Medical Imaging : Advances in nuclear medicine

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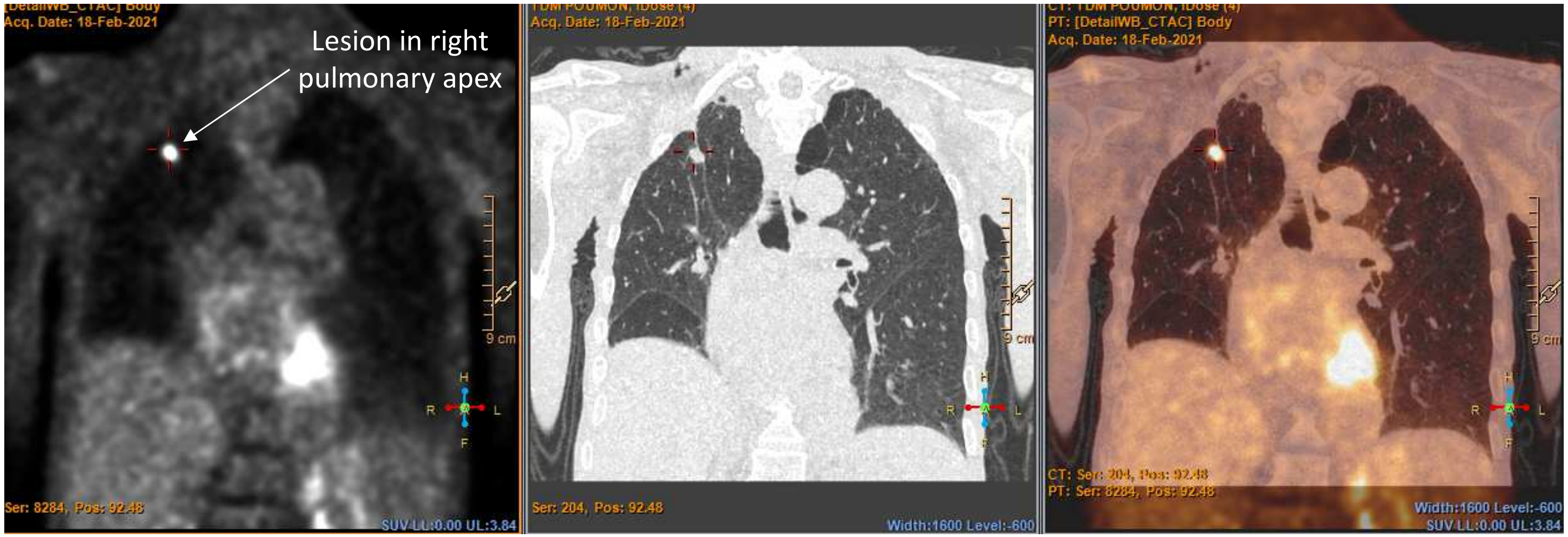
First clinical positron imaging device developed in **1953** by Dr. Brownell (left) and Dr. Aronow (right)

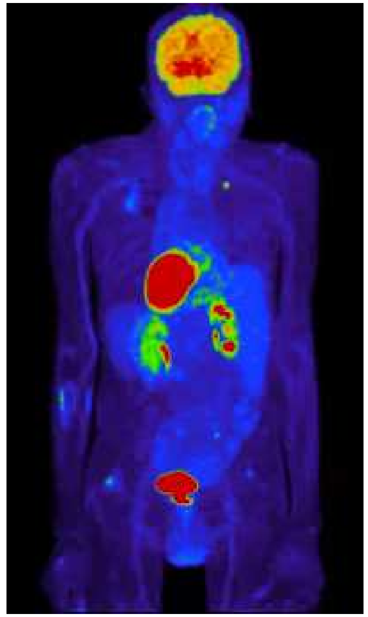
Advances in PET imaging

PET : Positron Emission Tomography

PET imaging

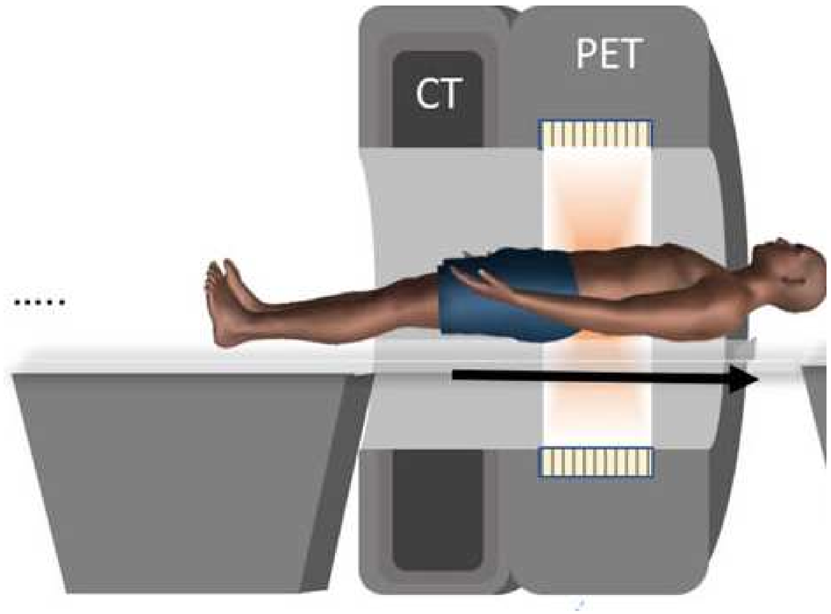
Positron Emission Tomography (PET) imaging is today the most sensitive functional imaging modality for studying the metabolic or molecular activity of an organ.

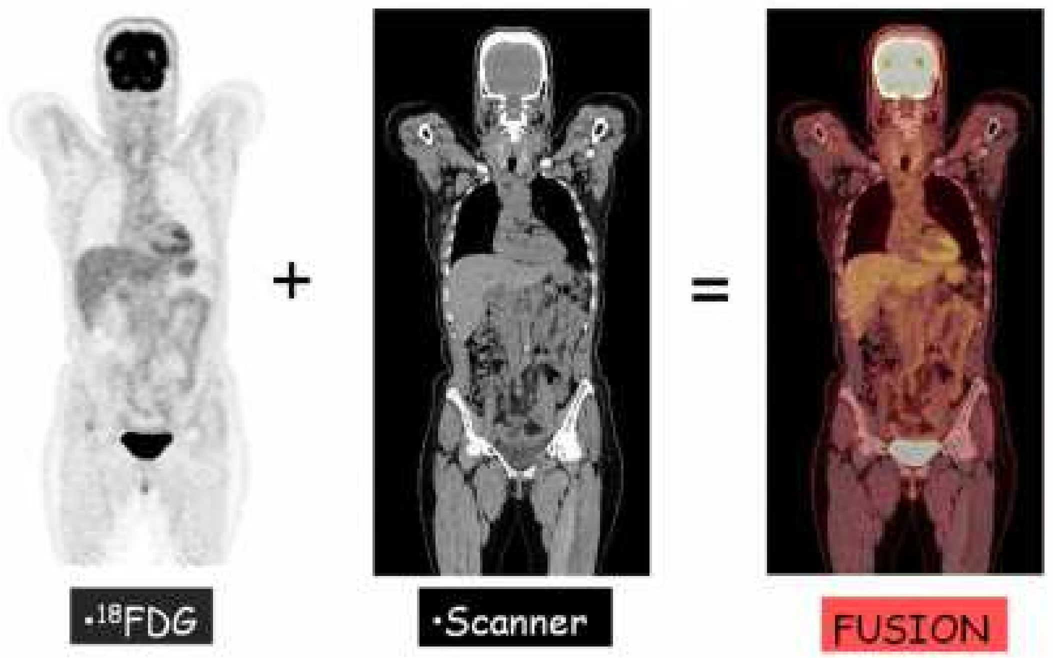




PET imaging… PET/CT imaging

Hybrid imaging : PET + CT





Clinical Workflow

Injection of the radiopharmaceutical
β+ decay

PET/CT Acquisition

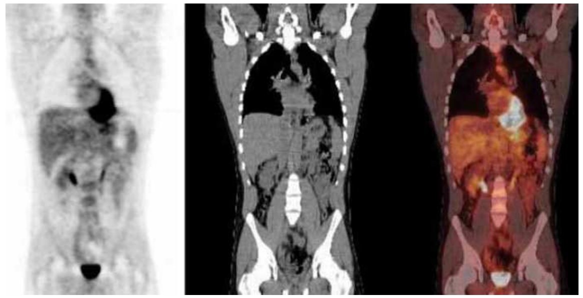
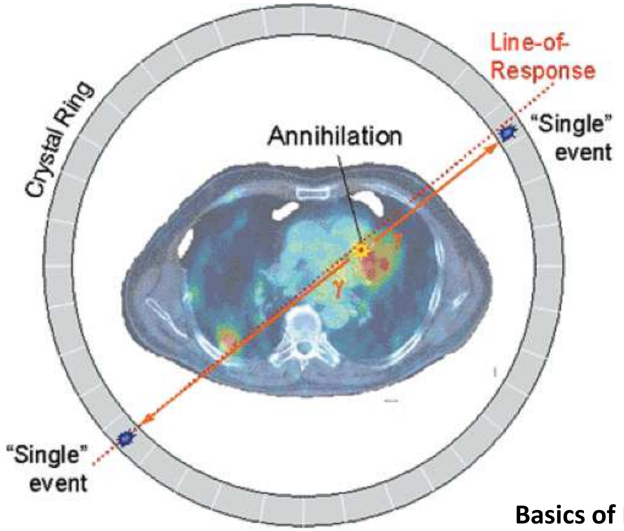


Image reconstruction and interpretation

The physics involved in PET imaging

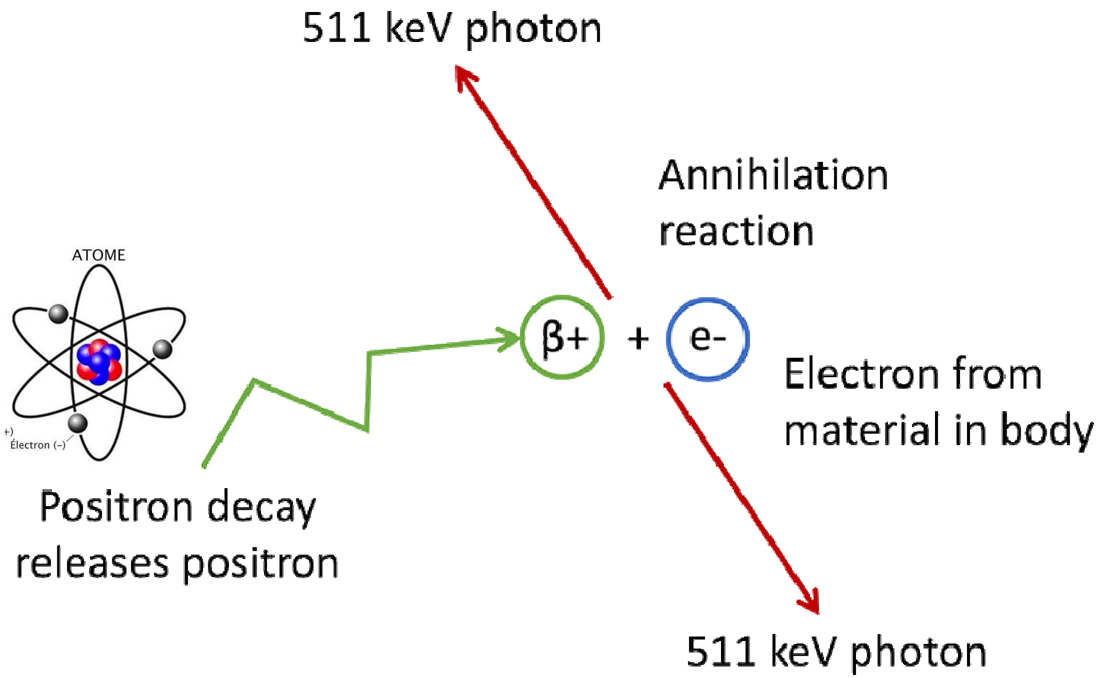
Principle: measurement of events corresponding to the **coincident detection of photons** created by the **annihilation** between a positron and an electron.



Basics of PET Scanning
Cyrill Burger
David W. Townsend

PET imaging does not detect positron particles but annihilation photons

Annihilation reaction



- The positron, produced from β+ decay, travels a few millimeters in the tissues, during which it loses all of its kinetic energy by collision with atoms
- At the end of the path, the positron combines with an electron to form a quasi-atom called **positronium**, which disappears by **annihilation** reaction
- The annihilation reaction products the emission of two photons in **opposite direction and of 511 keV** each

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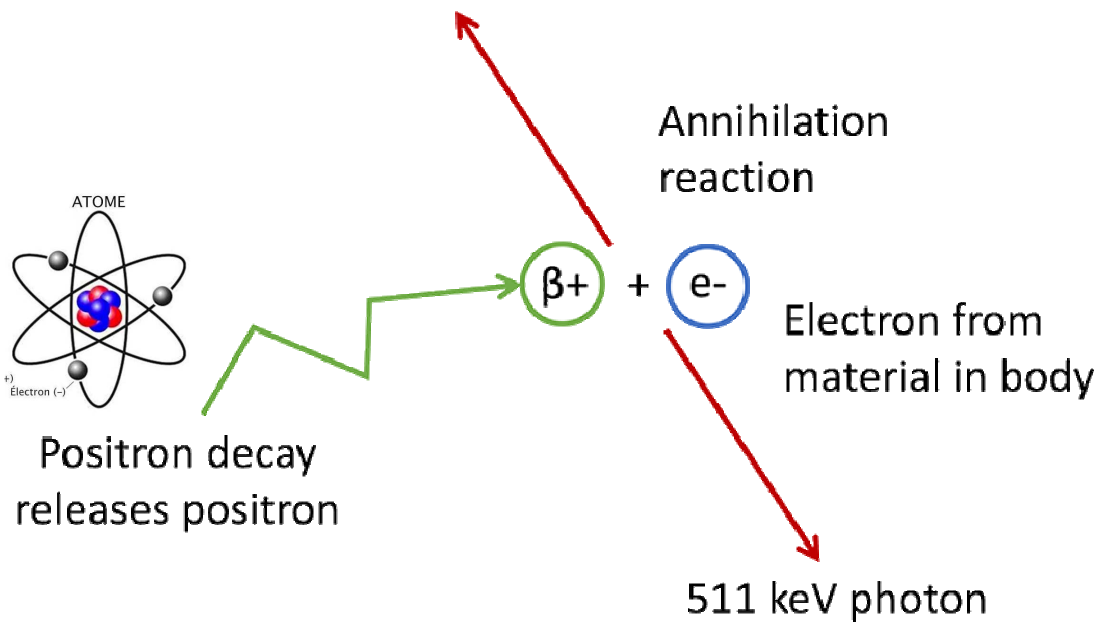
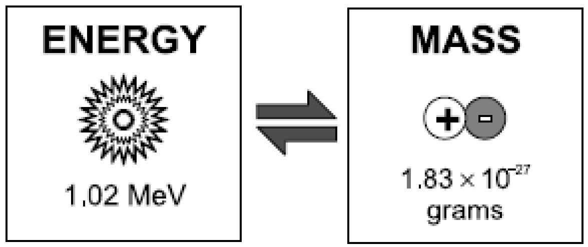
Annihilation reaction



Why do photons have an energy of 511 keV ?

Einstein equation $\mathbf{E = mc^2}$

$$E_{\gamma} = m_{e^-}.c^2 + m_{\beta^+}.c^2$$

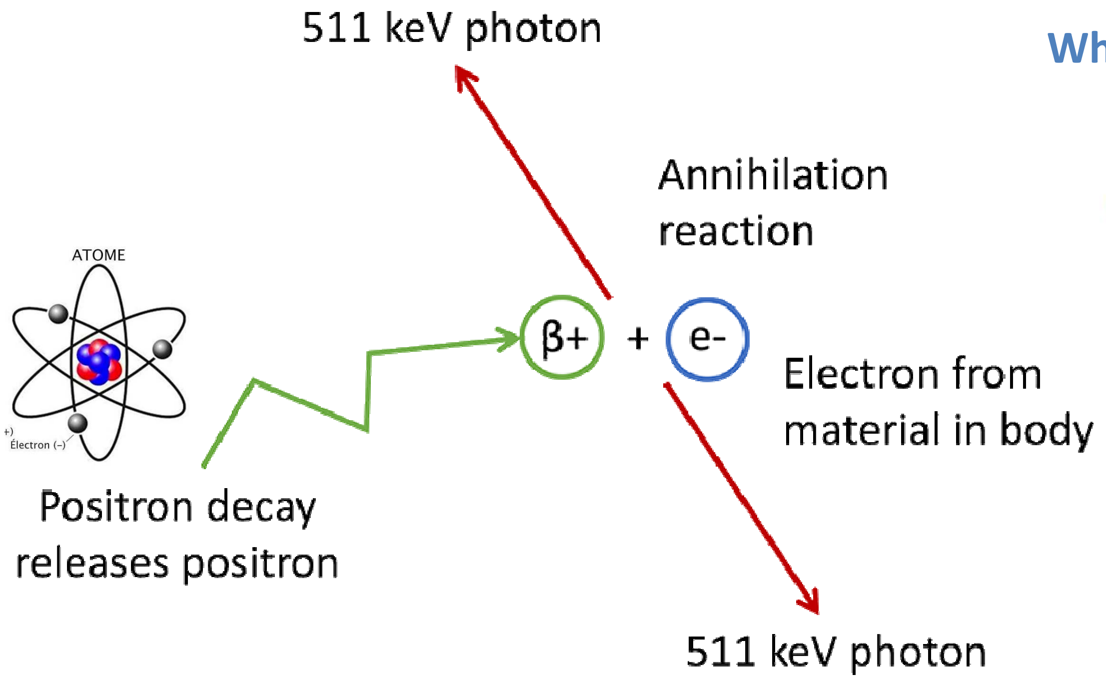


Mass of electron at rest, m = $9{,}109{,}10^{-31}$ kg

E (J) = 2 x $9{,}109.10^{-31}$ x $(3{,}10^{+8})^2$ (1 J = $6{,}242{,}10^{+18}$ eV)

E(eV) = 511 keV

Annihilation reaction



Why do photons have an opposite direction of emission ?

$$\vec{P}_{e^-} + \vec{P}_{\beta^+} = \vec{P}_{\gamma_1} + \vec{P}_{\gamma_2} = \vec{0} \leftrightarrow \vec{P}_{\gamma_1} = -\vec{P}_{\gamma_2}$$

The law of conservation of momentum imposes a collinear and opposite emission of the two photons

This annihilation radiation is what is detected in PET and what is used to form images of tracer concentration in the body.

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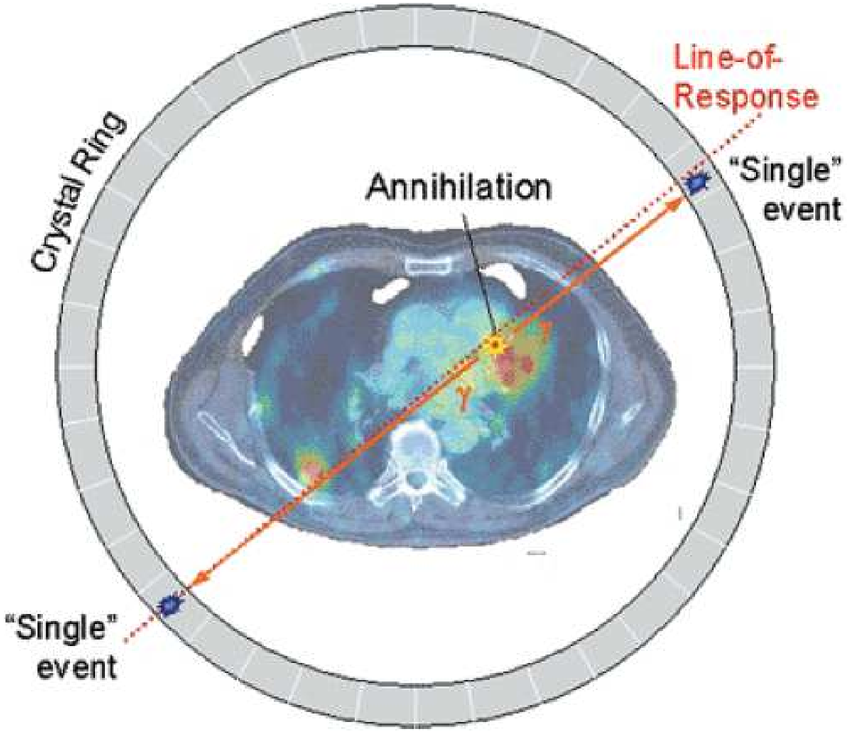
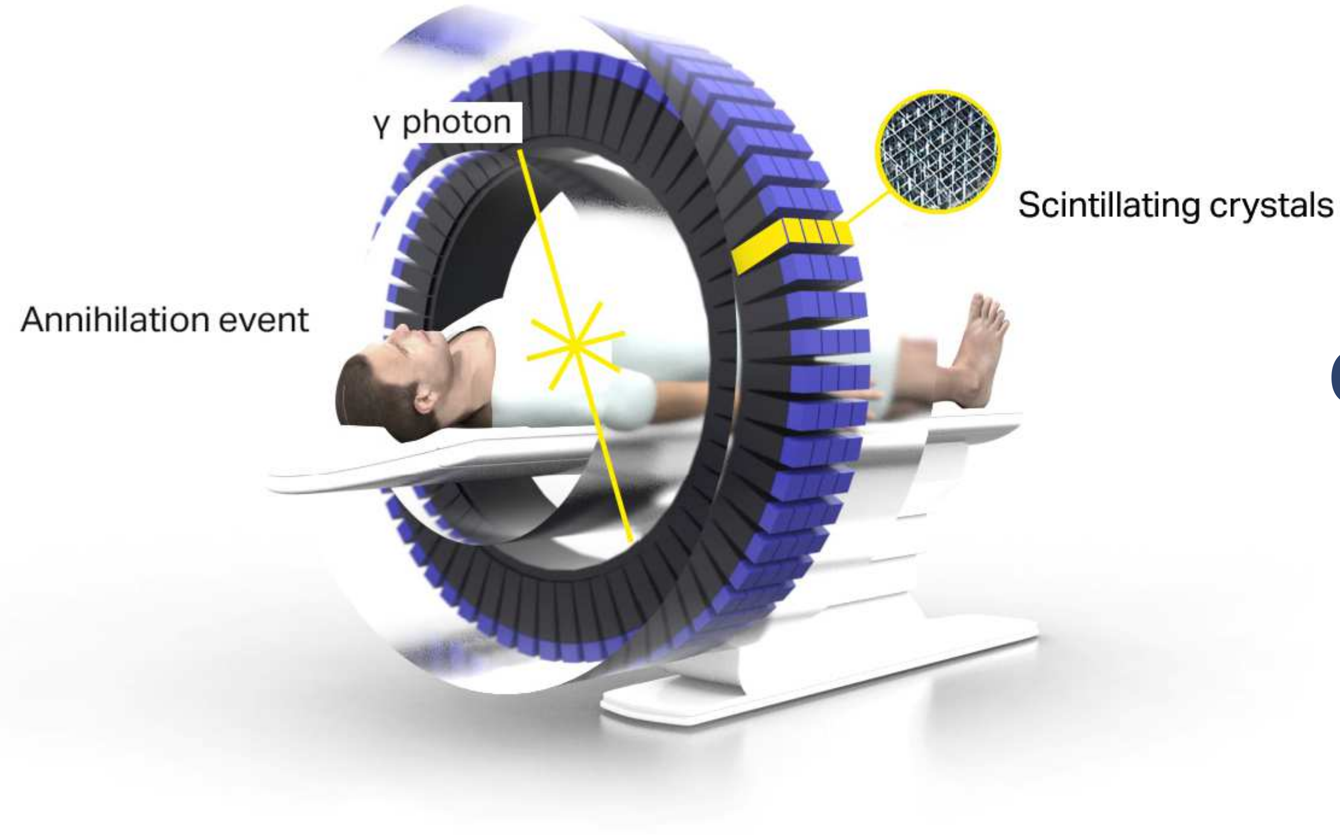
Detection in PET imaging



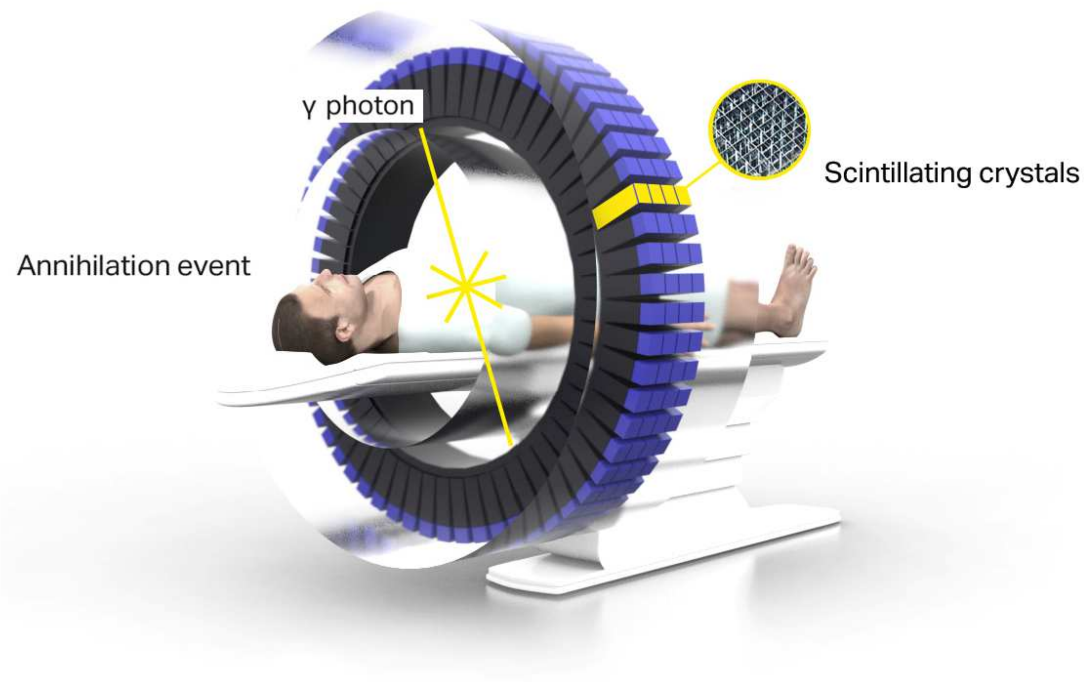
PET imaging is based on determining the projections of the sites of annihilation. It is obtained by means of two independent detectors which measure almost simultaneously the two 511 keV photons produced by annihilation

The simultaneous, or coincidental, detection of two photons indicates that they originate from annihilation that occurred within the volume. This simultaneous detection is also defined as a line of response between the two detectors.



Current PET detector

Current PET detector



- A full PET scanner is constructed as a cylindrical assembly of block detectors in a ring structure.

- The sensitive volume inside the detector cylinder that a patient can occupy is called the field-of-view (FOV), which in human scanners is typically 70 cm in diameter and 16 – 25 cm in axial length

block detectors

1 block detectors = small individual scintillation crystals coupled to four photomultiplier tube (PMT)

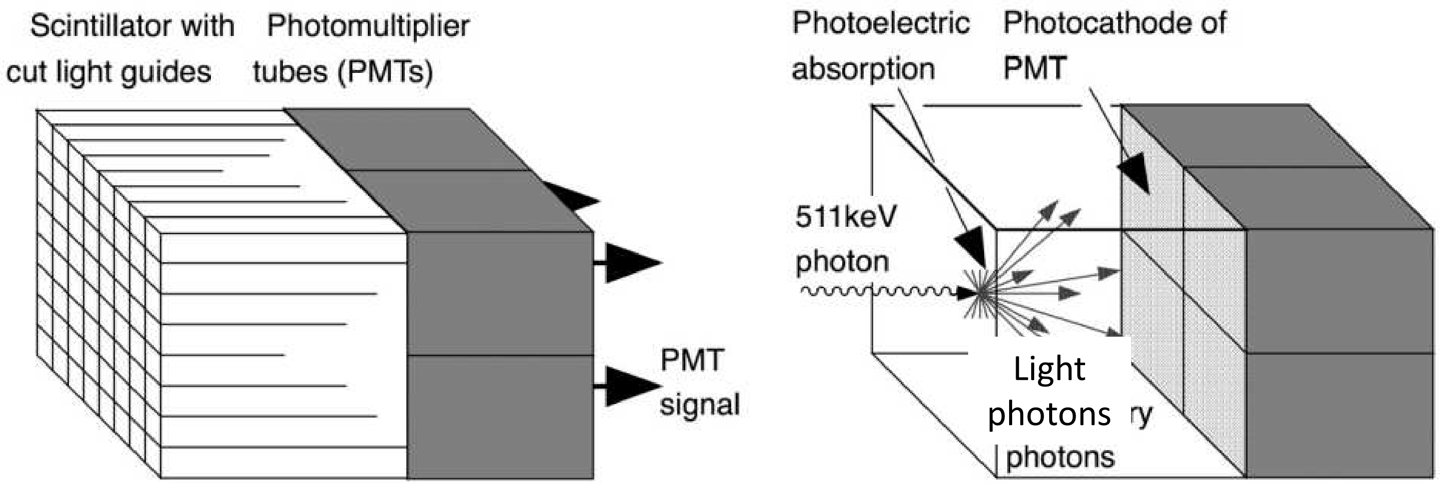
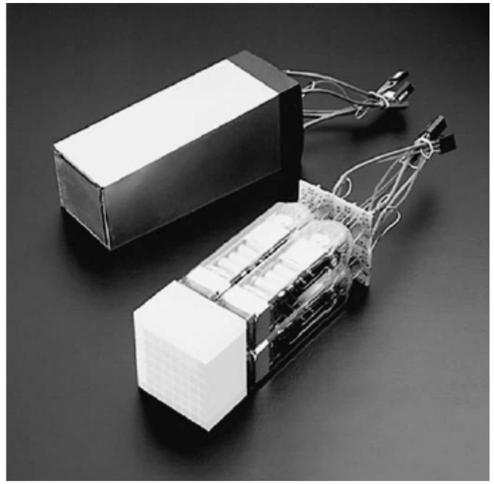
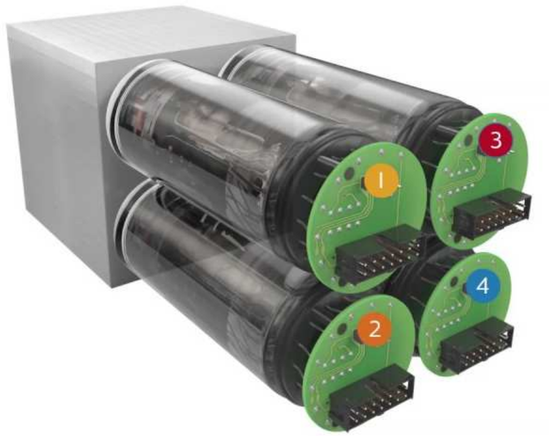


Fig. 2. Schematic of a block detector with finely segmented scintillator crystals read out by four photo-multiplier tubes.



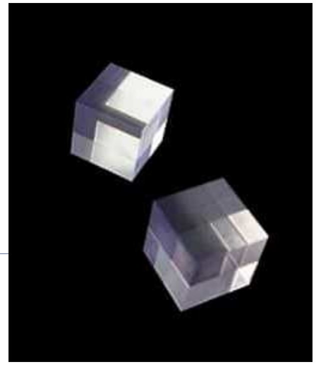


The Physics of PET/CT scanners

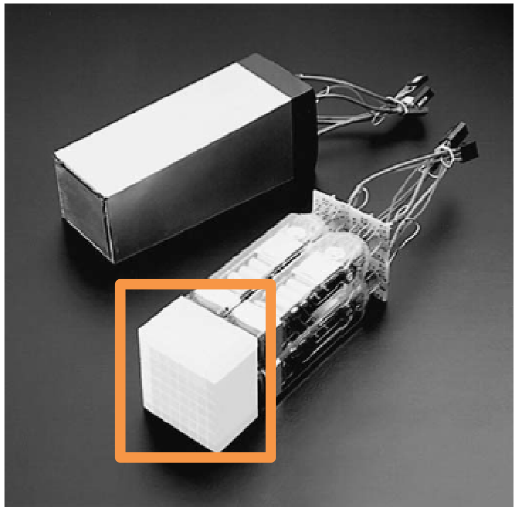
Ruth E. Schmitz, Adam M. Alessio, and Paul E. Kinahan

Imaging Research Laboratory
Department of Radiology
University of Washington

Scintillation crystal



Goal : to convert annihilation photons into light photons



Main properties :

- ❑ Stopping power
  - ❑ Depends on density and effective atomic number (Z) of the material
- ❑ Decay constant
  - ❑ describes how long the scintillation flash lasts in the crystal. Shorter decay constants are desirable.
- ❑ Energy resolution
  - ❑ allows to distinguish against PET photons that have Compton scattered (and lost energy) before being measured

Scintillation crystal

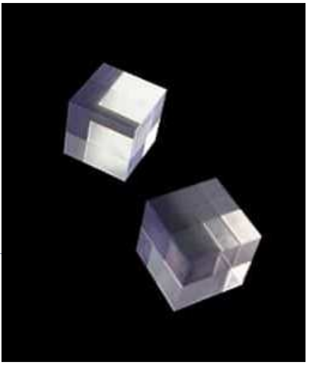


Table 1. Scintillators used in PET Scanners.

Material	Cost	Light Output[1]	Effective Density[2]	Light Decay Time[3]	Comments
NaI(Tl)	cheap (relatively)	highest	lowest	long	Hygroscopic No longer used
BGO	expensive	lowest	highest	long	Does not support TOF PET
LSO (or LYSO)	more expensive	high	high	very short	Some patent disputes
GSO	more expensive	very high	somewhat lower than LSO	very short	No longer used

[1] determines energy and spatial resolution
[2] determines scanner sensitivity
[3] determines scanner deadtime and random coincidences rate as well as ability to be used with time-of-flight (TOF) PET imaging

Abbreviations: BGO = bismuth germinate, NaI(Tl) = thalium-doped sodium iodide, LSO = lutetium oxyorthosilicate, LYSO = lutetium yttrium orthosilicate, GSO = gadolinium orthosilicate

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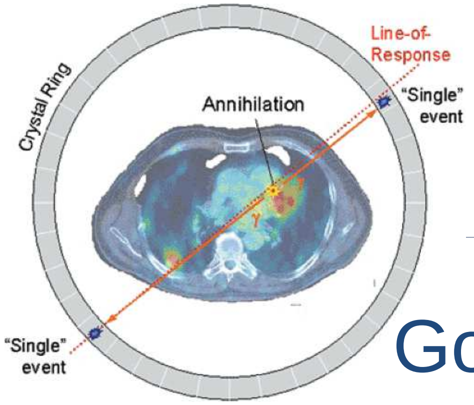
Manufacturers are divided on the choice of material:
Currently, BGO and LYSO is favored by GE, LSO by Siemens, and LYSO by Philips.



Photomultiplier Tube (PMT)

Goal : to convert light photons into electric current

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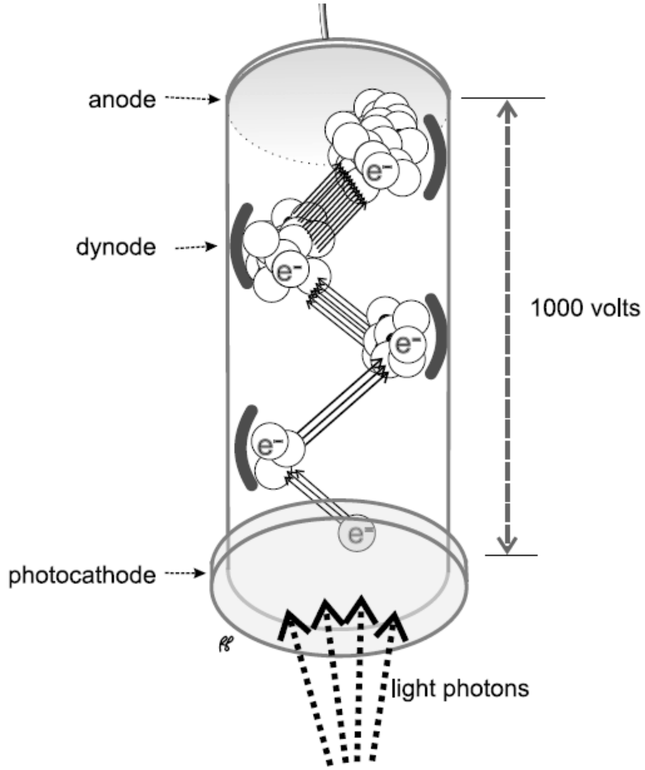
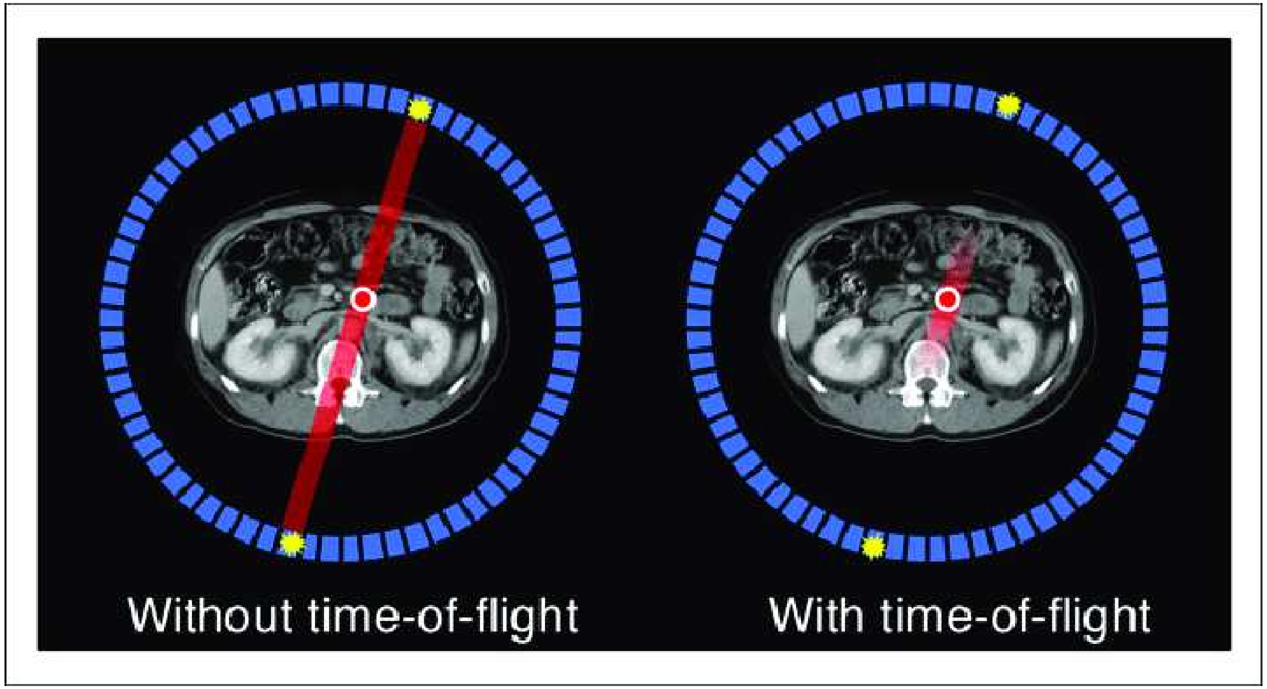




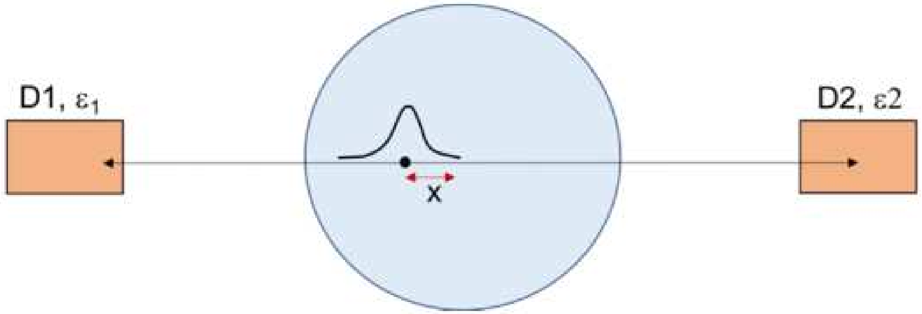
Time of light PET
A major development

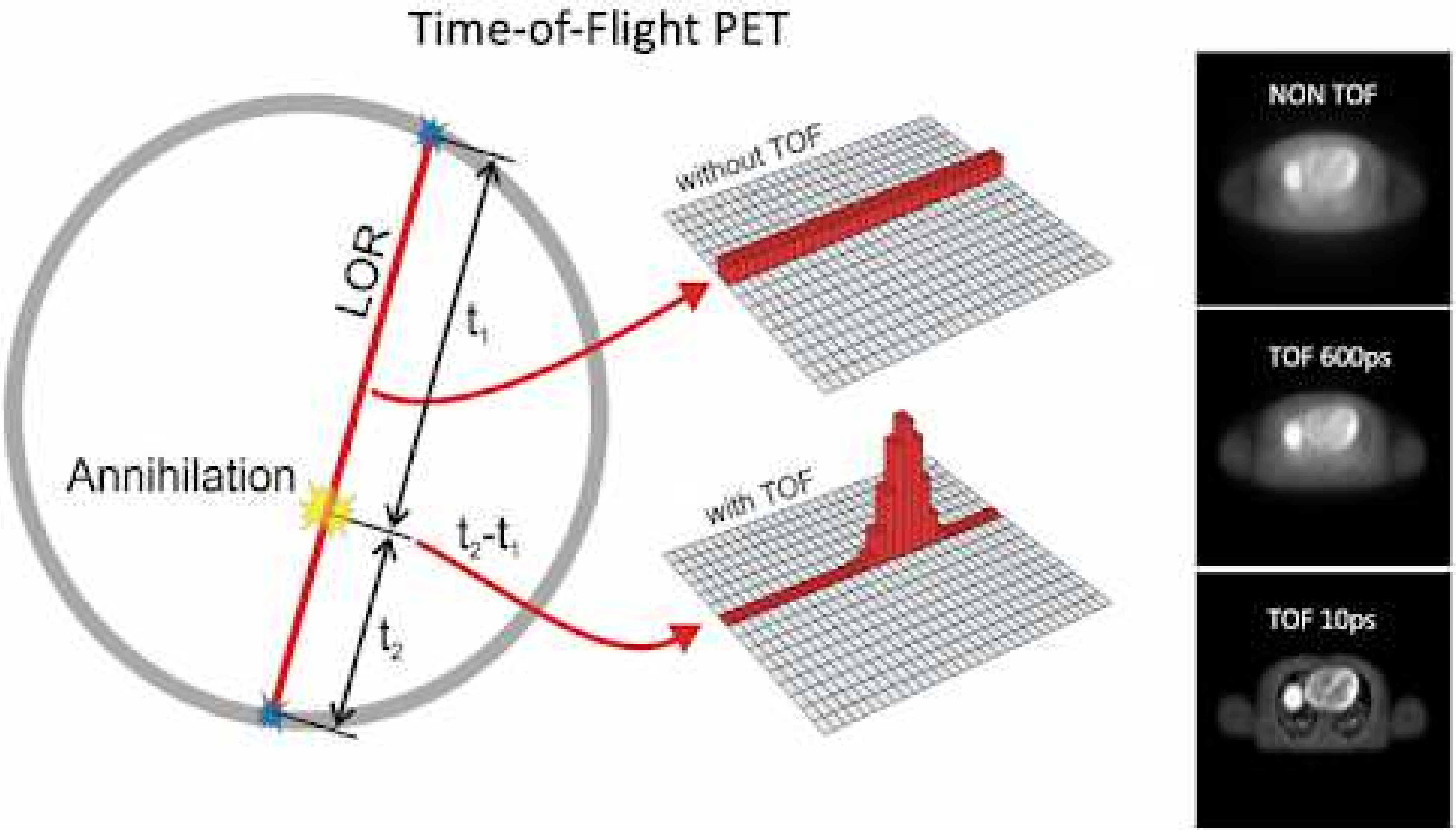
Time of light

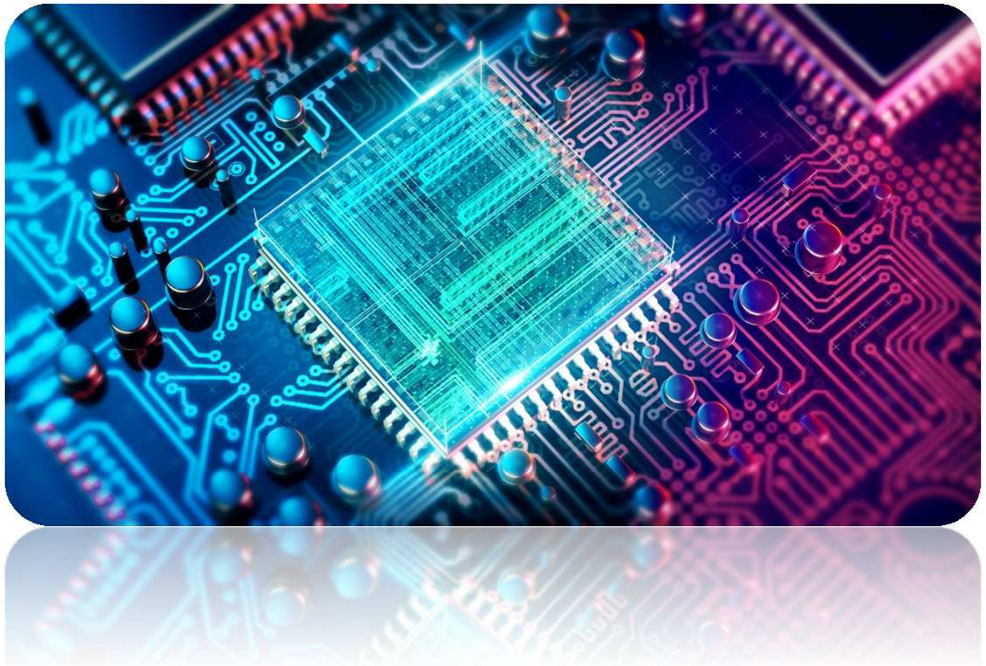
Principle :

If the difference Δt in time of arrival of the two coincidence photons is known, the position x of annihilation along a LOR with respect to the centre of the scan (FIG. 4) can be determined using the relationship:

$$x = \frac{c\Delta t}{2}$$




Time-of-Flight PET
LOR
Annihilation
t_1
t_2
t_2-t_1
without TOF
with TOF
NON TOF
TOF 600ps
TOF 10ps



SiPM PET technology
The new generation of PET

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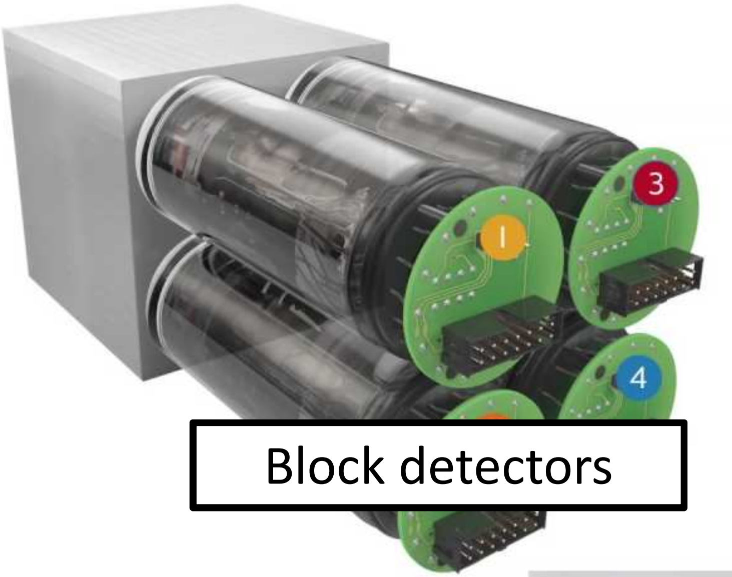
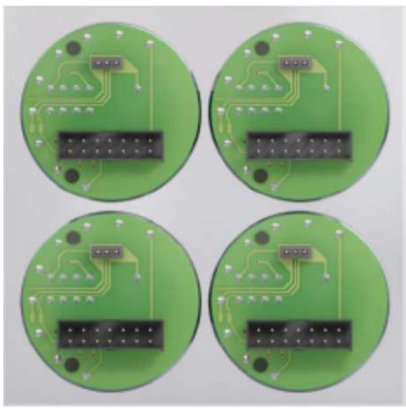
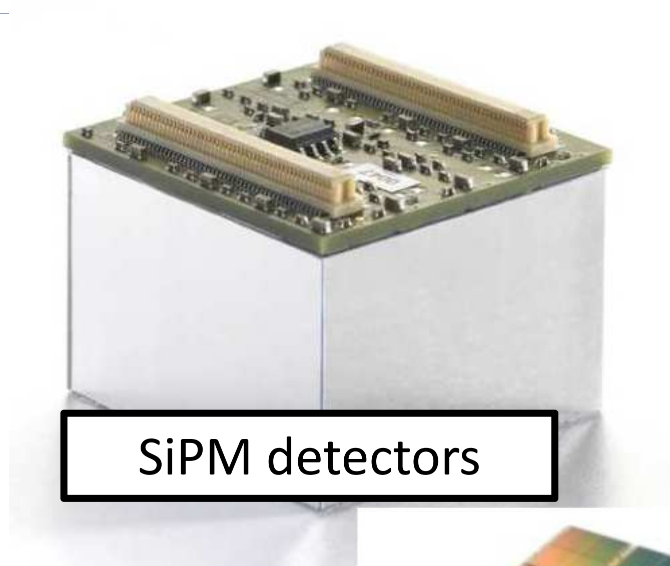
Analogic PMT→ Digital SiPM

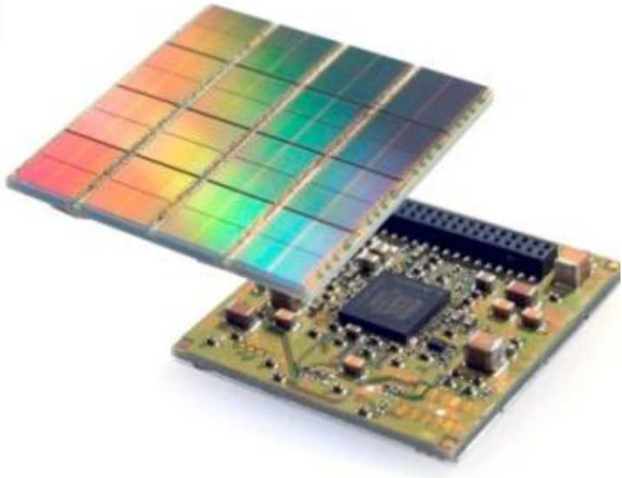


Block detectors



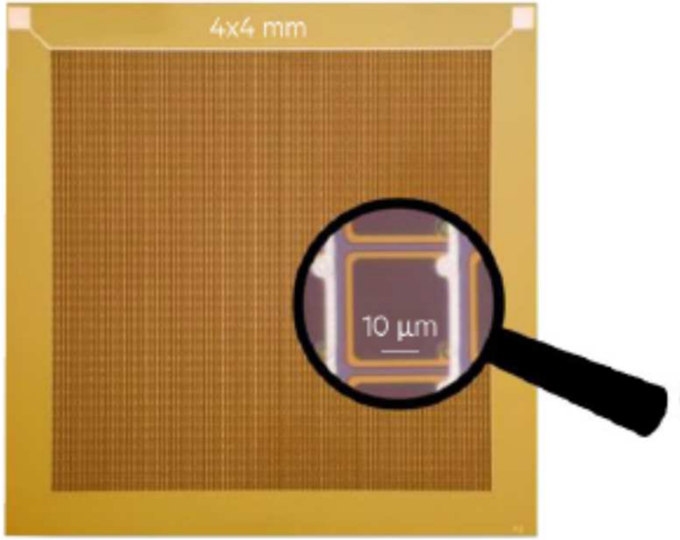


SiPM detectors



SiPM detectors

SiPM matrix



Silicon photomultiplier is a matrix of identical avalanche photodiodes (ADP or pixel) operating in Geiger-mode (G-APDs) :

- APDs are compact silicon devices, based on a modified p–n junction structure
- APDs are designed such that when a bias voltage is applied, a region with a very high electric field is created.
- The field is high enough that charges produced in this region, by the absorption of light photons from a scintillator, may be accelerated to create further electron-hole pairs in the region by impact ionization, thus causing a multiplication or “avalanche” of charges that are then collected to form an output pulse.
- The output pulse is proportional to the amount of scintillation light interacting in the APD.
- The cells are connected together on a common silicon substrate

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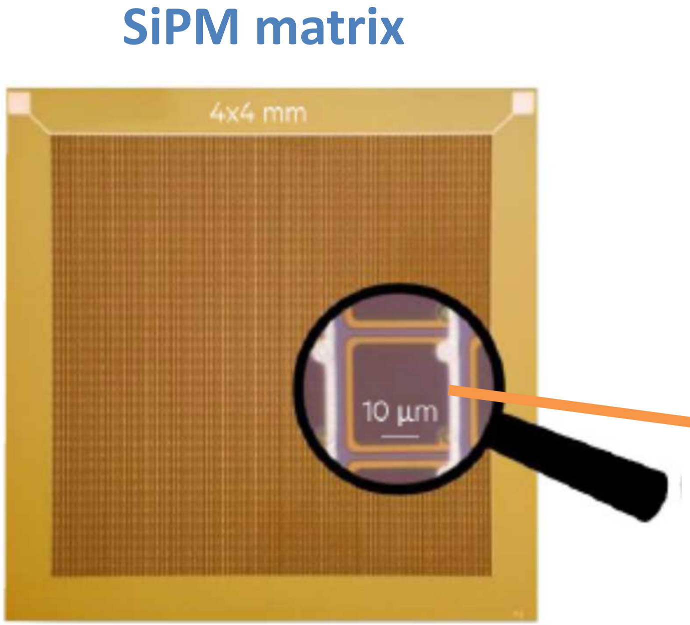
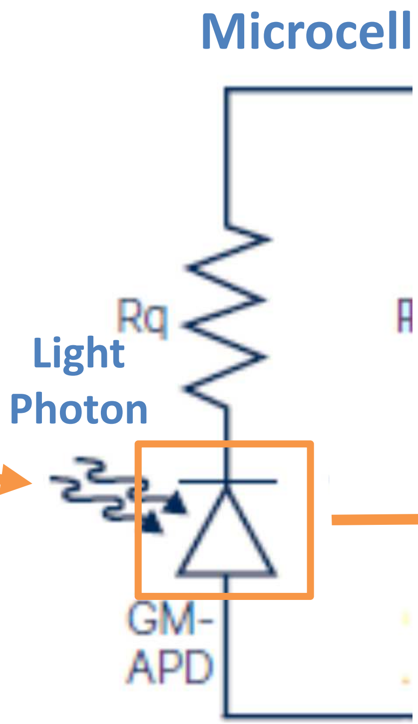
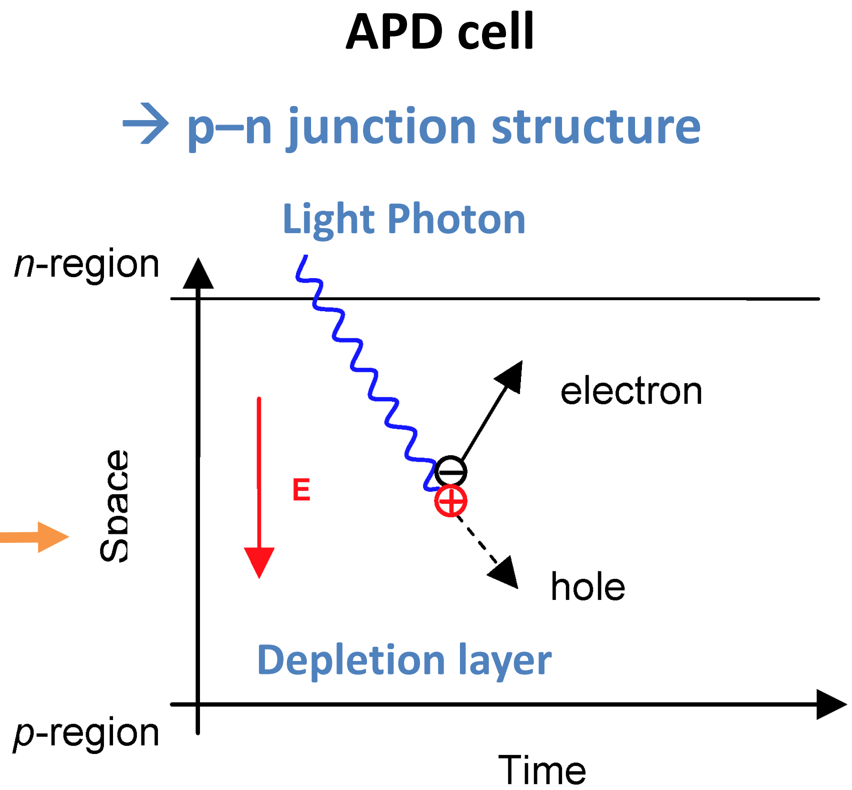
SiPM detectors

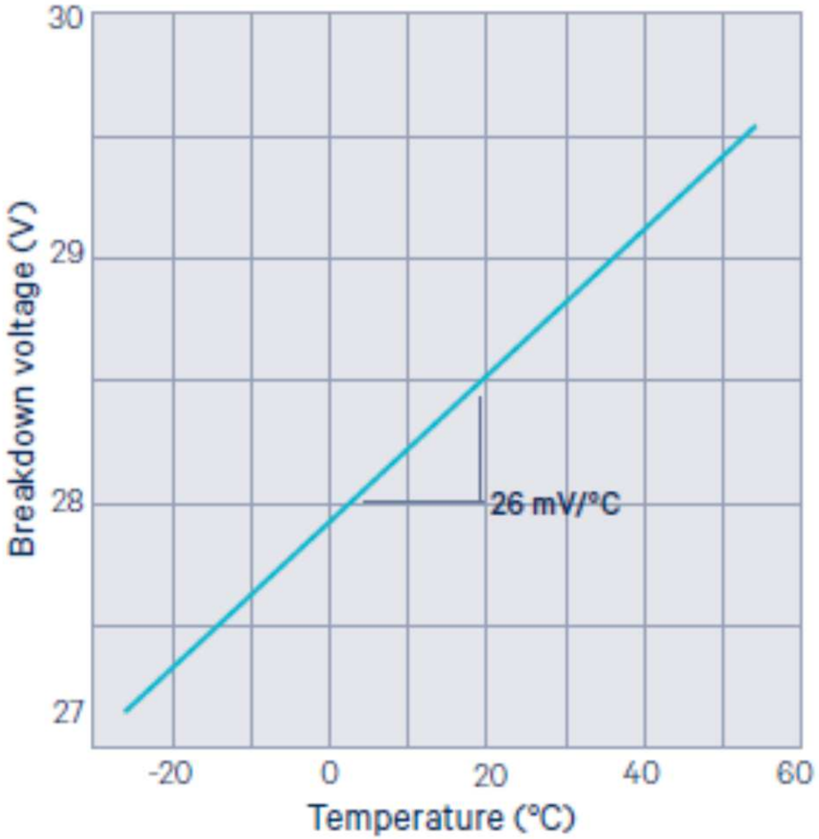






$$Q_{\text{cell}} = C_{\text{cell}} \times (V_{\text{bias}} - V_{\text{breakdown}})$$

Temperature effect on SiPM detection

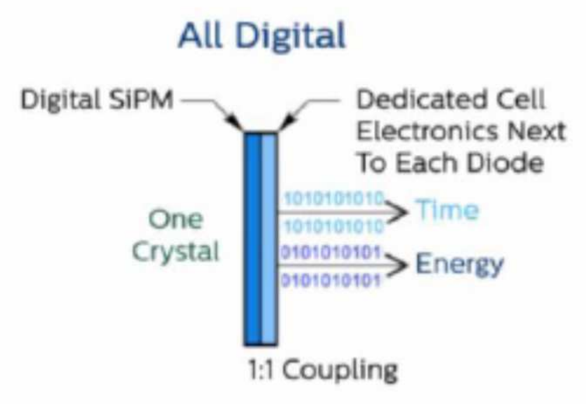


If the temperature increases the sensitivity of the photodiodes decreases
→ detection is degraded

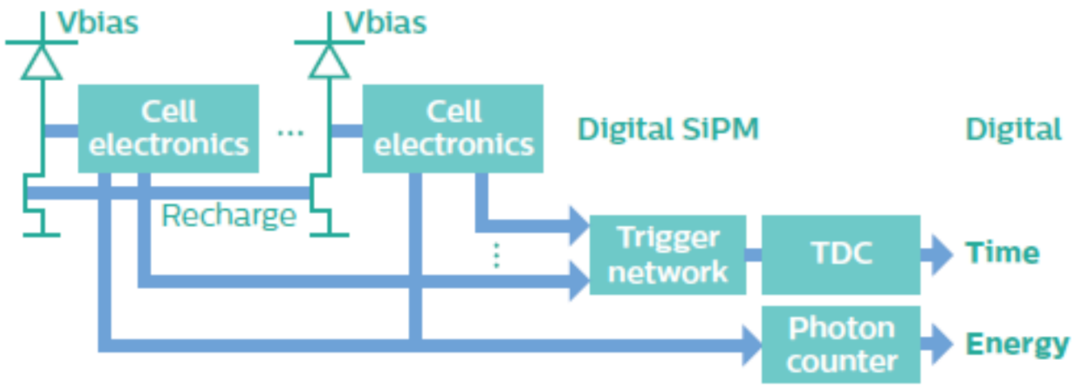
→ Need to cool the electronics and ensure a constant temperature
→ Technical Constraint for users

Philips PET Vereos case

Philips PET Vereos Technology



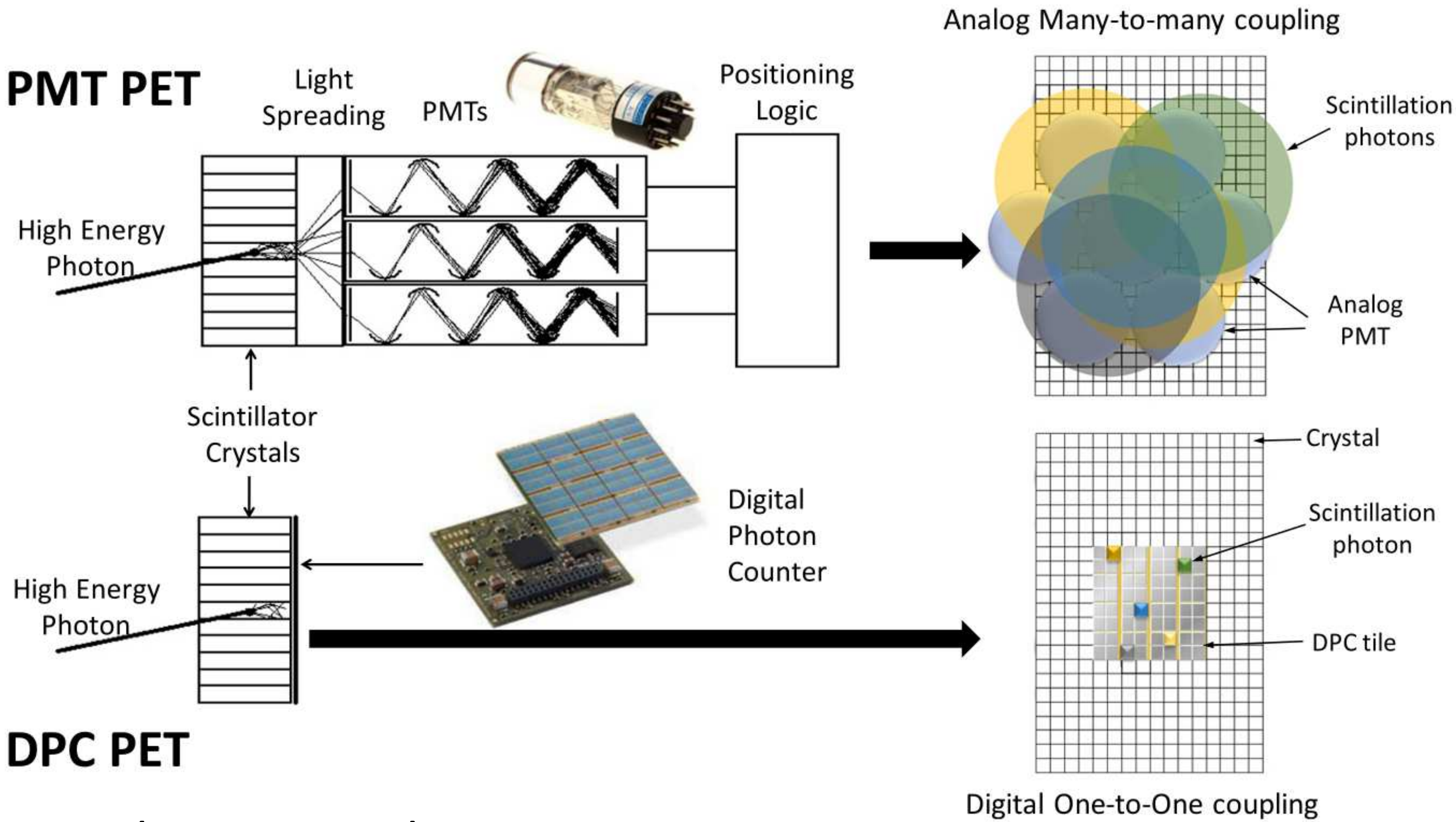
- Direct Photon Counting (DPC technology) 1:1 coupling
- Optical photons are counted one by one
  - No need amplification
  - No intermediate analog-numeric converter



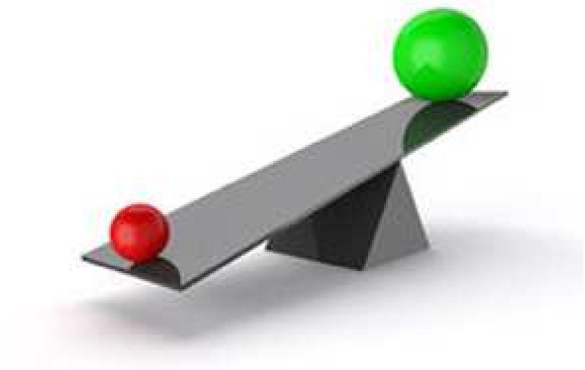
- SiPM : matrix of cells
  - Cell : Avalanche Photodiodes in Geiger-mode

→ Digitization of the signal as close as possible to the interaction in the crystal

PMT *vs* SIPM : Philips PET Vereos



Zhang *et al.* EJNMMI research 2018



Imaging comparison PMT vs SiPM

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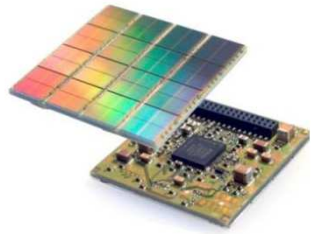
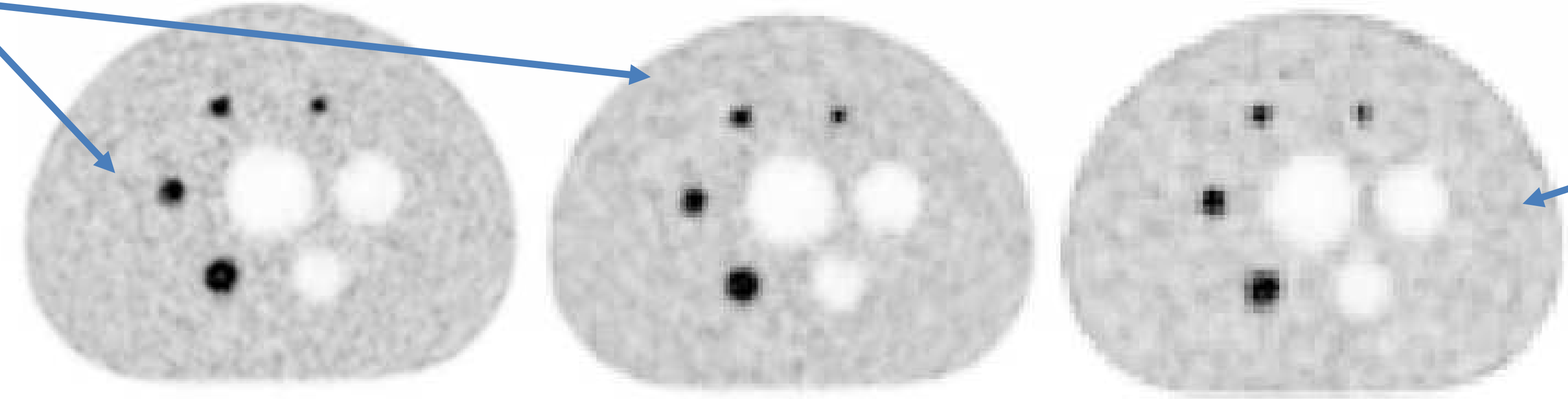
PMT *vs* SiPM



SiPM PET



PMT PET

Fig. 6 Reconstructed images of the IEC phantom with the same image roughness (IR = 0.15). The reference was for the mCT using 3 iterations, 21 subsets, no post-filtering, 200 × 200 matrix size, and 3.2×10^7 net trues (equivalent to a time acquisition of 120 s). Left: Vision using 4 iterations, 5 subsets, no post-filtering, 440 × 440 matrix size, and 2.4×10^7 net trues (reduction factor = 1.34, time acquisition = 89 s); middle: Vision using 4 iterations, 5 subsets, no post-filtering, 220 × 220 matrix size, and 1.7×10^7 net trues (reduction factor = 1.89, time acquisition = 63 s); right: mCT (reference). Gray scale level is identical for all images. Contrast improvement for the different spheres, as compared to the reference, is listed in Tables 4 and 5.

Carlier *et al.* EJNNMI 2020

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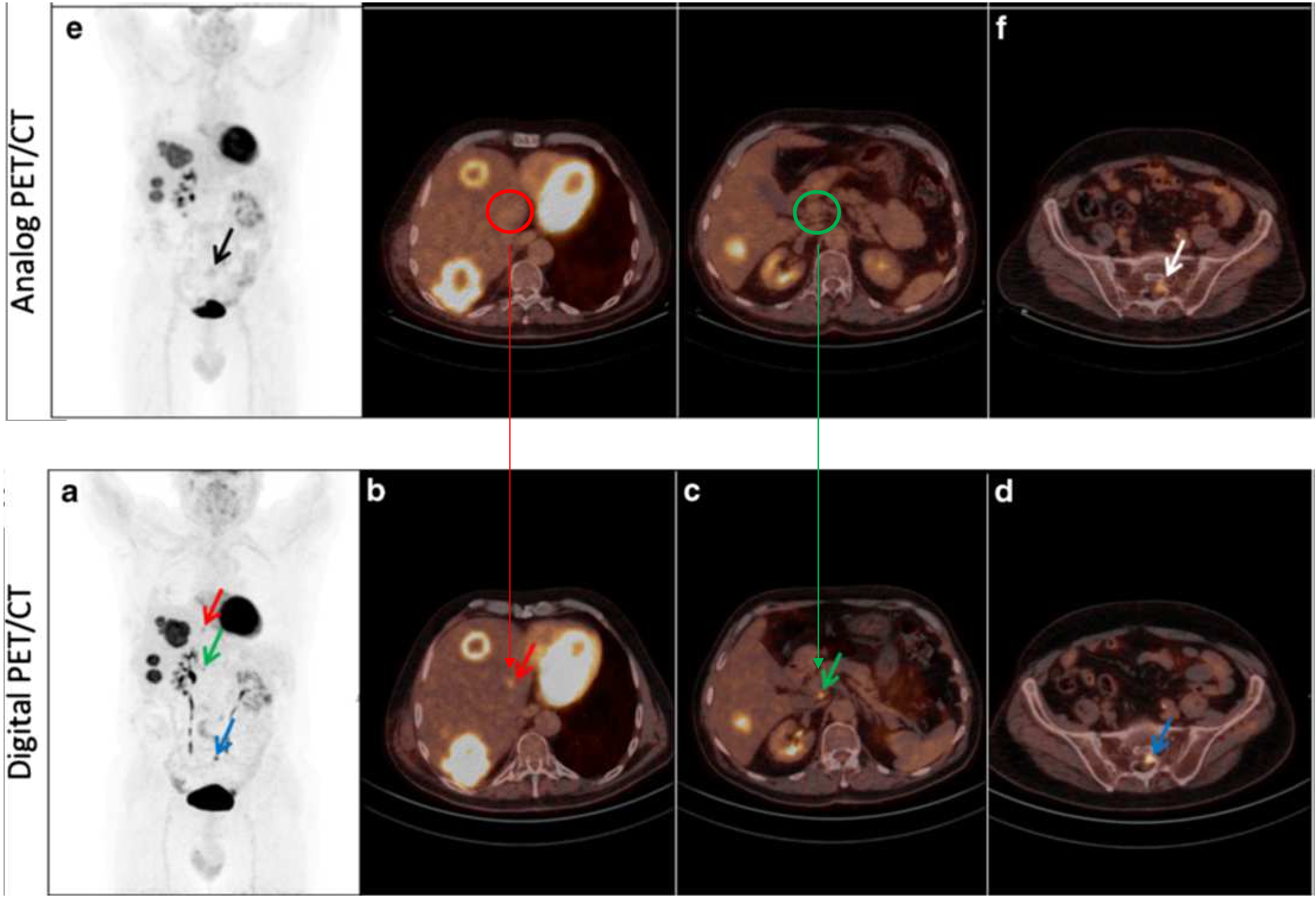
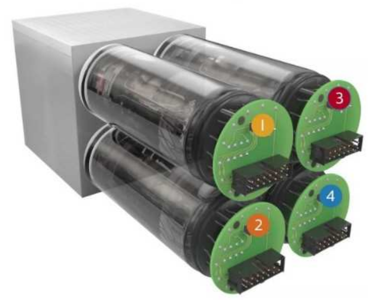
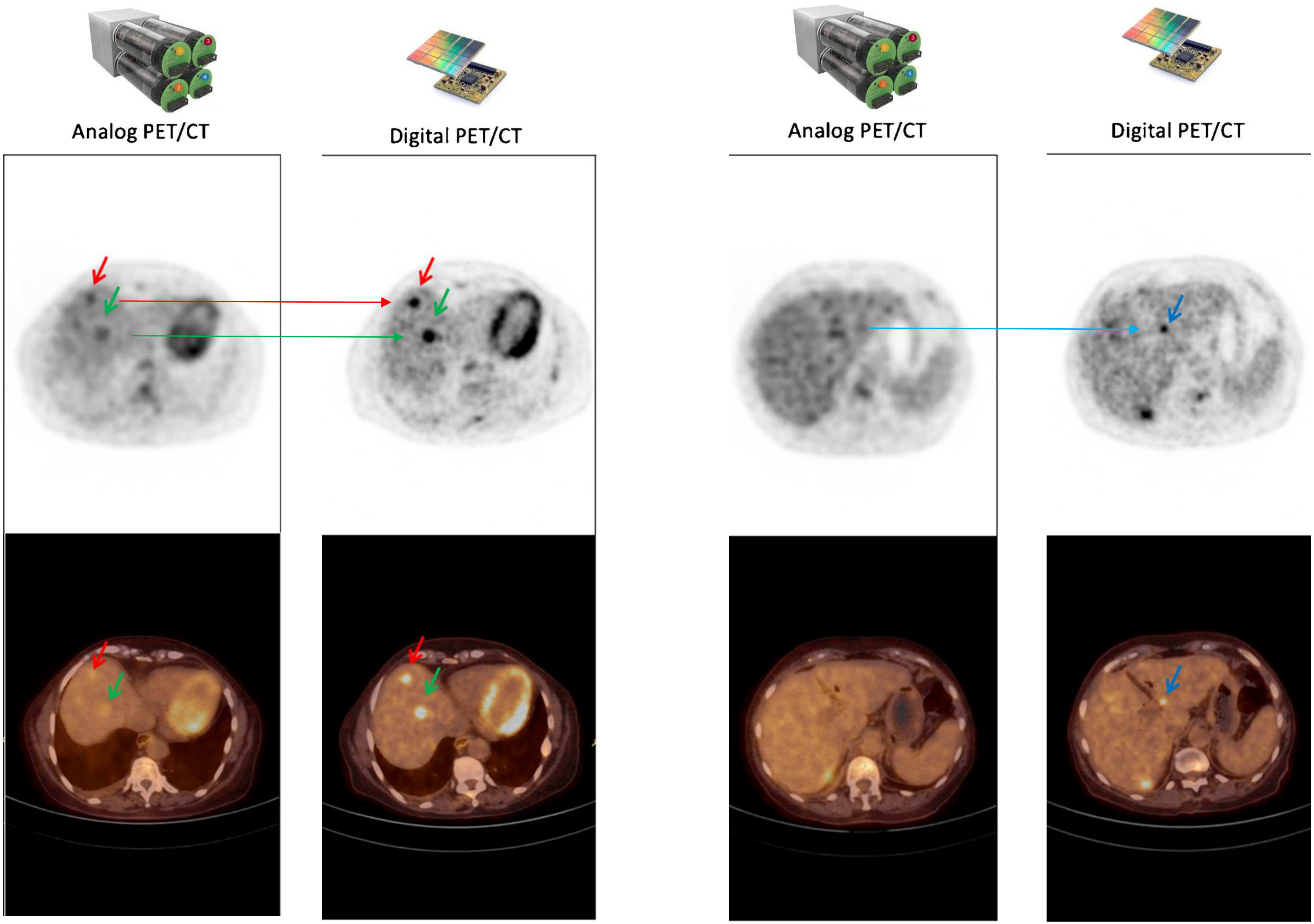


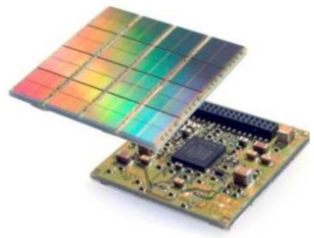


Lopez-Mora *et al.*
2018 EJNMMI



Lopez-Mora *et al.* *2018* EJNMMI

PMT *vs* SiPM



- Comparing to photomultiplier tubes (PMT), SiPMs are :
  - more compact,
  - insensitive to magnetic field → PET/MR
  - single photon response
  - high detection efficiency
  - high gain at low bias voltage
  - very good timing properties

- Gain in temporal resolution
- Gain in spatial resolution
- Gain in sensitivity

  → Better detectability of small lesions

  → Better quantification

Commercial clinical SiPM-PET

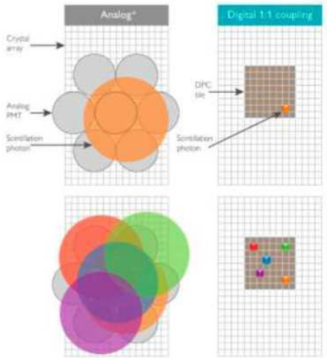
Light Shield

Scintillator (LBS) crystal array **with light guides** and Enhanced Spectral Reflectors (ESR)

Silicon Photomultiplier (SiPM) with electronics (ASICS) designed for Digital Compton Recovery

Philips exclusive Digital Photon Counting (DPC) technology

Our revolutionary digital breakthrough in PET imaging

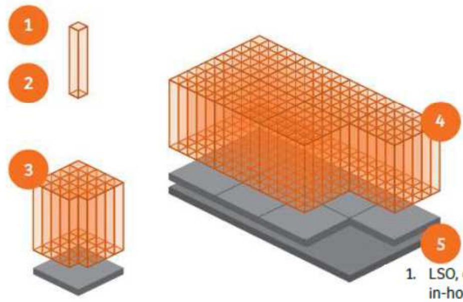


DPC converts scintillation light directly to a digital signal, with zero analog noise.

DPC reduces the traditional tradeoffs between sensitivity gains and resolution gains.

DPC compared to analog* enables:
- Faster TOF
- Faster timing resolution
- Faster post-processing and image fusion
- Faster throughput and workflow

Transcend digital with the Optiso UDR Detector



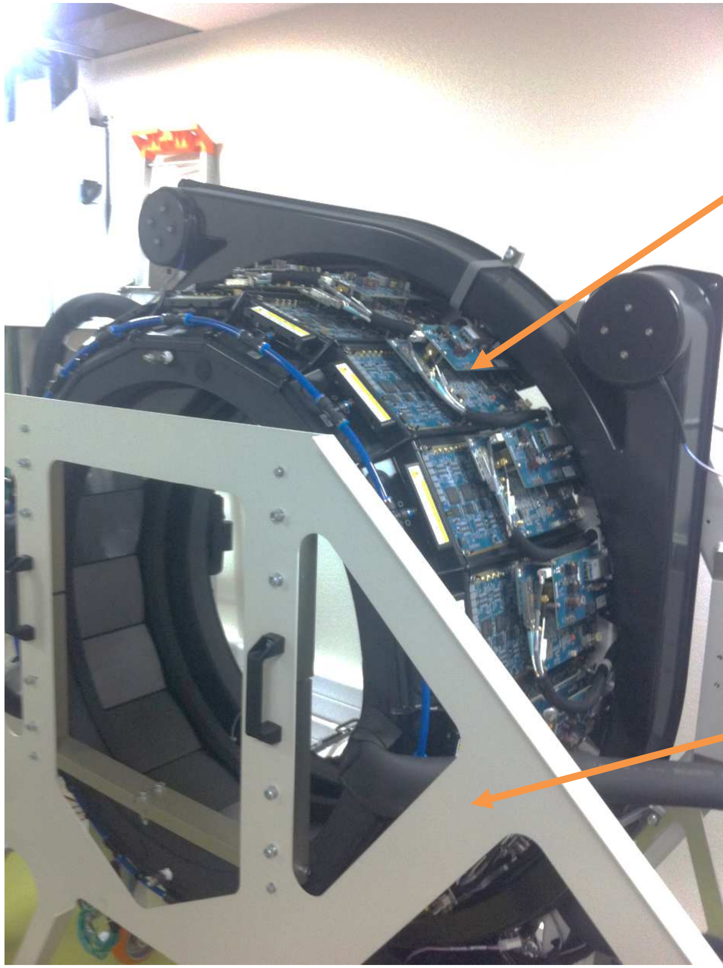
1. LSO, a fast and efficient scintillator, is grown and cut in-house through a vertically-integrated manufacturing process to ensure the highest quality.
2. 3.2 mm crystal elements are individually selected and deliver high isotropic spatial resolution; higher spatial resolution may result in improved lesion detectability.
3. 100% coverage[2] of the crystal area with SiPM sensors results in a timing resolution of 249 picoseconds[2] and 3.4 times higher effective sensitivity[3] for faster scans and lower dose.
4. A small block size delivers >1150 kilo counts per second[2] effective peak NECR for improved clinical performance.[3]
5. High-flow direct-cooling of the detector plate allows the detector to operate at room temperature[2] for outstanding performance, serviceability and improved patient comfort.

Installation of a PET Vereos in Léon-Bérard Center

Some pictures of our installation…

Statif

CT part



Ring PET

Support for setup

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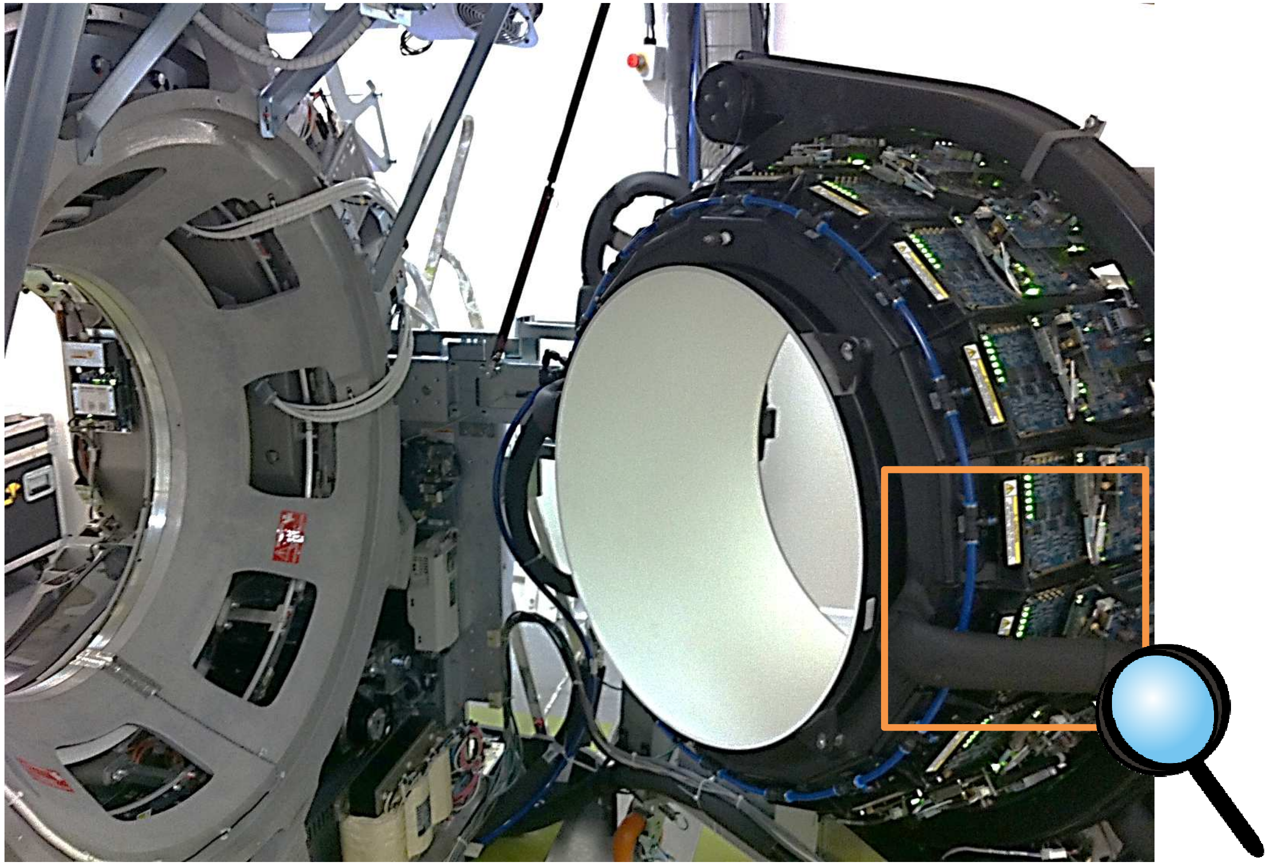
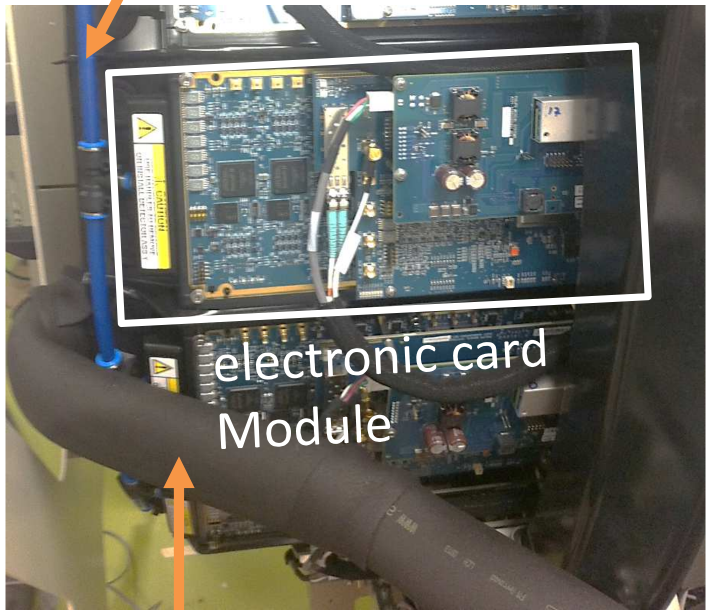
Some pictures of our installation…





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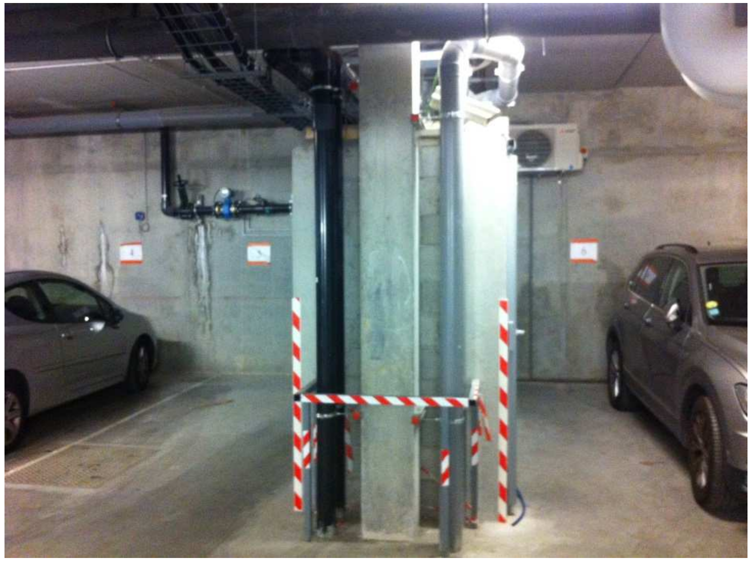
Some pictures of our installation…

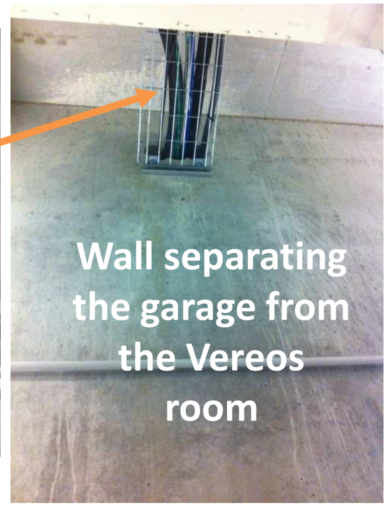
- Technical local



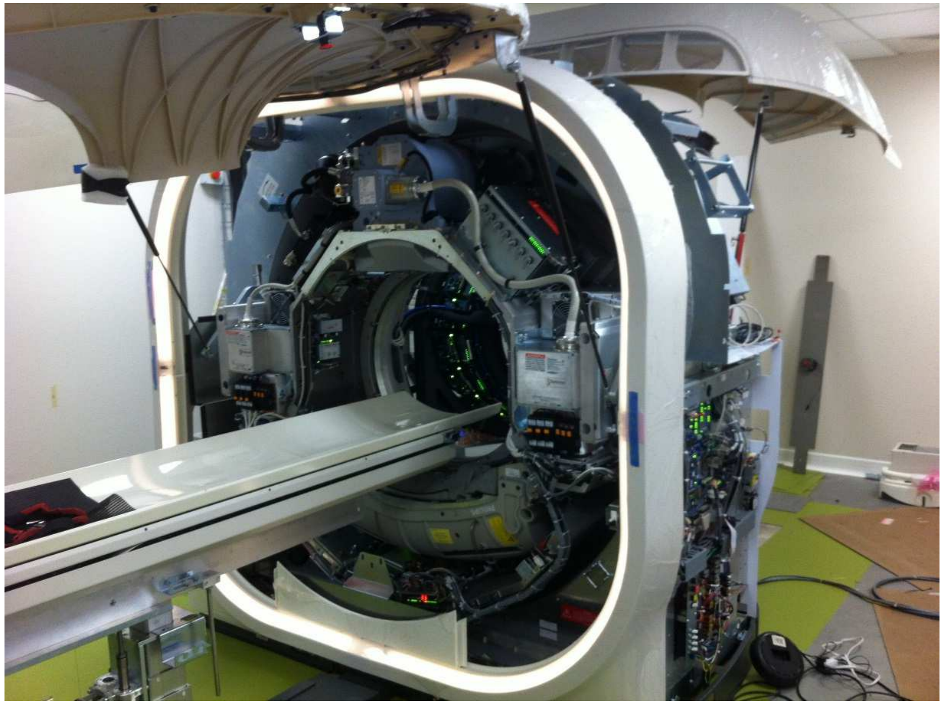
Dehumidifier

Chiller (water temperature at 18°C)

Passage of the piping through the ceiling



Some pictures of our installation…



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Main research axis in instrumentation…

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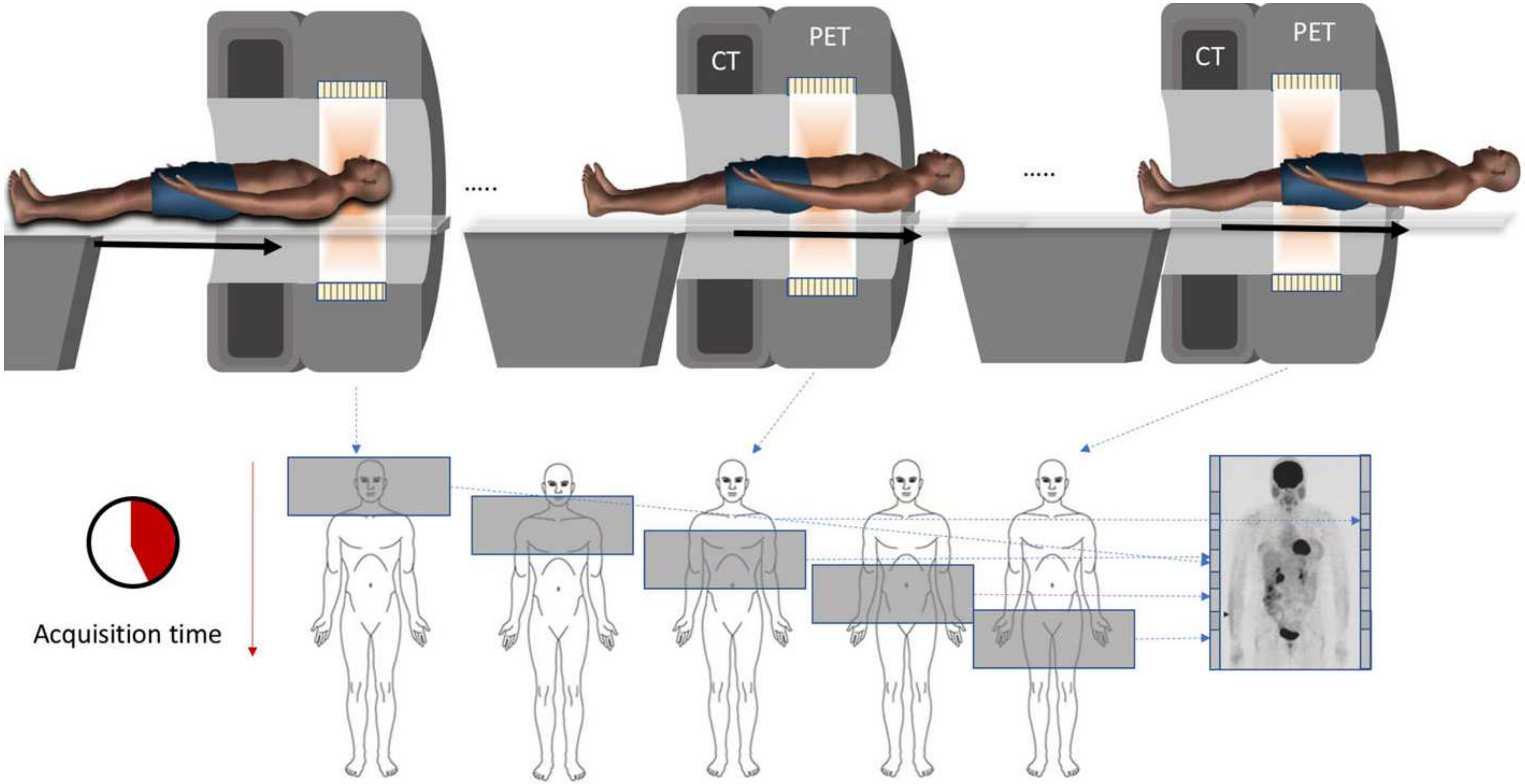
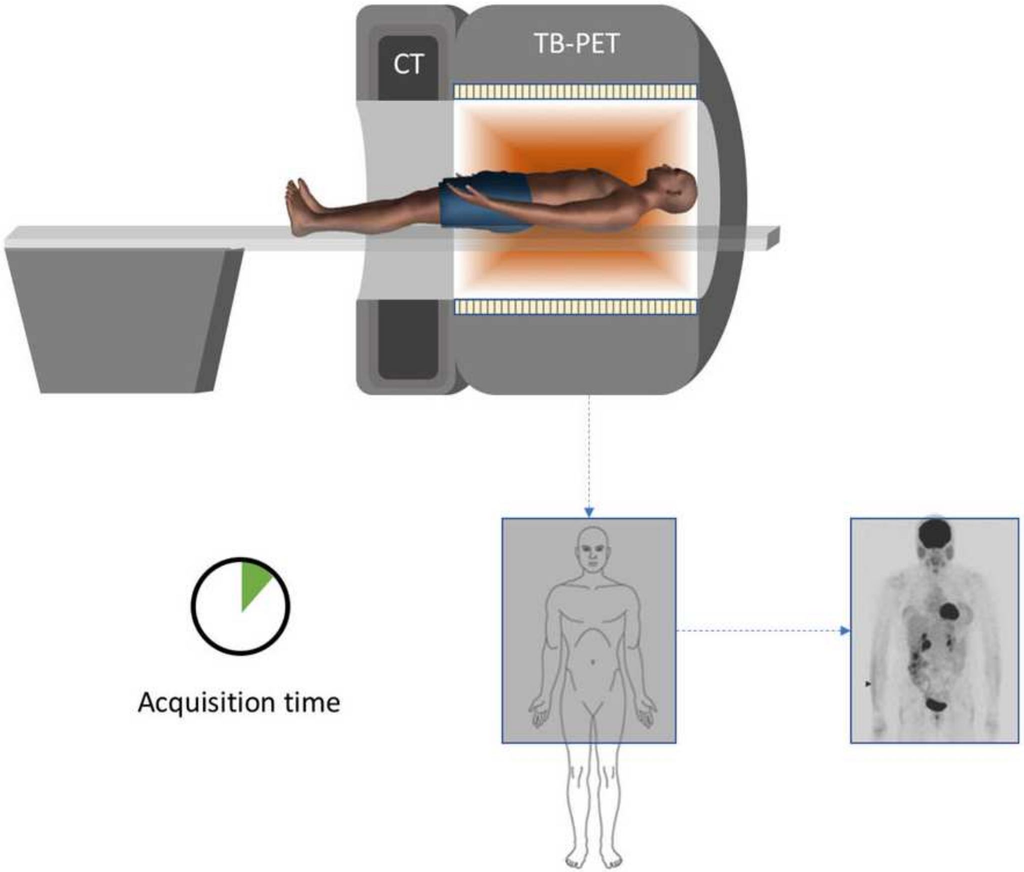
The concept of total body PET



Standard axial length of a PET ring : multiple bed positions are required

The concept of total body PET



The concept of total body PET is to surround the patient with much more detectors in the axial direction to increase the sensitivity with a large factor.

There are two improvements associated with such a design:

1. First of all, the detection efficiency of photon pairs emitted from a certain point already in the FOV is increased by the larger solid angle (longer axial extent).

2. A much larger fraction of the patient is seen in one bed position, so more FOV is covered in the same time frame.

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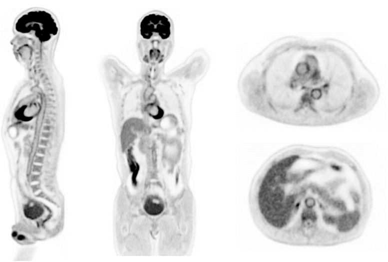
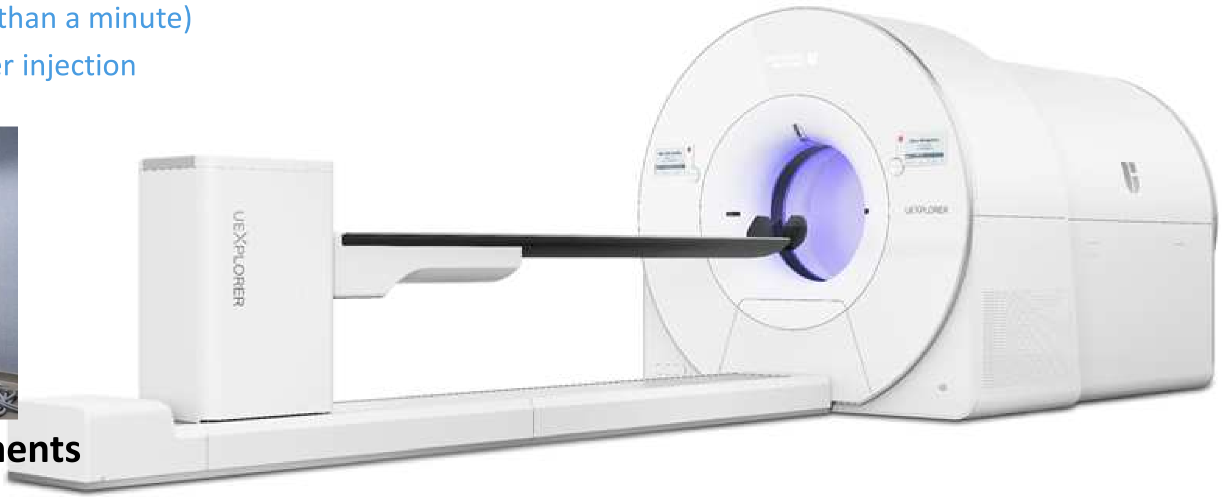
Total-body PET Scanner

UCDAVIS

- The **EXPLORER** consortium is a multi-institutional group established to design, build and utilize the world's highest sensitivity positron emission tomography (PET) scanners for a wide range of biomedical research applications in human patients and volunteers.
- The **EXPLORER** scanner has an effective sensitivity for total-body imaging that is 40-fold higher than current commercial scanners and is expected to open up completely new ways in which PET can be used in biomedical research and ultimately in clinical practice. This massive increase in sensitivity can be used in a number of ways, for example:
  - to perform scans at extremely low radiation doses (similar magnitude to the dose received from a round trip flight between San Francisco and London)
  - to perform scans much more quickly (potentially in less than a minute)
  - to track the fate of radiotracers for much more time after injection



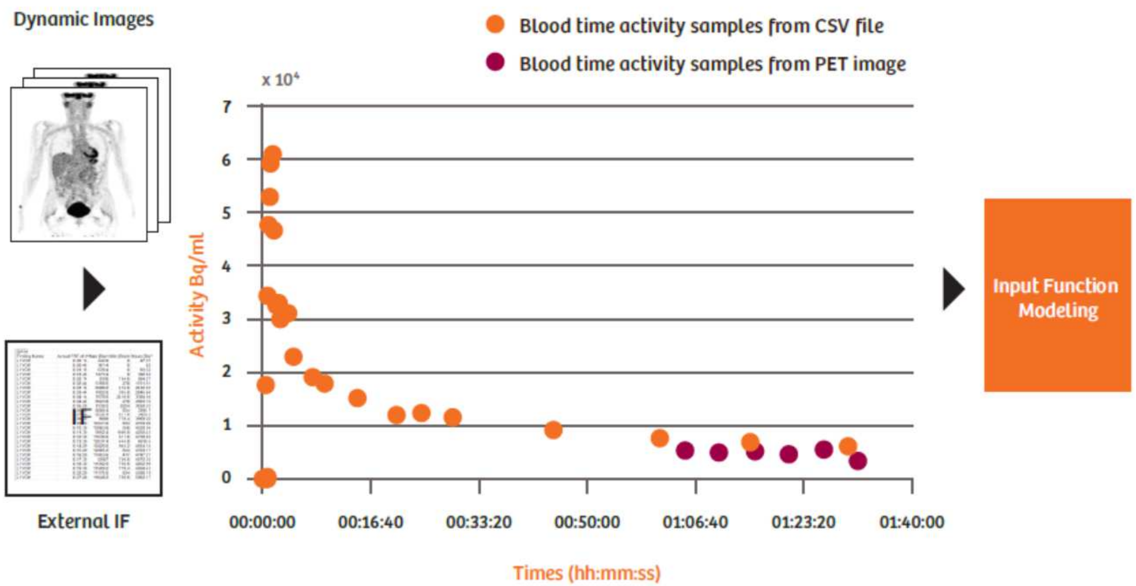
500 thousand detector elements



Clinical application : dynamic PET

New paradigm : whole-body real-time activity data will need to be acquired for all connecting tissues and organs of the body.

GOAL : to measure dynamic *in vivo* physiological processes such as 18F (18F FDG)* metabolism, blood perfusion, oxygen consumption, cell proliferation, and receptor density…



Thank you for your attention !

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