Nuclear chemistry is the study of changes associated with the nuclei of atoms. Positron emission tomography (PET) is one of the beneficial real-life uses of nuclear chemistry. Simply, it is a handy instrument that physicians use to take images of an individual's body to determine if a person is at risk for a certain disease or carries one. This module will focus on the procedures of a patient receiving a PET scan, the nuclear reactions associated with the images that are produced, commonly used tracer molecules, and useful applications of PET scans in clinical diagnosis.

History

The first PET camera was completed in January 1974 by Michael Phelps's and the first whole-body system for human and animal studies was finished in December of that year. The first commercial system, also designed by Phelps, was delivered to UCLA in December 1976. The research that went into creating the first PET scanner dates several decades back to the early 1950s. It was suggested by William Sweet, Chief at the Massachusetts General Hospital, that the radiation from positron emission has the potential to increase the resolution of nuclear images taken in detecting any brain damages. Soon after this proposal, many patients under the suspicion of brain tumors were imaged with a simple positron scanner and the image results were much clearer, as was predicted by Sweet. The simple positron imaging device uses two-dimensional arrays and only a few radiation sensors to trace the radioactive substances, so the images were very low quality.

In 1952, the first clinical positron scanner device was invented. This device was essentially the same as the first simple positron scanner from 1950 but with a few upgrades. It not only produced coincidence scans, but unbalance scans as well. The unbalance scan was a huge refinement because it produced a lower resolution image that allowed for easier determination of a brain tumor to the right or left of the midline of a patient's brain.

Then in 1962, the first multiple detector positron imaging device was invented. A few unique features on this new scanner include higher sensitivity as well as being able to obtain another three-dimensional image by focusing on different planes of the two detector arrays. This allowed for the imaging of lesions in two dimensions while the exact position of the tumor growth can be determined in three dimension. Refinement of the PET scanner focuses on increasing the sensitivity and adding features to find more ways to have the scanners produce images in higher definition.

In 1970, the PET scanner was formally introduced for use in the medical field. A few years following the introduction of the PET scanner, the radiopharmaceutical fluorine-18-2-fluoro-2-deoxyglucose (FDG) was made by chemists as a tracer so studying of the images were easier in locating brain tumors. Technological advances in the 1980s allowed for the invention of PET scanners with higher resolution than ever before that produced very precise, clear images.
Figure 1: This shows that increases in image quality were evident as refinements were added to previous PET scanners. Image courtesy of Brain and Mind.

Nuclear Reactions

The procedure of PET scans are made possible by nuclear reactions involving the emission of the positive beta particle known as the positron. The positron is a mass-less particle but has a positive charge of one. In other words, it is very similar to an electron (they have the same mass), but instead of a negative charge, it carries a positive charge. In nuclear reactions, it is commonly represented as any of the symbols \( ^0_{+1}e \), \( ^0_1e \), or \( _{+1}\beta \). The emission of a positron is represented by:

\[
^1_1p \rightarrow ^1_0n + ^0_1e^-\]

This shows that the positron (represented here by \( ^0_1e^- \)) speeds out of the nucleus while the neutron stays inside the nucleus. Consider the following nuclear reaction that is common in PET scans of the brain where carbon-11 is used as the tracer molecule.

\[
^{11}_6C \rightarrow ^{11}_{5}\beta + ^0_1e^-\]

Notice that in this example of positron emission, the nuclide changes into a different element and as it gives off a positron particle, the atomic number is lowered by one, but the mass of the new element stays the same as the carbon that has decayed.

General Procedure

The first step of the process is to inject the patient with a solution commonly used by the body to produce energy, such as glucose. It must be a positron-emitting substance because when the scanner with its array of detectors detect the
collisions of the positrons with electrons, the two species disappear, and in the process, create two gamma photons to move apart in opposite directions. The scanner's electronics record these detected gamma rays and map an image of the area where the active glucose is located. PET allows the physician to locate the exact areas where metabolic activities are occurring. For example, the PET scan shows exactly where the injected glucose is being used in the brain, the heart muscle, or a growing tumor. In a cancer patient, the cancer cells show up as denser areas on a PET scan due to the cells' high metabolic rates in comparison with normal cells.

Figure 2: Patient undergoing the process of getting a PET scan. A patient undergoing a SPECT bone scan. The patient lies on a table that slides through a scanner, while two gamma cameras rotate around him. Machine operators typically work remotely from another room, shielded from the radiation being emitted by the patient. from Wikipedia (CC-BY-SA-3.0, Ytrottier).

**Computed Axial Tomography (CAT) and Magnetic Resonance Imaging (MRI)**

Computed Axial Tomography (CAT) scanners are very similar to PET scanners. The major difference is that patients are scanned with x-rays in a CAT scan so they are at risk of developing cancer if exposure to the ionizing radiation is too long or too often. The Magnetic Resonance Imaging (MRI), which was invented after the CAT scanner, is an expensive test and uses radio waves and magnets that show information on a computer screen. Patients are not at risk with MRIs because the test does not use ionizing radiation of any kind. The reason CAT scans are still used is most likely because it is much more affordable than MRIs.

Compared to CAT and MRI scanners, PET is much more efficient in detecting the differences between benign and malignant tumors because it focuses on the metabolic activity of radiopharmaceutical chemicals (glucose).

**Radionuclides**

Radionuclides used in PET scanning are typically isotopes with short half-lives that stay active just long enough to trace its activities in the body effectively and produce corresponding images. Below is a list of some of the more common isotopes...
used as tracers in the body and what each of their primary uses are:

- Carbon-11: PET brain scan
- Copper-64: Lung and liver disease diagnosis
- Fluorine-18: Bone scanning and studying the cerebral sugar metabolism
- Krypton-79: Assessing cardiovascular function
- Nitrogen-13: Brain, heart, and liver imaging
- Oxygen-15: Lung function test

**Figure 3:** Graphic representation of a patient's PET scan shows abnormal activity in the abdominal region. Image courtesy of Wikipedia Commons.

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**Applications of PET Scans**

PET scanning is useful in the medical field as well as a research tool. In the medical field, it is heavily used in the clinical diagnosis of certain diseases and disorders because it is effective in targeting radionuclides (tracers) used in particular bodily functions. It is also useful in researching certain brain diseases and checking whether cardiovascular functions in
an individual are normal because the produced images map this out very clearly as shown in the graphic representation below.

1. Oncology

PET scanning using the tracer radionuclide fluorine-18 (commonly known as FDG) is used because glucose-using cells take this molecule up and the images show where the metabolism of glucose is abnormal. The FDG molecule is trapped inside of the cell that takes it up until it decays completely, so a relatively short half-life is important. The use of FDG in oncology PET scans make up the majority of all PET scans in current practice.

PET scanning is especially effective in the detection of cancer because the activity of the injected glucose is especially active and is easily traced in the produced images.

Listed below are a few reasons why PET scanning is effective in detecting cancer:

1. Early and immediate detection: PET scanners effectively produce images of the immediate activity of glucose, accurately distinguishing a tumor growth due to its significantly active form, as is shown on the images in higher resolution. However, a PET scan images the entire body, so if it catches the activity of secondary tumor growths first, this can change the treatment that a patient will undergo.

2. Stages of cancer: PET is very sensitive in determining the full extent of disease, especially in lymphoma, malignant melanoma, breast, lung, colon and cervical cancers. Confirmation of metastatic disease allows the physician and patient to more accurately decide how to proceed with a certain patient's treatment.

3. Checking for recurrences: PET scanning is considered to be one of the most accurate procedures in differentiating tumor recurrences. By being able to scan a patient without the risk of over-radiation, this particular procedure allows for the development of a treatment plan that works most favorable to the patient, while also incorporating all functioning data of the tracer chemical.

4. Effectiveness of chemotherapy: The levels of tumor metabolism are compared on PET scans before and after a chemotherapy cycle. A successful chemotherapy treatment is visible by a PET scan by comparing the images from before and after the treatment and noting whether there are any noticeable changes in the activity of glucose throughout the body.

2. Neurology/Neuropsychology

PET imaging of the brain is based on the assumption that brain activity is associated with high radioactivity. The tracer nuclide that is used is oxygen-15. Its short half-life of two minutes makes it so that PET scans of the brain must be processed immediately after the oxygen-15 is made. The brain’s rapid use of glucose produces very vividly colored images that indicate where the most activities in the brain are. This makes it relatively easy to narrow down where abnormal activity is occurring in a patient with a brain disease because the color on the image will be different in the areas where a disease has settled in.

3. Cardiology

Though relatively new, detecting patients at risk of stroke may have been suggested to be the next focus of the process of PET scanning. The tracer nuclides that are used include krypton-79 and nitrogen-13.
4. Psychiatry

Carbon-11 and fluorine-18 are two radionuclide tracers that selectively bind to receptors in the brain, thus are a target for further research in the biological aspects of psychiatry. The states of dopamine, serotonin, and opioid receptors have been studied in humans because of their affect in patients with psychiatric conditions such as schizophrenia and mood disorders.

Problems

1. Given the symbol for nitrogen-13 is $^{13}\text{N}$, using knowledge of positron emission, find which element the decay of nitrogen produces in the following nuclear reaction that takes place in PET scanning.

\[ ^{13}\text{N} \rightarrow \underline{^{13}\text{O}} + _{+1}\beta \]

2. Write the nuclear reaction for positron emission by oxygen-15, which takes place in a PET scan used to assess the efficiency of the lungs.

\[ ^{15}\text{O} \rightarrow \underline{^{15}\text{F}} + _{+1}\beta \]

3. Write the nuclear reaction for positron emission of a chemical used in bone scanning and studying the sugar metabolism of the cerebral (positron emission by fluorine-18).

4. Write the nuclear reaction for the reaction necessary to assess cardiovascular function in the human body, given that the nuclide krypton-79 emits a positron in the reaction.

Solutions

1. $^{13}\text{N} \rightarrow \underline{^{13}\text{O}} + _{+1}\beta$

2. $^{15}\text{O} \rightarrow \underline{^{15}\text{F}} + _{+1}\beta$

3. $^{18}\text{F} \rightarrow \underline{^{18}\text{Ne}} + _{+1}\beta$

4. $^{79}\text{Kr} \rightarrow \underline{^{79}\text{Rb}} + _{+1}\beta$

References


4. [http://jco.ascopubs.org/content/26/1/....full.pdf+html](http://jco.ascopubs.org/content/26/1/....full.pdf+html)