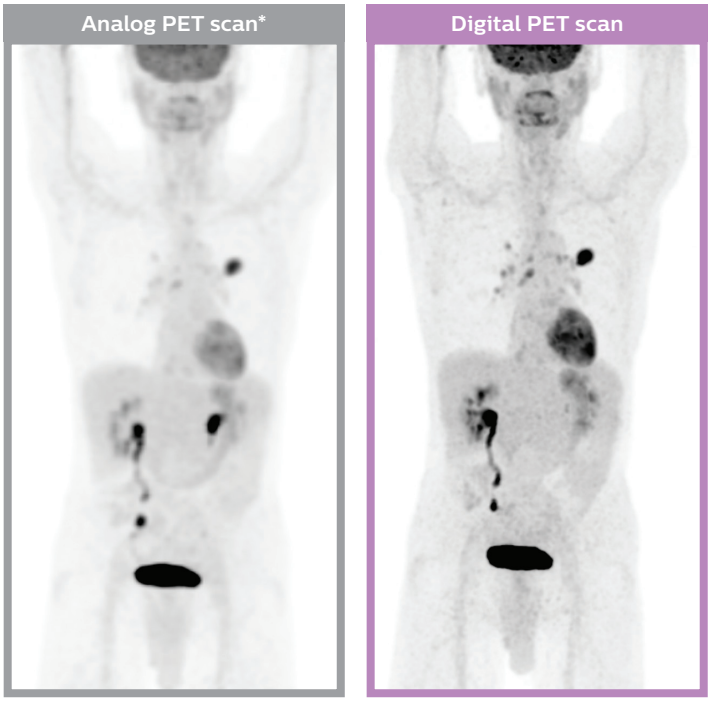

Figure 12 Sensitivity gain is approximately doubled with the Vereos system compared with the analog GEMINI TF 16 system.

> “With 1:1 coupling, we get not just more information but enhanced information and more certainty. We’re better able to identify the source of the annihilation event, improving the volumetric resolution.”
>
> *Chuck Nortmann, Clinical Product Manager Advanced Molecular Imaging, Philips*

*GEMINI TF
Sample images acquired in a clinical study of the Vereos PET/CT system at University Hospitals Case Medical Center.
Investigational device limited by law to investigational use.

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