MIDDLE EAST TECHNICAL UNIVERSITY

FACULTY OF ARTS AND SCIENCES

PHYS450 - HEALTH PHYSICS

TERM PAPER

Positron Emission Tomography (PET)

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Introduction

Introduction and historical developments

A brief history of Positron

A subatomic particle which existence of the particle was first postulated in 1928 by the famous Paul Dirac. However, the particle positron is first observed 4 years later in 1932 by a scientist named Carl D. Anderson, who gave the name of positron to the particle itself. Furthermore, Anderson wanted to rename the electron as “Negatron”, but his suggestion failed hence we still use the name electron for e^- particle[9][10][11][12].

What is a Positron?

Positron is the anti-matter complement of the e^-, electron, and has the identical mass to an electron but opposite to the electron, it has a +1 charge rather than -1. Positrons have many possible sources to be produced, but in the case of PET scanning, the Positron is sourced as a product of nuclear decays.

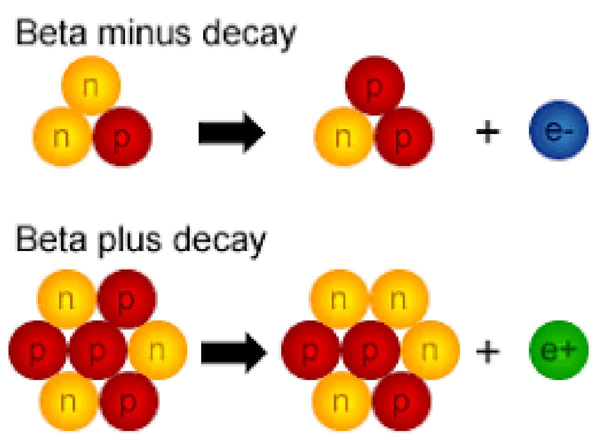

Figure 1 What is a Positron

[Positron Emission Tomography (schoolscience.co.uk)]

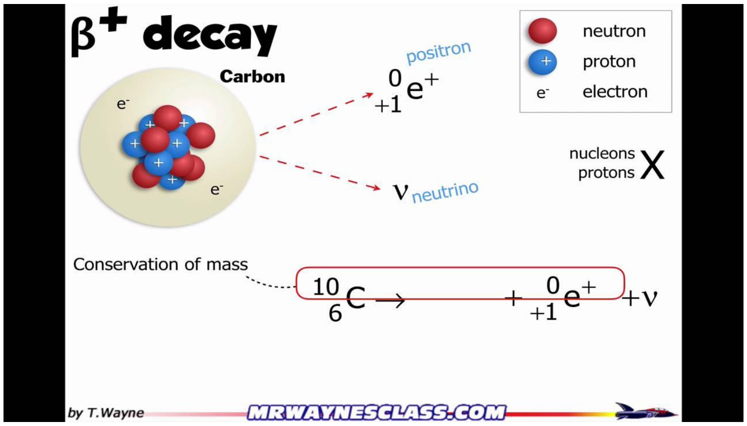

Figure 2 An example of positron (Carbon) decay or Beta-Plus Decay

[Beta plus introduction - YouTube]

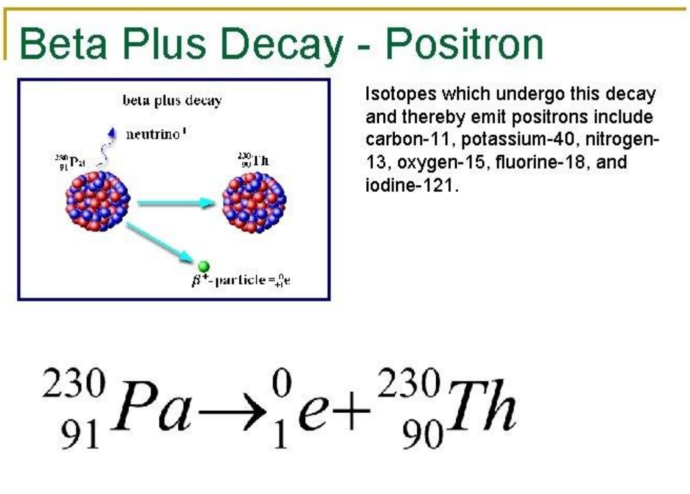

Figure 3 An example of positron (General) decay or Beta-Plus Decay

[Atomic Nuclear Physics IB Physics Life and Atoms (slidetodoc.com)]

Nuclear decay is basically when an unstable nuclei are produced in a cyclotron (will be covered later) by bombarding the target material with protons, then as a result a neutron is released.

$$^{18}O + proton => \ ^{18}F + neutron$$

In PET, the material that is targeted is chosen so that the product of the bombardment decays to a more stable state isotope by emitting a positron, e.g ^{18}F has too many protons, so one of these protons decays into a neutron emitting in the process a positron an a neutrino.

$$proton\ (+\ 1\ charge)\ \ =>\ \ neutron\ (0\ charge)\ \ +\ \ positron\ (+\ 1\ charge)\ \ +\ \ neutrino\ (0\ charge)$$

After decay, were left with ^{18}O[1].

Sources of Positron

There are two types of positrons to use;

First one is the Slow Positrons which have energy in eV and seen in positron annihilation spectroscopy in materials studies.

Second one is the Fast Positrons which have energy levels in MeV and can be seen in particle accelerator sources.

Technologies that are used for positron sourcing can be separated into 4 types as:

1) Radio-isotope source
2) MeV electron beam
3) GeV electron beam
4) Gamma-ray beam

Radio-isotope source can also be separated into 2 types with;

1) Long-lived such as ^{22}Na ($\sim10^6$ e^+/s)
2) Or beam-induced such as ^{13}N ($\sim10^9$ e^+/s)

Now let's look at the different types as mentioned above as Fast and Slow positron.

Fast-Positron

There are two types of sourcing of the Fast-Positron to delve further into, let's discuss them.

1) Conventional Sources (mentioned above and with nuclear reactions)
2) Advanced Sources (separated into 3 important sourcing)
    - Hybrid Target
    - Undulator Gamma-Ray
    - Compton Gamma-Ray

Bremmstrahlung and pair-production takes place when there is an incident electron beam enters a conversion target which is most of the time a solid.

There are certain major limitations to the technology which is most of the time the heat-load or the shockwaves in the conversion target.

Conventional Sources

Target in the system is 14mm of amorphous tungsten. In the system that is in the figure 4 on the right image, there is a beam spoiler used to keep the peak energy on the system deposited density below the $\frac{35J}{g}$. Emittance that is normalized is 2100 mm.mrad before the damping ring. Energy spread in the system is 0.1% at 4 GeV. Injector aims to produce 2 bunches per pulse at 50Hz rep rate with a bunch charge of $2.5 \times 10^{10} = 2.5 \times 10^{12} e^{+}/s$.

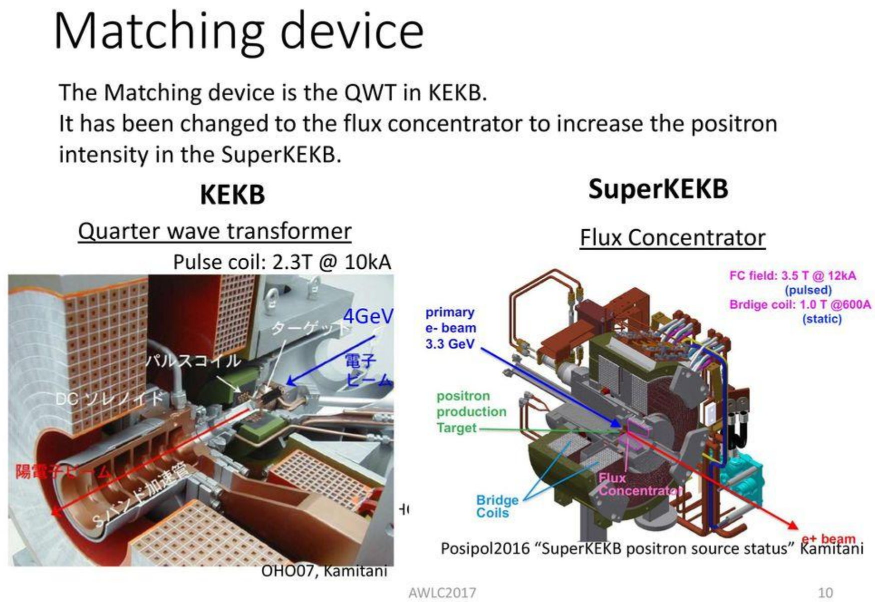

Figure 4 Conventional Source device (Super KEKB Positron Source)

KEKB/SuperKEKB positron source a review and the status - ppt download (slideplayer.com)

Advanced Sources (Hybrid Target Source)

As our second type of sourcing Fast-Positrons, the first one to come into our mind is Hybrid Target Sourcing. In Hybrid Target Sourcing, one of the strategies is to avoid any damage to the conversion target by separating the bremsstrahlung and pair-conversion processes into two separate targets.

Enhanced photon production becomes possible in a crystalline target due to the channeling of the radiation. The difference in the yield of photon for a 5 GeV electron beam incident on a 1.4mm thick amorphous W target compared with the crystalline target of the same thickness. (Artru et al., 2015)

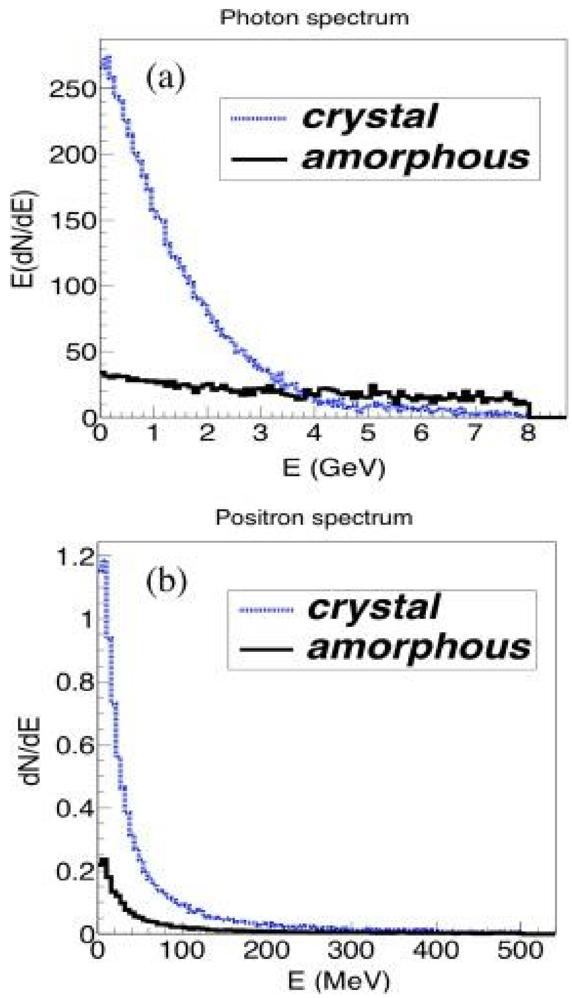

Fig. 5. (a) Energy Spectra for the photons, and (b) energy spectra for the Positrons. (Artru et al., 2015)

Sources such as CLIC from crystal => dipole (where e^+ produces and then) with gamma-ray to amorphous also a yield of ~$8e^+ / e^-$. these are the sources as considered as the kind of sources for SuperKEKB and for CLIC as mentioned above.

In this system heat dissipation can be improved by replacing the amorphous target with a granular target (for which experiments are undergoing at KEK)[14][15][16][17][18][19].

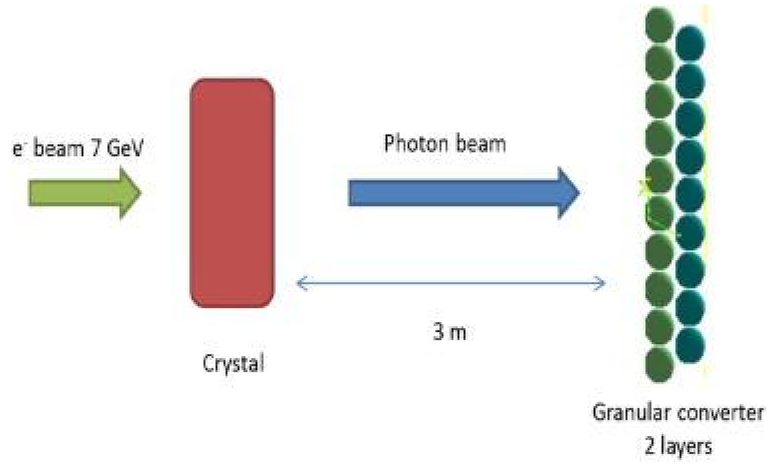

Figure 6 CLIC and KEK case
(Artru et al., 2015)

Advanced Sources (Undulator Gamma-Ray Source)

This method of fast-positron sourcing, which is named as undulator source and is and advanced technique is primarily considered as for the ILC, the undulator produces a gamma-ray spectrum with a series of harmonic peaks in the system. For this sourcing system normalized emittance after target is 0.13m rad[14][15][16][17][18][19].

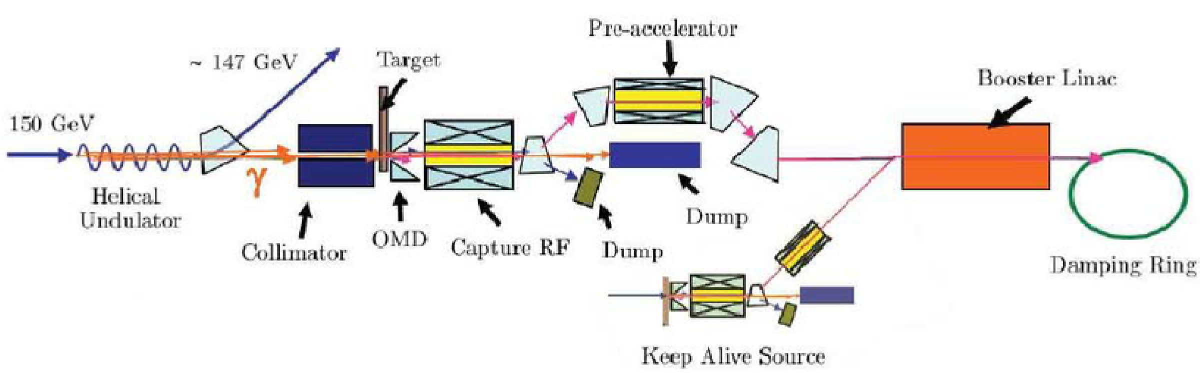

Figure 7 Positron Undulator Source
(Clarke et al., 2015)

Advanced Sources (Compton Gamma-Ray Source)

The last one that will be mentioned for this part is the Compton source which has the mechanism of compton backscattering of the laser beam that has been used for an electron beam that is as used in the most intense gamma-ray sources such as the ELI-NP.

The laser in the system is typically a YAG laser that is using one or many high finesse optical cavities.

In figure 8 one can see a Compton source that is designed as CLIC Injector Complex.

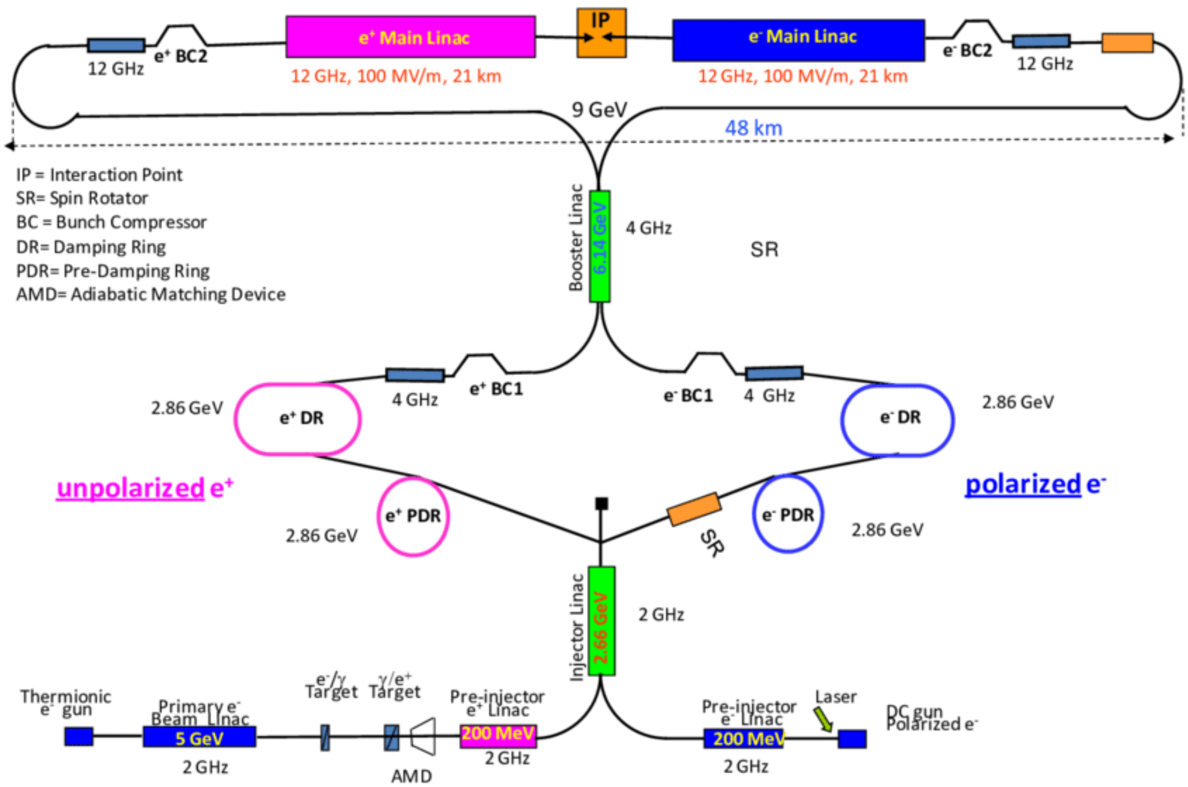

Figure 8 CLIC Main Beam Injector Complex for 3 TeV: Baseline configuration (Rinolfi et al., 2022)

By this Compton source built we now finished covering the parts that are intended to be covered for sourcing of positron, let's go back to the history of the positron, PET, and more [14][15][16][17][18][19].

Annihilation of a Positron and Electron

In the annihilation of a positron and electron, the positron will encounter an electron and completely annihilate each other resulting in a conversion of all their masses into energy. From this, it results in two photons, or gamma rays production.

Due to the conversation of energy and momentum, each photon has exactly the same energy and it is 511 keV, also the photon head is almost 180 degrees from each other.

511 keV is the ideal rest state of annihilation value.

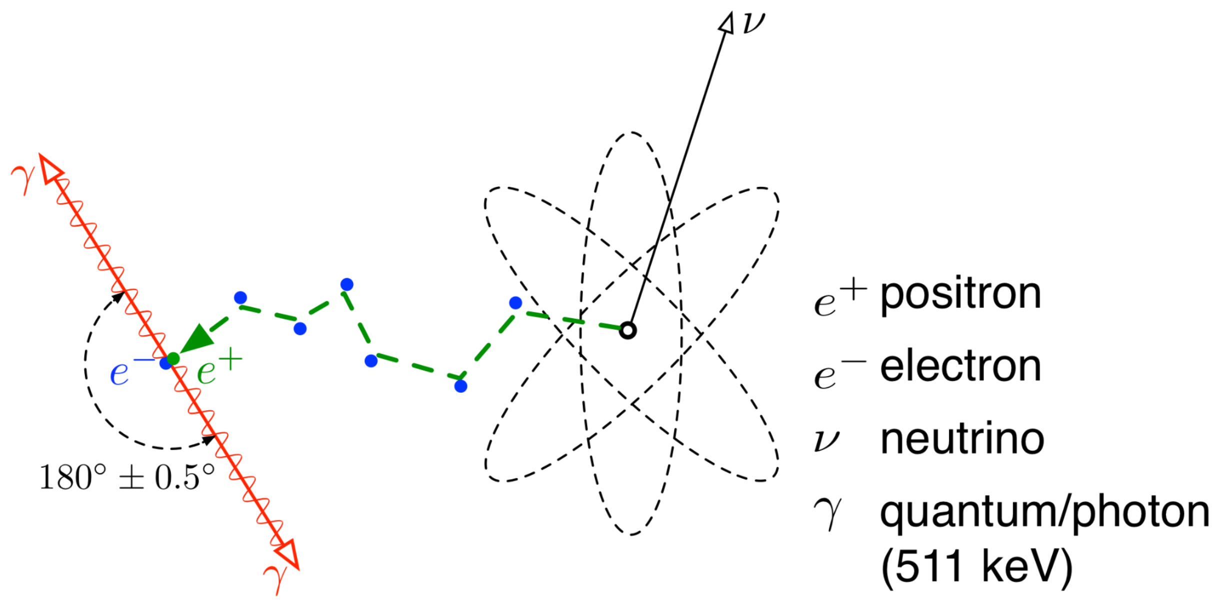

Figure 9 Annihilation of a Positron and Electron

[Electron–positron annihilation - Wikipedia]

How do we detect photons (gamma rays)?

The Positron-Emission Tomography device detects these photons that come from annihilation with a PET camera which allows it to determine where they came from, where the nucleus was when it decayed, and also knowing where the nucleus goes in the body.

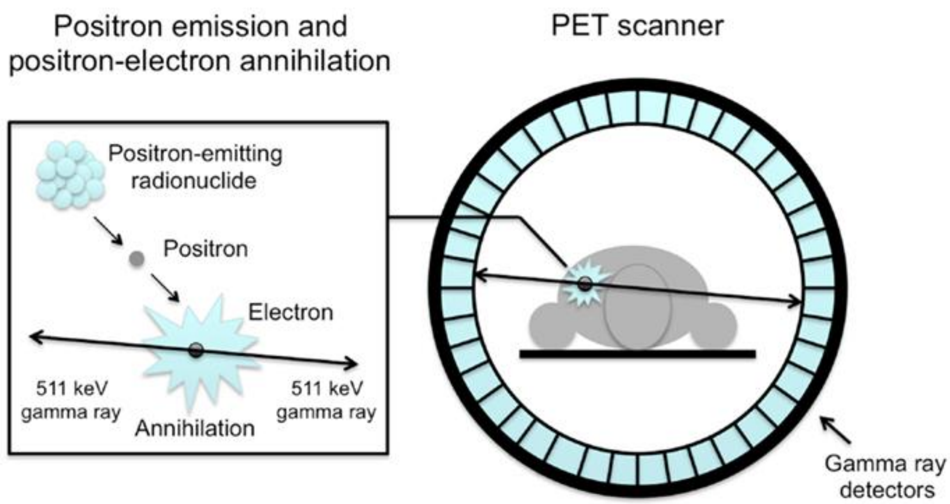

Figure 10 PET Gamma Ray Detectors

POZİTRON EMİSYON TOMOGRAFİSİ (PET) – TIP VE MÜHENDİSLİK (wordpress.com)

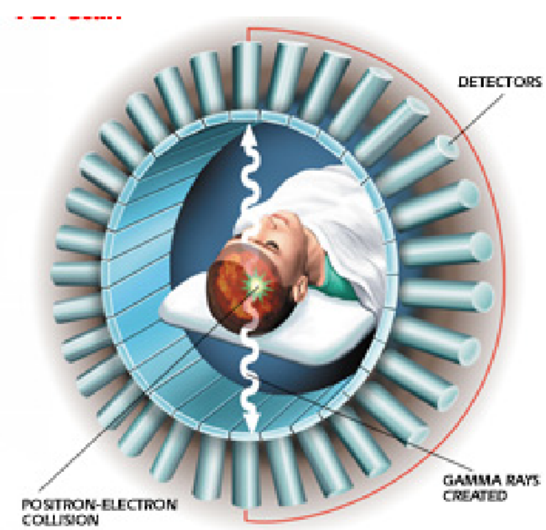

Figure 11 PET Gamma-Ray Detectors and collision illustration

(Crosetto, 2009)

History of PET scanners

Concept of the emission and transmission tomography was introduced by David E. Kuhal and Roy Edwards in late 1950s at the University of Pennsylvania.

In the 1970s, Tatsuo Ido from Brookhaven National Laboratory was the first to describe the synthesis of ^{18}F FDG, the most commonly used PET scanning isotope carrier. The ^{18}F FDG is chosen because of its half-life is hundred and ten minutes which is convenient for to carry isotopes of this material from a cyclotron to make the positron which is far away from the place or the city you are located at, hence it can be carried out to scan the patient conveniently without losing the material. Other positron emitted isotopes also could be used such as carbon-nitrogen-oxide, but they are not feasible to use since they have short half-lives they cannot be used if the isotopes are coming from far away cyclotron.

Also in conventional nuclear medicine and nuclear imaging, isotope of choice can be such as technetium-99m which is a metastable nuclear isomer of technetium-99 and is the most common medical radioisotope in the world, however when we talk about cellular imaging or molecular imaging then the isotope of choice becomes ^{18}F, there could be other isotopes of use such as ^{11}C, ^{13}N, ^{15}O, but ^{18}F is chosen due to it can be used for more than 90% of the imaging/examination also the compounds can be coupled with the element isotope itself.

One can clearly say that there is not only one person to name that developed the PET scan, but a collective of people made the system to come to this day.

Physical Principles

Physical Principles of Positron Emission Tomography

PET (Positron Emission Tomography) Definition

The PET or Positron emission tomography is a type of nuclear medicine imaging technique that produces a three-dimensional image of functional processes in the body itself. The method is a non-invasive diagnostic imaging technique to measure the metabolic activity of cells in the human body.

The method was developed in the mid-1970s and it can be said that it is the first scanning method to give functional information about the brain. There are also other types of imaging techniques such as like CT or MRI x-ray, but they were not intended to give functional information as PET does. To enhance the power of the PET one can use it together with CT or MRI[2][3][5]].

How PET works

PET working starts with a short-lived radioactive tracer isotope, which is injected into the living being and the injection application is usually done into blood circulation. The tracer is chemically incorporated into a biologically active molecule.

Later we will continue with a waiting period due to the active molecule getting concentrated in tissues that the medical doctor has an interest in to find out the issues. Then as the radioisotope undergoes positron emission decay (also known as positive beta decay), it emits a positron, an antiparticle of the electron with opposite charge (which is the main deal of PET as the name suggests.). After traveling up to a few millimeters the positron encounters an electron, and the encounter annihilates them both (both the electron and the positron which is electron-positron annihilation as known.) and produces a pair of (gamma) photons moving in opposite directions with 511 keV[6][8][9][11].

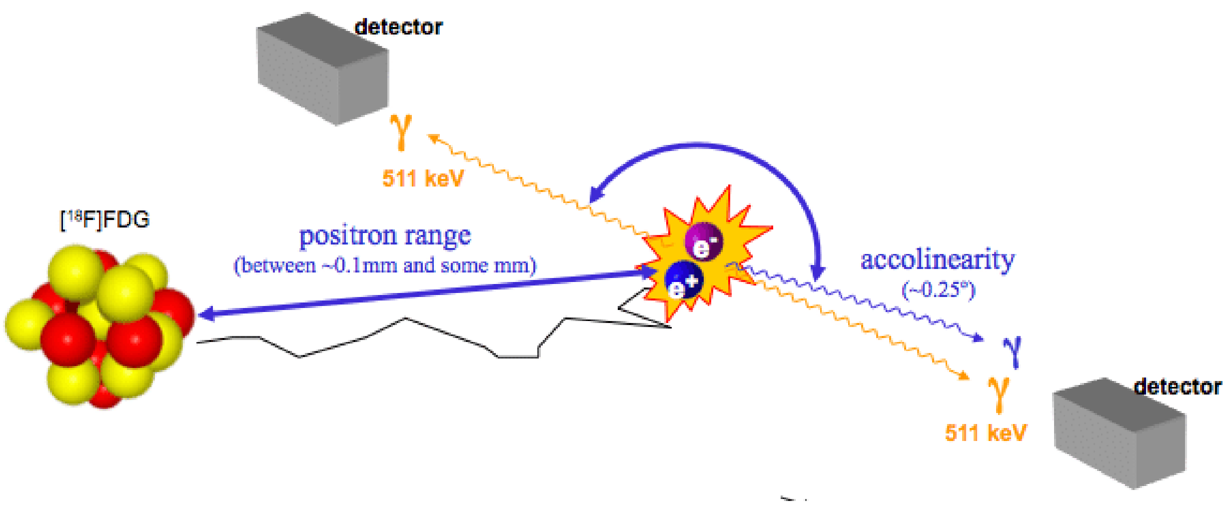

Figure 12 Positron-Electron Annihilation
(Branco, 2010)

These photons then are detected when they reach the scintillator in the scanning device creating a burst of light which is detected by photomultiplier tubes. The technicians therefore could then create an image of the parts of the brain, e.g which are overactive.

PET Scan

As mentioned before in the prior parts, why when there exist CT and MRI, and also other types of high technology methods that were available we have the PET scan developed, why did this science move forward. The reason behind the PET scan development is simplistic as living a regular daily life, which is functional information that you can get by the PET scanning. PET scanning enables one to get function information at the cellular level. Throughout the years' humankind developed these technologies and is now able to diagnosis disease at first steps rather than it is too late.

What Makes PET Useful

Positron emission tomography (PET) is offering a vast number of unique advantages compared to other imaging modalities. PET measures the two annihilation photons that are produced back-to-back after the emission of the positron from a radionuclide tagged tracer molecule, that is chosen to mark a specific function in the body on a biochemistry level. Henceforth, PET is known for providing molecular imaging to biological function instead of anatomy. The detection of the annihilation of both photons (gamma) in the coincidence yields increased sensitivity over all other forms of medical imaging. The imaging of the two high-energy annihilation photons that are time-coincident allows accurate attenuation correction from either a dedicated transmission scan or from CT information.

The system allows accurate extraction of the information from PET images. Only minute amounts of imaging substrate are needed to be injected (due to the tracer principle) because of the high sensitivity of PET. In addition to this, positron-emitting isotopes that are used in medical imaging (C-11, N-13, O-15, F-18, etc.) are relatively short-lived, this enables optimal use of the imaging photons while keeping patient radiation dose in a range that is not dangerous to the patient. Moreover, most of these isotopes that are discussed are can be incorporated into biological substrates (glucose, H_2O, NH_3, CO_2, O_2, etc.) and pharmaceuticals, without altering their biological activity.

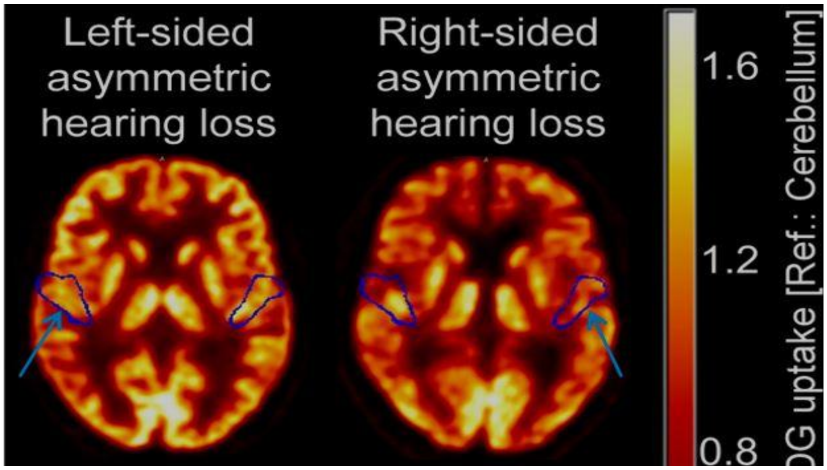

Figure 13 PET Application to show neural nonfunctioning

High-Resolution PET/CT Imaging May Help Predict Effectiveness of Cochlear Implant (hearinghealthmatters.org)

Compared to CT and MR images, PET images appear much blurrier and or noisier, due to the relatively limited number of photons that can be collected during an imaging study. In addition, detector resolution is poorer due to the detector physics. X-ray CT scanners can easily resolve the points less than 1 mm in size, while PET scanners cannot be said to reliably resolve point sources such that are smaller than 4-5 mm at best, and closer to 10 mm in practice. However, this system does not impair their high sensitivity to focal tracer concentrations or their usefulness in accurate quantitative functional imaging (Schmitz et al., 2013).

Data Acquisition for PET

Photon detection and Scintillation detectors

Photon's general goal is to detect and measure the total energy deposited by the photon when it traverses the detector. For the highest sensitivity and accuracy, all of the photon's energy should be deposited, but in practice, this is not always possible.

In most PET scanners today, scintillation detectors are used as detection elements. They couple inorganic scintillation crystals that emit visible or near-ultraviolet light after interaction with an incident high-energy (511 keV) photon, to photodetectors that detect and measure the scintillation photons.

Scintillation crystals, the incident annihilation of a photon (nominally 511.000 eV energy) interacts and create photons that are tens of thousands which are in the visible wavelengths (about 1 eV energy each) in a very short flash or "scintillation". The number of scintillated photons produced in the crystal is proportional to the energy deposited by the annihilation photon (Schmitz et al., 2013).

There are many things to continue with the data acquisition, but I believe for the sake of the continuity and general goal of the paper will not continue with it.

Uses of the PET scanning

- Detects Cancer
- Determines whether cancer is malignant or benign and has the potential to spread in the body
- Assess the effectiveness of a treatment plan, such as cancer therapy
- Determines if cancer has returned after treatment
- Determines blood flow to the heart muscle

- Determines the effects of a heart attack, or myocardial infarction, on areas of the heart.
- Identify areas of the heart muscle that would benefit from a procedure such as angioplasty or coronary artery bypass_surgery (in combination with a myocardial perfusion scan).
- Evaluate brain abnormalities, such as tumors, memory disorders, seizures, and other central nervous system disorders.
- To map normal human brain and heart function.

The PET scanner can be used in patients with conditions affecting the brain, or heart diseases. Also can be used in the detection of Alzheimer's disease, certain types of cancer, lastly some neurological disorders. (Portnow, 2013)

Cyclotron

- Is a charged particle accelerator
- Accelerates the charged particles in a cycle path and these particles gain energy.
- Energetic particles then hit a target material get absorbed in to the nucleus, converting the target in to the different species.
- E.g, a proton of hydrogen, when hits ^{18}O-water converts it to the ^{18}F-fluoride with emission of a neutron other insignificant "sub-atomic" particles to balance the energy equilibrium. (Youtube, 2018)

Tracer

- Radioisotopes used in PET scans are isotopes of carbon, nitrogen, oxygen, gallium and ^{18}F used as a substitute for hydrogen.

- Only radioactive forms of natural elements that will pass safely through your body and be detected by the scanner.

- The scanner type that is used depends on what your doctor wants to measure, so; if your doctor is looking for a tumor, he might be wanting to use radio-labeled glucose (FDG) and watch how it is metabolized by the tumor.

Mutual Annihilation after Positron Decay

The positron later annihilate a free electron, generate two gamma photons in opposite directions.

- The two photons each have energy 511 KeV, which is the energy equivalent to the rest mass of an electron or positron

- These gamma rays that are produced are used for medical imaging (Positron Emission Tomography), detected using a coincidence detection circuit. (Portnow, 2013)

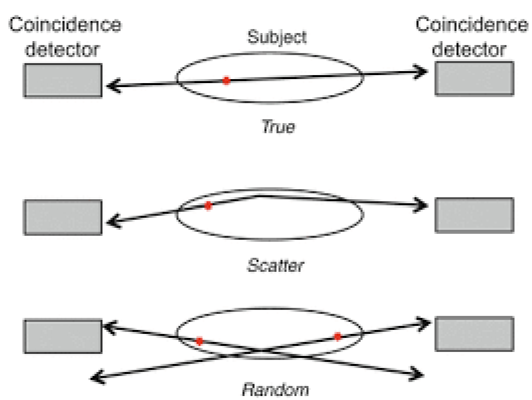

Figure 14 PET Detected Events

[PET Physics and Instrumentation | Radiology Key]

(The Radiology Key is really good website to understand instrumentation principles of PET.)

Coincidence Timing

In the coincidence of timing there are three classes of events which are;

- True coincidence
- Scattered coincidences
- Random incidences

Which are given in figure 14. One must tune the sensitivity in the PET otherwise can detect too much noise since the measurement capability of the system is able to detect “trues” and reject “randoms”. (Youtube, 2018)

Combined PET/CT scanner

- It is used to detect the structure and function of the wanted body part simultaneously.

- Greater detail with a higher level of accuracy is achieved; due to both scans being performed at one time without the patient having to change positions, hence there is less room for error.

- Greater convenience for the patient who undergoes two exams (CT & PET) at one sitting, rather than at two different times.

- CT part is a high-resolution anatomical (structural information) information giver and PET now enhances this with additional functional imaging (with low-resolution). (Youtube, 2018)

Benefits of PET Scan

- The information that is provided by nuclear medicine examinations is unique and often unattainable using other imaging procedures.

- For many diseases, nuclear medicine techniques that make scanning yield the most useful information needed to make a diagnosis or to determine the appropriate treatment. If any exist.

- Nuclear medicine is less expensive and may yield more precise information than exploratory surgery.

- By identifying changes in the body of the patient at the cellular level, PET imaging might detect the early onset of disease before it is evident on other imaging tests such as CT or MRI, so it can be an early bird for the patient itself. (Youtube, 2018)

But there are still limitations to this technique let's discuss those.

Limitations of PET Scan

- It is time-consuming

- Resolution of the structures that are attained from the body by nuclear medicine might not be as clear as with other imaging techniques, due to low-resolution, such as CT or MRI.

- It can give false results if the chemical balances in the body are not at regular levels.

- Since radioactive substances decay quickly and are effective only in a short period of time, it is important to have the patient be there on time for the appointment and receive the radioactive material at the scheduled time.

- A person who is highly obese may not fit into the opening of a conventional PET/CT unit.

- It is needed to be considered that the patient will remain still for a very long time, hence it is hard to attain.

- Claustrophobic people may feel anxiety and may not remain silent or hormone levels may rise due to fear.

- Even though you may feel the desire to feel something due to the radioactivity, there won't be any and you will be disappointed unless it is the plutonium gas that they are injecting into you mistakenly, and if it's the case, it is highly unlikely you will get out alive from that day. (Youtube, 2018)

Conclusion

Conclusion

The PET scanning produces images of the body of the patient by detecting the radiation emitted from radioactive substances, there positron-electron annihilation occurs with 2x511 KeV photon created to opposite directions.

These substances that are mentioned above are injected into the body, and are usually tagged with a radioactive atom such as ^{11}C, ^{18}F, ^{15}O or ^{13}N, that has short decay time. These radioactive atoms are formed by bombarding standard/regular chemicals with neutrons to create short-lived radioactive isotopes.

PET detects the gamma rays (photons) given off at the site where the annihilation occurs, positron emitted from the radioactive substance, and collides with an electron in the tissue (annihilation). Then these results are acquired with an instrumentation system that has data acquisition machinery in it and evaluated by a trained expert such as MD.

These results may contain false information and these false information also with the caring the patient to not panic them is the duty of the health providers, which is elaborated in the techniques part, due to it might effect the results of the system which will lead into bad results.

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* Some of the citations are shown with superscript [] and some shown with APA just because I was tired of writing some of them.