Swayam Course - Analytical Techniques

Week: 15, Module 39 - PET and its diagnostic Applications

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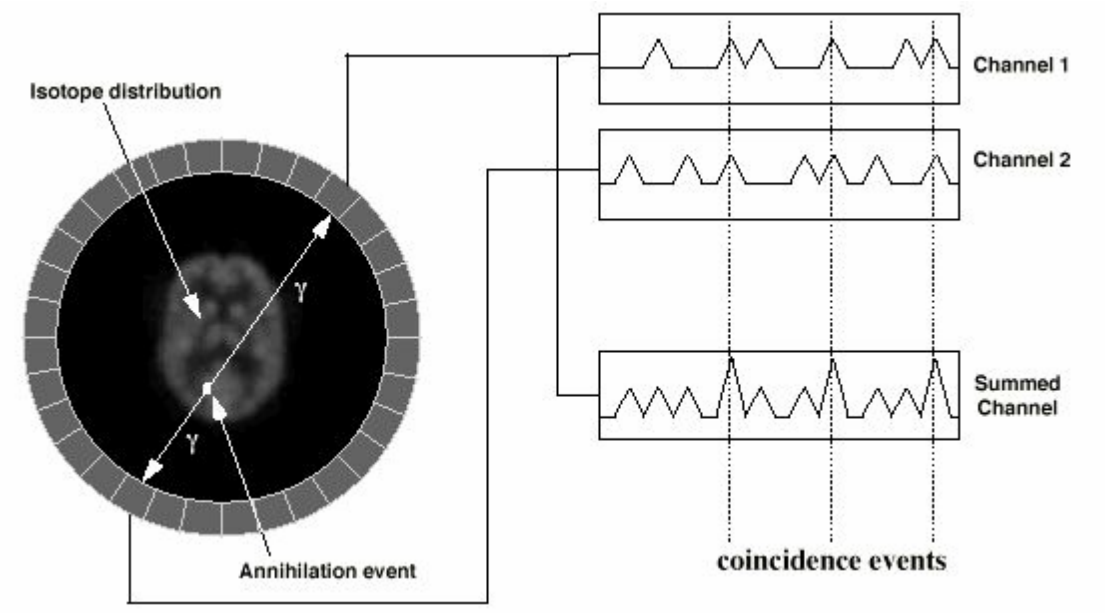
1. Objective:

1) To understand the principle of Positron Emission Tomography (PET).
2) To understand the detection principle of gamma rays emitted from the patient.
3) To understand the mechanism of coincidence detection circuitry working.
4) To know the various types of events detected by the detector and which one is important for formation of image.

2. Introduction:

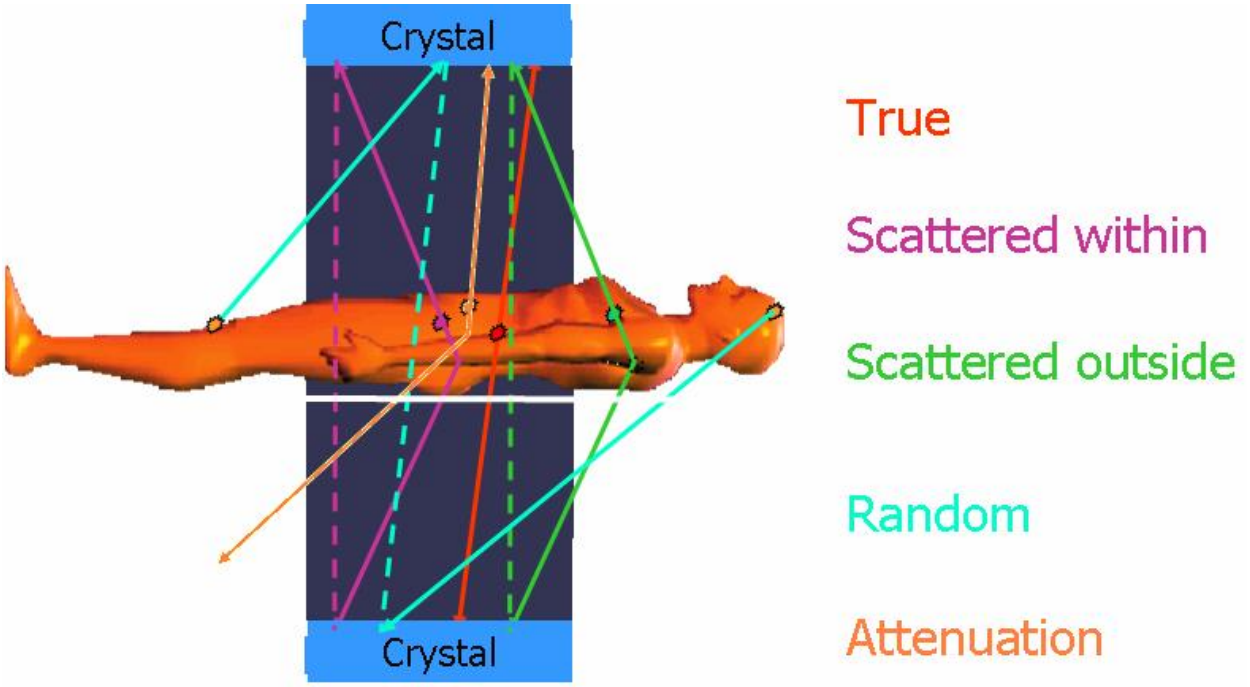
The Positron Emission Tomography (PET), is the most sensitive method for quantitative measurement of physiologic processes in vivo. It only uses positron-emitting radionuclide. PET detectors detect the back-to-back annihilation photons that are produced when a positron interacts with an ordinary electron



Coincidence detection in a PET camera

As seen in the figure, the geometry of PET detectors consists in a ring detect the coincidences emitted from the patient. Several parallel rings form the complete detection panel of the system. A coincidence event is assigned to a line of response (LOR) joining the two relevant detectors. In this way, positional information is gained from the detected radiation without the need for a physical collimator. This is known as electronic collimation. Electronic collimation has two major advantages over physical

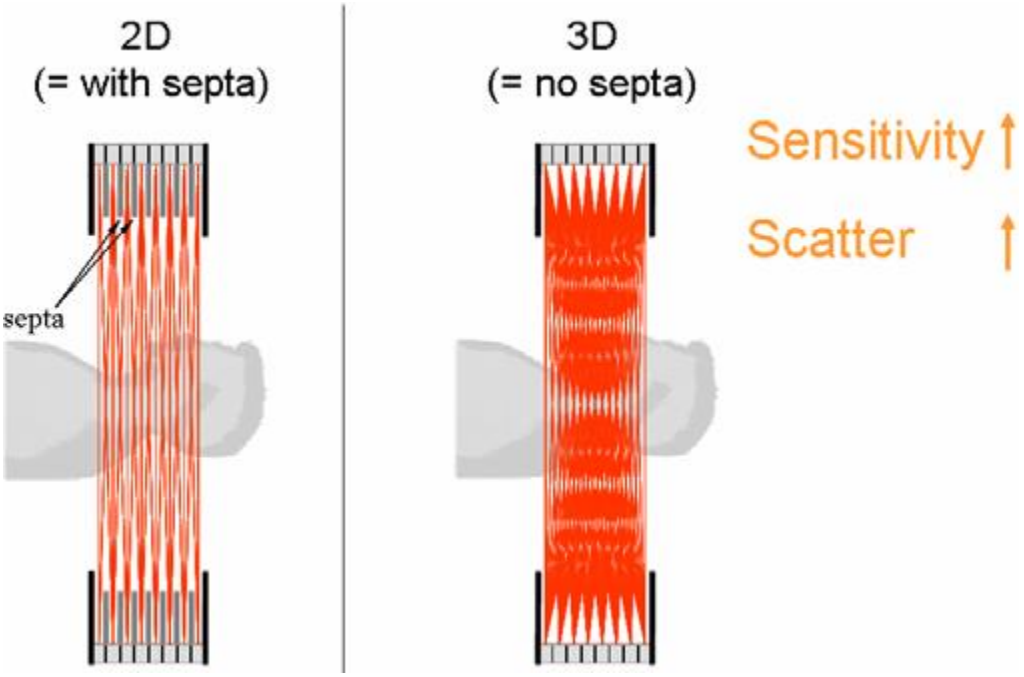
collimation. These are improved sensitivity and improved uniformity of the point source response function.
Coincidence events in PET can be of four kinds: ***true, scattered, random and multiple***. As shown in the following figure;



PET Coincidence

True coincidences occur when both photons from an annihilation event are detected by detectors in coincidence, neither photon undergoes any form of interaction prior to detection, and nor other event is detected within the coincidence time-window. A scattered coincidence is one in which at least one of the detected photons has undergone at least one Compton scattering event prior to detection. Since, the direction of the photon is changed during the Compton scattering process, it is highly likely that the resulting coincidence event will be assigned to the wrong line of response. Scattered coincidences add a background to the true coincidence distribution, which changes slowly with position, decreasing contrast and causing the isotope concentrations to be overestimated. They also add statistical noise to the signal. The number of scattered events detected depends on the volume and attenuation characteristics of the object being imaged, and on the geometry of the camera. Random coincidences occur when two photons not arising from the same annihilation event are incident on the detectors within the coincidence time window of the system. The number of random coincidences in a given LOR is closely linked to the rate of single events measured by the detectors joined by that LOR and the rate of random coincidences increase roughly with the square of the activity in the FOV. As with scattered events, the number of random coincidences detected also depends on the volume and attenuation characteristics of the object being imaged, and on the geometry of the camera. The distribution of random coincidences is fairly uniform across the field of view, and will cause isotope concentrations to be overestimated if not corrected for. Random coincidences also add statistical noise to the data. Most cameras employing block-detector technology may be operated either in "2D" mode or "3D" mode. In 2D mode, thin septa of lead or tungsten separate each crystal ring and coincidences are only recorded between detectors within the same ring or lying in closely neighboring rings. Coincidences between detectors in closely neighboring rings are summed or rebinned to produce a dataset consisting of 2P+1 co-planar sets of LORs normal to the

axis of the camera, where P is the number of detector rings. Such a data set may be reconstructed into images using tomographic techniques like the ones discussed by SPECT.

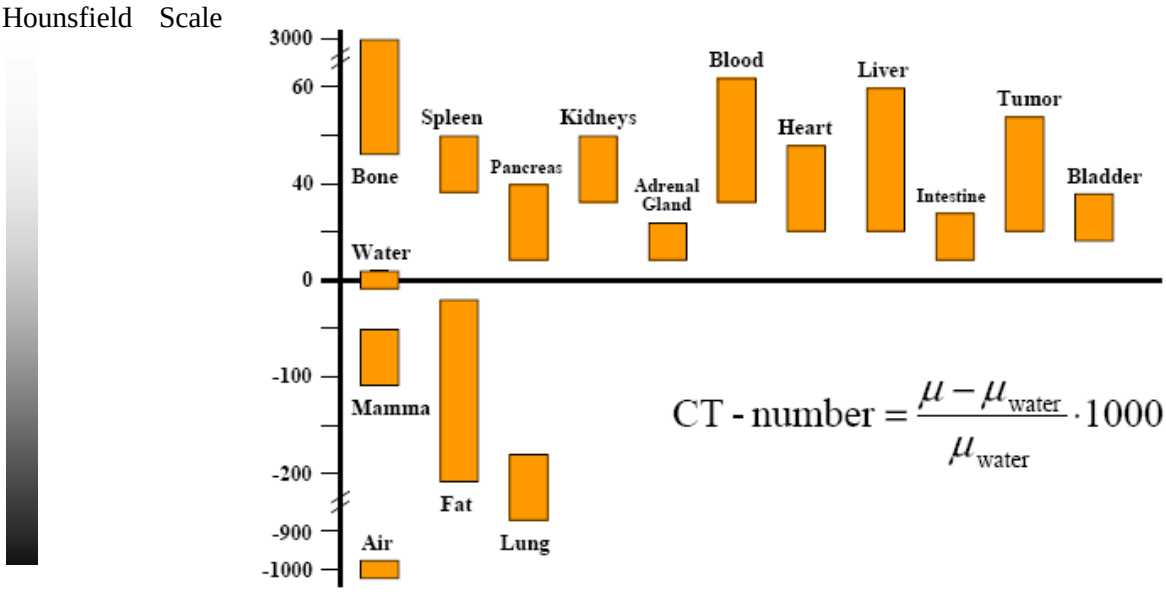


Corrections for scatter, randoms and the effects of attenuation are applied to data acquired in a PET camera then the number of counts assigned to an LOR joining a pair of crystals is proportional to a line integral of the activity along that LOR. Parallel sets of such line integrals are known as projections. Reconstruction of images from projections is a problem to which much attention has been paid over the last 30 years, and many analytical and iterative reconstruction schemata exist on in the computational burden. One way to get attenuation correction is by running a transmission scan. It uses a radioactive source to produce attenuation "map" of the body of the patient. A reference scan called "blank" is always done in order to obtain the ratio of the blank counts that is used for corrections and quality assurance.

3. CT Principles:

The principles of CT are conceptually simple. Physically, X-rays can traverse a cross-section of an object along straight lines, are attenuated by the object, and detected outside it. During CT scanning, the cross-section is probed with X-rays from various directions; attenuated signals are recorded and converted to projections of the linear attenuation coefficient distribution of the cross-section. These X-ray shadows are directly related to the Fourier transform of the cross-section, and can be processed to reconstruct the cross-section.

Hounsfield Scale

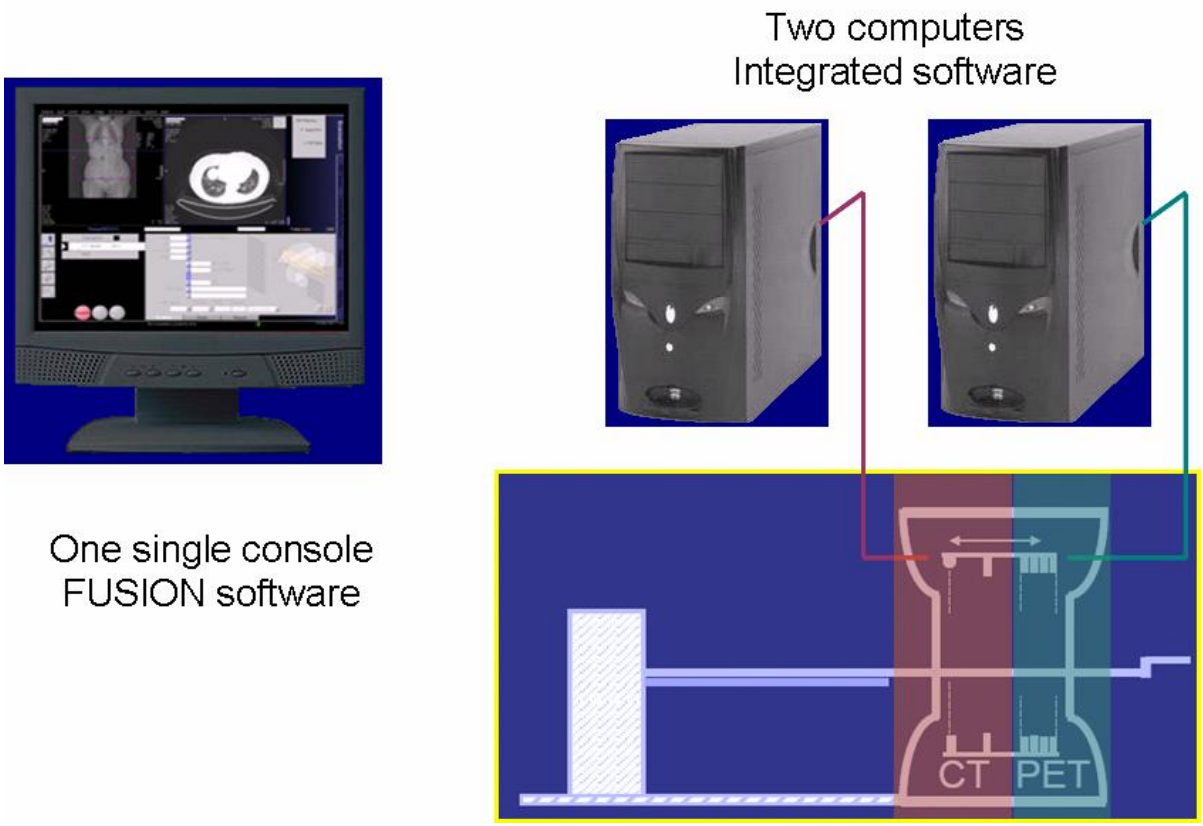


The measured attenuations of the X-rays passing through the patient are converted into pixels and converted into CT numbers (Hounsfield units (HU)). The 3D CT images are obtained from 2D transverse slices, which show anatomical information in terms of tissue densities (HU). Because we cannot see the difference between 2000 different shades of grey it would be pointless to produce an image which covered the whole range of Hounsfield numbers. In order to produce a useful image of the area of interest a system of windowing and levels is used. The available grey scale is spread over the chosen range of Hounsfield numbers. The window defines the upper and lower limits of this range. To produce an image, which shows up most major structures, a large window is used. For more detailed information about tissues with very similar density, a small window is used. The smaller the window the more detailed the image but the range of tissue density that is seen is reduced.

The level is the Hounsfield number at the centre of the window. This is chosen so that the window covers the type of tissue you are interested in. To image dense tissues, a high level is used and to image low density tissues, a low level is used. Multi-slice detector geometries allow whole-body imaging, reduces scanning times (of a few seconds) which brings that the patient discomfort is reduced and movement artifacts in images are minimized. To enhance some structures with similar tissue density values, contrast media (high density substances) are used.

4. PET/CT principles:

The PET images offer a great functional contrast but don't provide too good anatomical resolution. On the other hand, the CT images provide a very good anatomical representation but it is difficult to find out functional information out of it. The combination of PET and CT in a single device provides simultaneous structural and biochemical information (fused images) under almost identical conditions, minimizing the temporal and spatial differences between the two imaging modalities.



Basic components of a PET/CT system

Among the advantages that having this two modalities together offers we can find that the patient stays on the same table for both acquisitions minimizing any intrinsic spatial misalignment; the total examination of PET is notably reduced; because of the transmission scan is being done by the CT reducing in this way the costs of maintenance and of replacing the radioactive source available in the standard PET scanners.

The PET/CT examination starts with the injection of the radionuclide. After an uptake time the patient is positioned as comfortable as possible on the table of the PET/CT scanner. Normally, a CT-topogram follows and then the table moves into the start position of the PET system and the emission scan is initiated. By the time the emission PET scan is completed, the CT transmission images have been already reconstructed and available for the attenuation and scatter corrections of the emission data. The total time for the images to be ready for diagnostics is restricted to the reconstruction time which is more or less the time taken to have enough counts for each bed position of the PET acquisition.

5. Radionuclides and Radiotracers

Radionuclides used in PET scanning are typically isotopes with short half-lives such as carbon-11 (~20 min), nitrogen-13 (~10 min), oxygen-15 (~2 min), fluorine-18 (~110 min), gallium-68 (~67 min), zirconium-89 (~78.41 hours), or rubidium-82(~1.27 min). These radionuclides are incorporated either into compounds normally used by the body such as glucose (or glucose analogues), water, or ammonia, or into molecules that bind to receptors or other sites of drug action. Such labelled compounds are known as

radiotracers. PET technology can be used to trace the biologic pathway of any compound in living humans (and many other species as well), provided it can be radiolabeled with a PET isotope. Thus, the specific processes that can be probed with PET are virtually limitless, and radiotracers for new target molecules and processes are continuing to be synthesized; as of this writing there are already dozens in clinical use and hundreds applied in research. At present, however, by far the most commonly used radiotracer in clinical PET scanning is fluorodeoxyglucose (also called FDG or fludeoxyglucose), an analogue of glucose that is labeled with fluorine-18. This radiotracer is used in essentially all scans for oncology and most scans in neurology, and thus makes up the large majority of all of the radiotracer (> 95%) used in PET and PET-CT scanning.

Due to the short half-lives of most positron-emitting radioisotopes, the radiotracers have traditionally been produced using a cyclotron in close proximity to the PET imaging facility. The half-life of fluorine-18 is long enough that radiotracers labeled with fluorine-18 can be manufactured commercially at offsite locations and shipped to imaging centers. Recently rubidium-82 generators have become commercially available. These contain strontium-82, which decays by electron capture to produce positron-emitting rubidium-82.

6. Safety:

PET scanning is non-invasive, but it does involve exposure to ionizing radiation. 18F-FDG, which is now the standard radiotracer used for PET neuroimaging and cancer patient management, has an effective radiation dose of 14 mSv. For comparison, radiation dosage for other medical procedures ranges from 0.02 mSv for a chest x-ray and 6.5–8 mSv for a CT scan of the chest. Average civil aircrews are exposed to 3 mSv/year, and the whole body occupational dose limit for occupational radiation workers in India is 20mSv/year. For PET-CT scanning, the radiation exposure may be substantial—around 23–26 mSv (for a 70 kg person—dose is likely to be higher for higher body weights).

7. Limitations:

The minimization of radiation dose to the subject is an attractive feature of the use of short-lived radionuclides. Besides its established role as a diagnostic technique, PET has an expanding role as a method to assess the response to therapy, in particular, cancer therapy, where the risk to the patient from lack of knowledge about disease progress is much greater than the risk from the test radiation. Limitations to the widespread use of PET arise from the high costs of cyclotrons needed to produce the short-lived radionuclides for PET scanning and the need for specially adapted on-site chemical synthesis apparatus to produce the radiopharmaceuticals after radioisotope preparation. Organic radiotracer molecules that will contain a positron-emitting radioisotope cannot be synthesized first and then the radioisotope prepared within them, because bombardment with a cyclotron to prepare the radioisotope destroys any organic carrier for it. Instead, the isotope must be prepared first, then afterward, the chemistry to prepare any organic radiotracer (such as FDG) accomplished very quickly, in the short time before the isotope decays. Few hospitals are capable of maintaining such systems, and third-party suppliers of radiotracers that can supply many sites simultaneously support most clinical PET. This limitation restricts clinical PET primarily to the use of tracers labeled with fluorine-18, which has a half-life of 110 minutes and can be transported a reasonable distance before use, or to rubidium-82 (used as rubidium-82 chloride) with a half-life of 1.27 minutes, which is created in a portable generator and is used for myocardial perfusion studies. Nevertheless, in recent years a few on-site cyclotrons with integrated shielding and "hot labs" (automated chemistry labs that are able to work with radioisotopes) have begun to accompany PET units to remote hospitals. The presence of the small on-site cyclotron promises to expand in the future as the cyclotrons shrink in response to the high cost of isotope transportation to remote PET machines.

Because the half-life of fluorine-18 is about two hours, the prepared dose of a radiopharmaceutical bearing this radionuclide will undergo multiple half-lives of decay during the working day. This necessitates frequent recalibration of the remaining dose (determination of activity per unit volume) and careful planning with respect to patient scheduling.

8. Summary:

Positron emission tomography/computed tomography (PET/CT) has an important role in the diagnosis and treatment of cancer. The technique can aid in the detection of an unknown primary tumor, assist in locoregional staging, evaluate for distant metastases or second primary tumors, and be a component of restaging and tumor surveillance. This article reviews the basic principles, pitfalls, and uses of PET/CT in cancer, as well as potential future applications.

End of Module

Quadrant III

Self Learning:

Multiple Choice Questions

Q1) Which of the following isotopes has the shortest half life?

a) Carbon-11
b) Nitrogen-13
c) Oxygen-15
d) Fluorine-18

A: c

Q2) What is detected during positron emission tomography (PET)?

a) Positrons
b) Neutrons
c) Electrons
d) Photons

A: d

Q3) The Positron Emission Tomography (PET), is the most sensitive method for quantitative measurement of physiologic processes in vivo.

a) True
b) False
c) Depends on the situation

A: a

Q4) Electronic collimation has two major advantages over physical collimation.

a) Improved sensitivity
b) Improved uniformity
c) Bothe (a) and (b)

A: c

Q5) Coincidence events in PET can be of four kinds ***true, scattered, random and multiple.***

a) True
b) False
c) Depends on the type of interaction

A: a

Q6) True coincidences occur when both photons from an annihilation event are

a) detected by detectors in coincidence
b) detected after attenuation of one photon
c) detected after attenuation of both the photons
d) all the above

A: a

Q7) The isotopes used for PET Scan are produced in

a) cyclotron
b) reactor
c) generator
d) linear accelerator

A: a

Q8) The effective dose received by the patient during PET-CT scanning is in the range of

a) 0.02 – 1 mSv
b) 2-5 mSv
c) 10-15 mSv
d) 15-25 mSv

A: d

Q9) Positron-emission tomography (PET) is a nuclear medicine functional imaging technique that is used to observe metabolic processes in the body.

a) True
b) False
c) Depends on the cancer

A: a

Q10) A positron is an antiparticle of an electron with identical mass and charge.

a) False
b) True
c) Depends on the type of emission

A: b

Quadrant IV

Weblinks and Additional Sources of Readings:

1) www.sciencedirect.com/science/article/pii/S0375947405002265/pdf
2) https://en.wikipedia.org/wiki/Positron_emission_tomography
3) https://link.springer.com/chapter/10.1007/978-0-387-22530-2_1
4) www.pitt.edu/~super4/40011-41001/40811.ppt
5) www.science20.com › Applied Physics › Medical Physics Notes