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Dedicated to Professor Ionel Haiduc
on the occasion of his 65th birthday

POSITRON EMISSION TOMOGRAPHY (PET) – PRINCIPLES AND GENERAL CHARACTERISTICS

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ABSTRACT. Positron Emission Tomography (PET) is a powerful nuclear medicine technique. Nuclear medicine techniques allow the visualization of physiological phenomena *in vivo*, and most important in a non-invasive way, through an external detection. The steps required in PET are the following: synthesis of labeled molecules; administration of these labeled molecules to the subject; scanning process with PET camera; data acquisition and subsequent processing; and finally image assessment. The goal of this paper is to briefly review the essential aspects concerning the PET technique, focusing on its principles and characteristics.

1. Introduction

Positron Emission Tomography (PET) presents two useful specific characteristics concerning *in vivo* determination of physiologic, biochemical and pharmaco-kinetics parameters, applied to humans.

On one hand, PET performs a quantitative autoradiography of positron emitters' distribution by using the method of standardized tomography reconstruction, which means that the images of PET correspond to an evaluation of region radioactivity expressed in the quantity of radioactive element on mass unit or tissue volume.

On the other hand, among the positron emitters there are short-lived radioisotopes (like oxygen, carbon, nitrogen), which allow the marking of the majority of the metabolic substratum without introduction of any heteroatoms. Oxygen-15 (produced in a cyclotron) is a short-lived isotope and offers a real possibility to study the cerebral blood flow and the local oxygen consumption of brain, making PET investigation a true non-invasive method.

Speaking about the principle of operation, in Positron Emission Tomography the electron-positron pair suffers an annihilation process in order to form two γ photons of 511 keV energy each; these γ rays are simultaneously emitted in two quite opposite directions. The detection process is made electronically, since both photons are detected due to their interaction with mineral crystals (the detector chain) resulting in photoelectric effect; a photomultiplier chain detects the scintillation photons. The schematic diagram of a PET chamber is given in Figure 1, while the annihilation process is presented in Figure 2.

A PET chamber may be defined as a 3-D detection instrument for coincident 511 keV γ-rays. This chamber is a high-tech, very complex device, which includes: the instrument body (with the detectors and all the subsequent electronics); the bed for the patient (which may be x-y moved); and the computer used to drive the instrument, to store the acquired images, and finally to reconstruct these images.

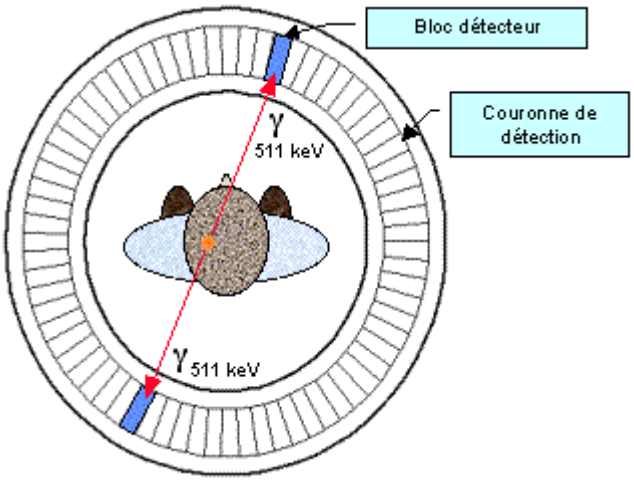

Fig. 1. Schematic of the PET chamber

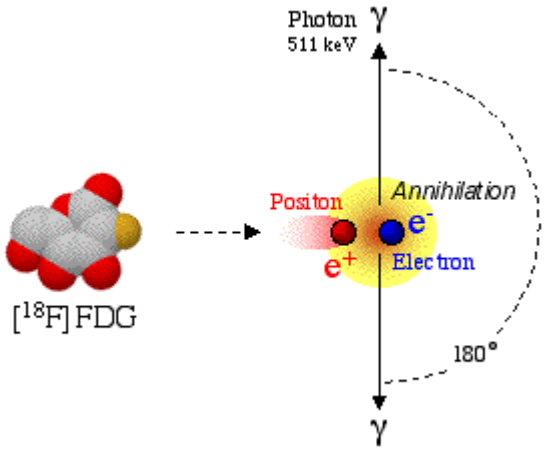

Fig. 2. Diagram of the annihilation process

It is important to remind that the calculation of the physiologic parameters using PET images is a difficult approach, which necessitates the elaboration and validation of the methods and models using numerical analysis appropriate to the studied systems and also to the technical performances of the detectors [1].

2. General characteristics of Positron Emission Tomography

2.1. Principles of PET

2.1.1. Principle of emission

After the synthesis process of the labeled molecules, the molecules of short-lived radioisotopes (positron emitters) are injected or inhaled into the human body and then follow either a metabolic process (glucose or protein syntheses, etc.), a physiological process (flow, distribution volume), or a pharmacological process (being fixed on a ligand, for instance). During the time, the isotopes incorporated in these molecules suffer a radioactive disintegration with positron emission. This is an isotrope emission proportional to the activity, and in fact with the local concentration of the tracer. The positron covers a certain distance within the subject in concordance with its maximum emission energy, until it meets and suffers an interaction with a free electron [2].

The electron-positron pair, having a 1.022 MeV/c^2 repose mass, suffers an annihilation in order to form two gamma (γ) photons of 511 keV energy each. These γ rays are simultaneously emitted in two quite opposite directions, according to the residual quantity of movement after the collision. In reality, the detectors dimension and the quantity of the collected events do not allow measuring this angular scatter, hence the directions are considered as opposed.

The magnitude of time interval of the process is on the order of 10^{-9} seconds (nanosecond range) for both disintegration and β^+ (positron) emission detection. Thus, as an example, if the interaction has taken place in the center of a 90-cm diameter tunnel, the time needed by the photon to reach the detector is equal with 1.5 ns.

2.1.2. Principle of detection

In PET the detection process is made electronically; both photons are detected due to their interaction with the mineral crystals, resulting in a photoelectric effect. Each of the interactions will produce a scintillation photon, which is detectable by a photomultiplier that in turn transforms the light impulse into an electric impulse.

An event is recorded in concordance with its spatial direction, at that moment when two detectors of the ring get independently a signal in coincidence (or in others words at the same time). It is very important to note that in reality the probability of detection at an instant time *'t'* is zero, so that is why one takes into account a Δt, time domain, called “coincidence window”, which is electronically commanded and which records the coincidence events included in the Δt period.

This type of detection presents a number of limits, due to the fact that a same pair of detectors can accept a number of different types of coincidences:

1. True coincidences - the pair of detected photons via electronic signal corresponds effectively to the β annihilation process.
2. Coincidences measured after the diffusion process of the rays: one or two photons of 511 keV suffered a modification of initial direction, due to Compton scattering in the subject.

3. Random coincidences: when two radioactive disintegration events take place simultaneously in different points of scanned object, and consequently a pair of photons (one from the first, and the other from the second disintegration) will be recorded as a coincidence.

It is obvious that all these obstacles concerning image quality should be taken into account, meaning that the technique characteristics of tomography will try to reduce these types of coincidences. To limit scattered coincidences one should choose one of the following methods:

- Increasing the minimal (threshold) energy of selection: the higher the better, because the photon loose energy in diffusion process.
- Window of coincidence should be as narrow as possible, because due to diffusion the time difference between the impact of two photons detected will be increased.
- Introduction of the collimators will reduce the diffusion from a tomograph plane to another.

On the other hand, there are two variants to limit the random coincidences:

a) By reducing the window of coincidence (Δt), because the probability to measure random coincidences increases with time; thus a reduced coincidence window will lead to an increase of the image's quality but in the same time to a lower number of recorded events.

b) By using posterior calculus, based on two type of measurements. In the first case, the counting rate of simple events recorded by some detectors placed on the ring around the subject is used; this rate is proportional with the activity seen by each detector, so that the probability of simultaneous counting by a detector is proportional with the product of both activities: $N_{random} \sim Activity^2 \, \Delta t$. In the second case, a second counting window is open immediately after the first one was stopped (or after a well known delay time), and because the photons have not enough time to arrive to detectors, all the recorded events are random coincidences and should be subtracted from the total data.

2.1.3. Time-of-flight principle. Comparison between TOF systems vs. conventional PET

The basic principle of adding time-of-flight (TOF) information to conventional coincidence counting in PET is to measure the time difference between the two annihilation photons arriving on coincident detectors:

$$\Delta t = 2 x / c,$$

where x is the difference of range and c the light velocity. It allows the spatial localization of the emission event in the vicinity of the positron source, instead of spreading it over the coincidence line. The method supposes that the very fast time-coincidence technique is used, and for this purpose the choice of the crystal and associated electronic circuit used is crucial. As an example, if x= 15 cm

and t= 1 ns, thus an accuracy of 50 ps for Δt would correspond to a 7.5 mm spatial resolution and is equivalent to that obtained with scintillators 15 mm in size, without any reconstruction procedure. In a few words, by using TOF information a coincidence event will be not only localized by lengthways of the coincidence line, but also it will be localized more accurately by the difference of path lengths of annihilation photons between the each coincident detectors. Thus, it is necessary to build up a faster window of coincidence.

The essential advantages of TOF information when used in PET are:

1) As a consequence of the very short scintillation time delivered by fast crystals, a TOF system is able to handle very high counting rates without a pile-up effect and consequently enables for fast dynamics studies.
2) The short range of γ-ray TOF (on the order of 2 ns for a 30-cm object) enables a good elimination of random events.
3) Approximate localization of the source positron results in an improvement of the S/N ratio, which provides a good sensitivity gain [3,4].

Random coincidence rate with TOF:

It is obvious that high random rates introduce dramatic image contrast degradation and even if they are correctly evaluated and subtracted the additional noise could increase the quantitative uncertainty. One of the advantages of random rejection is that one can use more active transmission sources and therefore reduce the acquisition time necessary for an accurate attenuation correction in quantitative studies.

Sensitivity:

TOF can substantially improve the S/N ratio of the tomographic images obtained and qualitatively illustrates this S/N improvement as compared to that obtained with a PET conventional back-projection procedure. The information is much more concentrated in the vicinity of the point source in the TOF technique than in the conventional method, where the information is back-projected only on a fraction of the object. In practice this is equivalent with a substantial decrease in the number of pixels concerned in the reconstruction procedure [4].

Spatial resolution:

Spatial resolution of TOF systems is limited by the size of the detectors for at least two reasons: their lower intrinsic stopping efficiency, and unavailability of small, very fast commercial photomultipliers.

For these reasons, small high spatial resolution detection elements cannot be used currently in TOF-based PET system and a compromise should be chosen between spatial resolution and resolving time. There are essentially two major advantages of the use of TOF over conventional PET, namely its ability to handle very high-count rates without saturation, and a good rejection of random coincidence rate [5].

On the other hand, the sensitivity gain can hardly balance the intrinsic lower efficiency of a fast scintillator compared to that of BGO (bismuth germanate oxide) used in conventional PET, and spatial resolution of TOF system is limited

by the relatively large detector size. As to the first point BaF_2 scintillator being non-hygroscopic, the compact arrangement of such crystals on ring detectors will improve the overall sensitivity, especially when expressing it in terms of counts per seconds / μCi / cm of axial length. Moreover, with BaF_2 the resolving time of a ring detector with a large number of crystals will be on the order of 300 ps (FWHM), thus corresponding to an equivalent sensitivity of 4 to 10 fold greater than conventional PET system (with a comparable geometry) as a function of the object dimensions.

2.1.4. The sensitivity of detection in PET

Sensitivity of detection is defined as the number of the detected events per second for a given radioactivity concentration enclosed in a volume unit. The sensitivity actually determines the counting statistics.

Crystal sensitivity:

The sensitivity of the crystal varies with:

- the nature of the scintillation crystal. Studies are conducted to more efficient detectors than NaI/Tl, such as bismuth germanate ($Bi_4Ge_3O_{12}$ or BGO), cesium fluoride (CsF) or barium fluoride (BaF_2). Factors such as light randament of scintillation (which establishes the number of photons sent to the photomultiplier PM - see Table 1) and stopping capacity of γ photons in connection with density of detection mineral (for BGO, after a pathway of 25 mm up to 90% of 511 keV photons are stopped) have to be considered.
- crystal size, essentially in two modes [6]:
  - section surface increases the sensitivity but decreases spatial resolution;
  - high energy of rays detected imposes the use of thick detectors (Table 1)
- threshold of energy selection: the lower is energy selection, the more photons of annihilation are restrained but there will be a higher number of scattered or random coincidences.

Table 1.

Detectors characteristics over sensitivity

Material	Scintillation time constant	Window of coincidences (ns)	Light yield (mm)	Crystal density (g/cm^3)
BGO	300 ns	12 – 20	8 – 12	7.13
BaF_2	0.8 ns (TOF)	4.1	5	4.89
CsF	3 ns (TOF)		8	4.64
Na/Tl	230 ns	12 – 20	100	3.67
GSO	60 ns		16	6.71
$YalO_4$	31 ns		24	5.35
$PbSO_4$	135 ns		67	6.20

Sensitivity of the photomultiplier tubes (PMT)

The PMT intervenes in sensitivity with both its selection (which allows him to collect the light according to its surface), and respectively the quantum yield of the cathode.

The chain detectors - PM has a determinant importance in counting statistics. If for example the number of photons produced by a γ (511 keV) interaction is up to 2000 then the measurement has an error of 5% [7].

2.1.5. The resolution of positron emission tomography

a) Intrinsic spatial resolution

For the newest PET devices for animal studies, a spatial resolution of 2-mm full width at half maximum (FWHM) is attained; for human studies a 5-mm resolution is achieved. High resolution is needed in order to measure tracers' flow in vascular spaces and the uptake and clearance of tracers in small structures. A high-resolution image will appear to be noisier, but the placement of reconstructed activity will more accurately reflect the true distribution. This accuracy is compromised for a low resolution image, no matter how many events are taken.

Intrinsic spatial resolution is fully determined by the machine geometric characteristics – crystal disposal around the ring and especially the size of elementary crystal section.

To achieve a high spatial resolution while retaining a good temporal resolution and detection efficiency, it is necessary to consider the following factors [5]:

- multiple rings of closely packed detectors of high density and atomic number for a good detection efficiency;
- small crystal for a good spatial resolution;
- a minimum of detector sampling motion (stationary or two position claim) for short imaging time ($\leq$ 2s);
- many parallel detectors channels for low dead-time and high rates;
- photopeak light selection on each crystal for rejection of tissue–scattered annihilation photons and multiple crystal interactions;
- good timing resolution (3-10 ns full coincidence window) for accidental background rejection;
- optimal shielding design for the rejection of prompt scatter and accidental backgrounds.

The factors that influence the resolution of PET are:

1- size of crystal – the smaller is the crystal, the better is resolution (this effect is inverse to that one concerning sensitivity);

2- initial energy of positron emission (isotope energy), which increases positron range before the interaction (Table 2).

Table 2.

Correlation between energy of positron emission (isotope energy) and positron range before the interaction

Isotope	Eβmax (MeV)	Δ(FWHM) $FWHM_0$=11mm	Free distance covered (mm) 75%
18-F	0.64	0.22	1.29
11-C	0.96	0.28	2.10
15-O	1.72	1.10	4.80
82-Rb	3.35	2.60	12.40
13-N	1.19	0.50	3.00
68-Ga	1.90	1.35	5.40

The annihilation events distribution at a point source has an approximately Gaussian form, having FWHM (in mm), approximately equal to ratio of maximum energy E_{max} (MeV) of positron and tissue density. In brain, image degradation due to positron range for the most usual isotopes (C-11; O-15; F-18) will be up to 1 cm (for F-18 2.3 mm, O-15 over 8 mm). Certain isotopes such as 38-K or 82-Rb provide positrons of high energy, which is an impediment, due to the decrease of the resolution. Additionally, even though γ rays of annihilation are generally emitted in opposite directions (at 180°), there would be a deviation from the direction and also the resolution quality will decrease (there is an uncertainty concerning collinearity of $\pm$0.25°). At 50-cm diameter rings may appear deviations that provide a decrease in resolution up to 1 mm, and for 100-cm diameter a resolution damage of 2 mm could occur. Even if the detector is made by discrete elements, all these form a continuous cylindrical detector (ring) and this fact leads to problems in accuracy of localization of scintillation events due to Compton scatters and others interactions. The range of this effect is up to 1 or 2 mm. It is important to underline here that an important phenomenon takes place when the annihilation photon arrives on detector surface under an angle: this will lead to a decrease of radial resolution for large distances from the image center.

3- object position over the tunnel center (Table 3).

Table 3.

Intrinsic resolution

0		10	20	Distance by center (cm)
BaF_2	5.4×5.7	5.4×6.2	6×8.6	Tangential and radial resolution (mm)
	8.9/7	10.2/10.4	12.5/21.4	Axial resolution (mm)
BGO	6.0	6.3	7.1	Radial resolution (mm)
	5.4	6.3	7.1	Axial resolution (mm)

The ring size in the slice plan (x,y) determines if the scanner should be used for cerebral exploration only, or for the whole body. Diameter of ring will modulate the resolution (peak), the homogeneity at FWHM as a function of distance to the center (a ring for whole body will provide a more homogenate

center), and the sensitivity. In accordance with the number of rings, z-axis is more or less explored which involves a movement or not of the patient within the tomograph for visualizing the whole organ (Table 4).

Table 4.

Ring size and slices to be explored

	Axial field	Elements
BaF_2	8.4 cm	7 cups of 9 mm , space of 12 mm
BGO	10.8 cm	31 cups 3.375 mm
	16.2 cm	47 cups of 3.125 mm (67 cups of 2.64 mm- to be developed)

Summarizing, the spatial resolution limits in PET could be briefly reviewed as a function of: positron range; deviation from 180° emissions; detectors size and detection efficiency; linear density of detectors in use; and multiple interactions within the crystal.

b) Temporal resolution:

Temporal resolution depends not only by the limits imposed by counting statistics, but also by the cycle of elementary sampling. With a rotational speed maximum of one round (circle) per second we can obtain one image each second.

In practice it is necessary to have a sequential mode for collecting data on a support and also to perform the reconstruction after choosing the optimal sequences.

For a bolus injection of 20 mCi of labeled water (with 15-O) for cardiac study, an image of right ventricle can be done by accumulating the coincidence events within the 2 seconds and in 4 seconds for left ventricle.

3. Conclusions

In this work the general characteristics and principles of PET were briefly discussed.

One should realize the increasing importance of this particular technique over the conventional nuclear medicine, from several points of view. First of all, PET may offer a non-invasive investigation method, being in fact the best method in brain disorders investigation [8]. Furthermore, PET technology uses short-lived radioactive isotopes and biocompatible-labeled molecules as markers, so that the tracer carrier is extremely fast and well assimilated by the body; therefore, PET is a very suitable technique for metabolic studies [7].

PET technique presents the auto-attenuation feature, which is not yet available for other conventional nuclear medicine techniques; also, the possibility of quantification has a crucial importance for the comprehension of the physiological mechanisms' studies.

Last, but not least, PET technique offers a pretty fast imaging response (the whole cycle of investigation takes from few minutes to few hours).

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