Positron Emission Tomography (PET)

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PET imaging can provide comprehensive and accurate staging information.

Positron Emission Tomography (PET) is an exciting modality, still in the early stages of general clinical acceptance [1]. The procedure has the potential to reduce healthcare expenditures for patients who have been diagnosed as having cancer. This is because PET imaging can provide comprehensive and accurate staging information which is not available from CT or MRI. Appropriate use of PET studies can lead to modification of treatment, for example from an aggressive approach to one of palliation when the staging information suggests a poor prognosis.

PET images the metabolic activity within various types of cancer by detecting the uptake of a radioisotope. This is a reflection of the characteristics of the cancer, indicating the maturation rate as well as the vascularization. The information obtained is complementary to the anatomical information provided by CT, MRI or ultrasound.

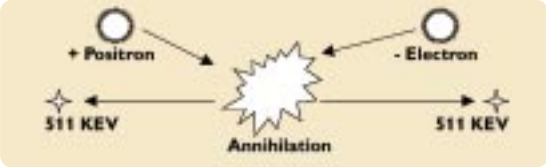

Figure 1. The positron-electron annihilation process.

Since increased metabolic activity occurs before anatomical changes, and can be detected many months earlier, PET imaging can provide an earlier diagnosis of cancer and accurate staging. In addition, the PET studies can provide data for improving the accuracy of radiation therapy treatment planning, as well assessing the effects of various forms of therapy.

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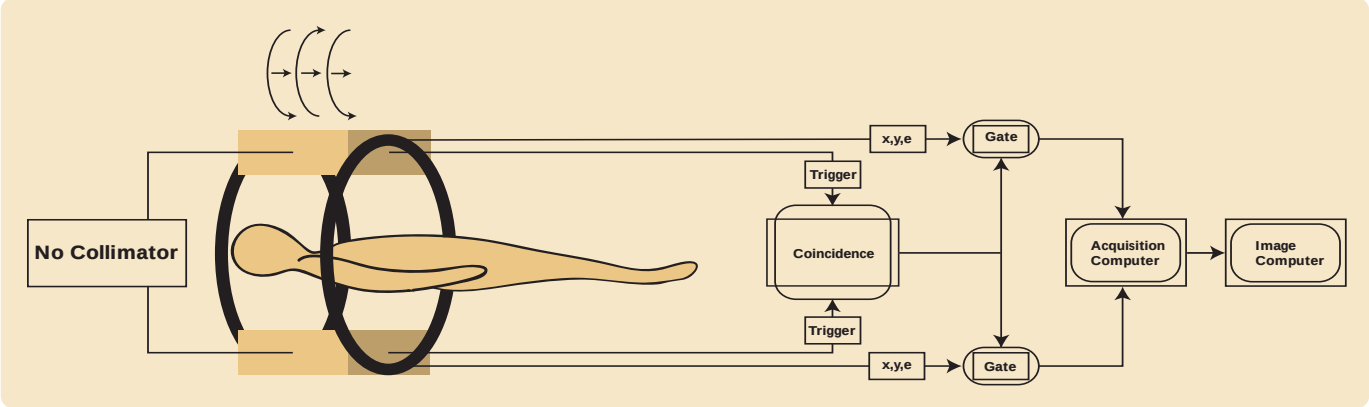
PET imaging systems

There are two types of PET imaging systems: dedicated PET, and single-photon emission computed tomography (SPECT) systems with coincidence imaging capabilities (coincidence systems). Both detect the presence of a radioisotope introduced into the body, and the principle of detection is the same. When a radioisotope decays it emits a positron - a positively charged electron- that immediately interacts with an electron. The combined particles undergo an annihilation reaction, which results in the release of two 511-keV photons in opposite directions. The imaging system is equipped with two detectors directly opposed to each other, i.e. in coincidence. Further, the annihilation event is known to occur along a line connecting the points of interaction in the two detectors (Figure 1).

In the dedicated PET system, banks of detectors are located at fixed positions around the body, resulting in paired sets of opposed detectors. The Philips ADAC-CPET system uses six detectors located in a hexagonal arrangement that encircles the patient (Figure 2). For SPECT systems like Philips ADAC-MCD MCD system, the two opposing detectors are rotated about the body, with coincidence imaging taking place at specific locations throughout a 360° rotation (Figure 3). In both the CPET and the MCD system, whole-body imaging requires relative motion between the patient and the detector field, so that images are acquired at different bed positions axially down the patient. In general, dedicated PET systems are considerably more expensive than SPECT coincidence systems (typically by a factor of 4 – 6 x). However, for equal

Figure 2. Schematic illustration of a SPECT coincidence imaging system.



imaging times, the dedicated PET systems provide higher quality images and are capable of detecting smaller lesions than the SPECT systems. In addition, whole body imaging with the dedicated PET system requires 45-60 minutes compared to 75-90 minutes for the SPECT system. The main advantages of the SPECT system are its lower cost, and its ability to perform general nuclear medicine procedures as well as PET studies. This system has its greatest acceptance in volume PET utilization (5-10 studies per week), whereas a dedicated PET system could be justified with volumes of 3 - 6 studies per day.

PET imaging applications

The primary application of PET imaging today is the detection and staging of various cancer types using the imaging agent F-18 fluro-deoxy-glucose (FDG). The fundamental mechanism for FDG localization in cancer cells relates to the increased rate of glycolysis in tumor cells, due to their anaerobic state relative to normal tissue. FDG metabolism is faster in tumors than in surrounding tissue, resulting in a high countrate differential between tumors and the background. This characteristic makes it possible to detect a malignancy in the presence of post-surgical changes, or determine whether a mass observed on a CT or MRI scan is benign or malignant. In addition, serial PET scans may be used to determine the efficacy of tumor treatment using chemo- or radiotherapy.

It is often difficult to determine whether a solitary pulmonary nodule seen on a chest X-ray or CT scan is benign or malignant. If the nodule is malignant, then the patient's care further care will be guided by the stage of the lung cancer. If the cancer has spread to the other lung, or appears below the diaphragm, then the patient is not a surgical candidate and should be treated by chemotherapy. Wahl et al. [2] reported an accuracy of 81% in detecting lung cancer with PET, versus an accuracy of 52% for CT.

PET studies can also be used to detect recurrent disease. If a patient has undergone surgery for colon cancer, it can be difficult to detect recurrence of the disease in a CT scan, due to the presence of scar tissue and the disturbed anatomy. FDG PET studies show recurrent disease as hot spots. Schiepers et al. [12] reported an accuracy of 95% in detecting colon cancer with PET, compared with an accuracy of 68% for CT (Figure 4).

PET studies can be used to follow patients undergoing chemotherapy. It is common to treat lymphoma by chemotherapy, and to follow the treatment with serial CT scans to look for a reduction in the size of the lymph nodes. However, when a physician sees an enlarged lymph node on a CT scan, it can be difficult to determine whether the treatment is effective. Sometimes the lymph nodes remain enlarged due to residual dead tumor. Functional FDG imaging can help differentiate between viable and non-viable tumors.

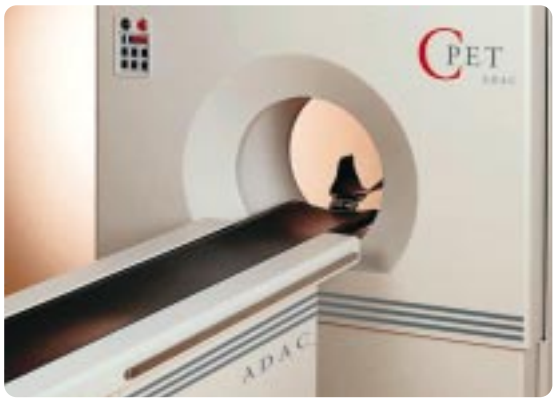


Figure 3.
The C-PET Imaging System.

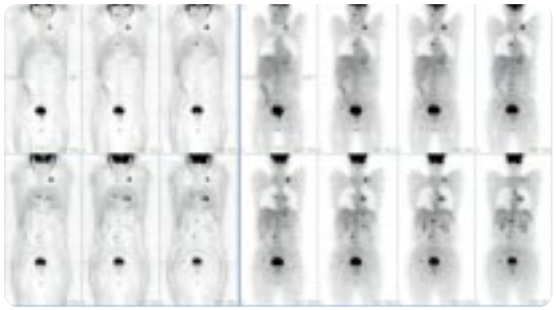


Figure 4.
PET scan on patient with confirmed colorectal cancer. The multiple sites of metastatic lesions resulted in the patient being placed on conservative medical management as the only therapy.

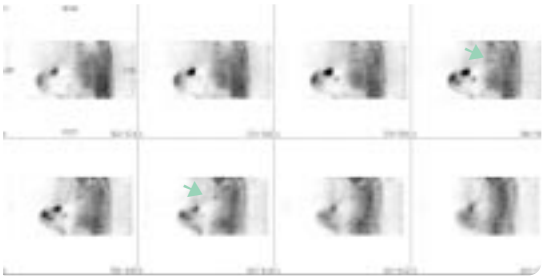


Figure 5.
PET images of patient with breast cancer showing multiple lesions in the breast and adjacent lymph nodes.

Several studies have been published that demonstrate the increased accuracy of PET imaging in detecting various cancer types in comparison with the other modalities. For example, Hoh et al. [13] reported an accuracy of 85% in detecting breast cancer with PET, compared with an accuracy of 67% for mammography (Figure 5).

PET imaging has a high accuracy in detecting cancer types.

Evolving future directions for PET

Now that PET imaging has become a reality, and is receiving routine oncology application, users of the technology are making recommendations to define

the future direction of PET imaging. These include technological changes to improve the performance of the imaging system, as well as new configurations of the technology to improve the accuracy of diagnostic information.

Accurate staging can save unnecessary pain and stress.

Technological advances

The clinical application of PET imaging in oncology has created a reality in which staging of patients with a primary diagnosis of cancer can save unnecessary pain and suffering for patients and their families, as well as healthcare dollars, by allowing the most appropriate therapy to be applied. This has resulted in a significant increase in the volume of procedures ordered by referring physicians. Since a typical study requires 45 - 60 minutes of imaging time, the PET centers are experiencing severe throughput problems, with an upper limit of 6 - 8 patients per day. Technological advances, leading to faster scan times, are needed to solve this problem.

Philips Adac is developing a new scanner (Allegro) which is intended to reduce the imaging times. Allegro will utilize a new detector which has greater stopping power and higher countrate capabilities than existing detector materials. The detector material is gadolinium oxyorthosilicate (GSO). Images from this system were shown at the 2001 Society of Nuclear Medicine meeting in Toronto.

A new detector can reduce imaging times.

A second consideration, after the choice of material, is the imaging geometry. PET systems can be operated with two-dimensional (2D) or three-dimensional (3D) imaging geometries. The 3D geometry is approximately 500% more efficient than the 2D geometry. In older BGO detector systems, imaging is typically performed in 2D using lead septa to shield the detectors. These septa limit the acquired data to a small axial region, or a limited number of transaxial slices. The 2D approach reduces scattered radiation. An alternative method to reduce scatter is the use of a detector material such as NaI (Tl), with its high-energy resolution (12%). This method rejects scattered radiation by using an energy window. Systems such as Philips ADAC-CPET and Allegro use this method and operate in 3D mode. The new detector material, GSO, was selected because it combines increased stopping power, higher counting capability and improved energy resolution, creating the necessary conditions for 3D imaging. This combination will result in an increased countrate and a corresponding decrease in scan time. It is anticipated the new detector materials can increase sensitivity by a factor of two, and counting rates by a factor of two as well. This could reduce whole-body imaging time to approximately 30 minutes.

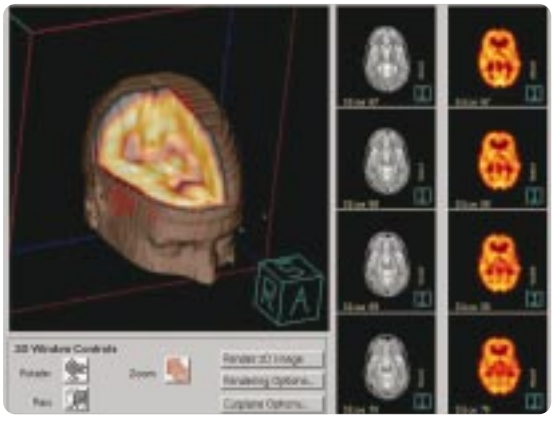


Figure 6. Example PET/MRI Fusion Images in a patient where PET demonstrates a metastatic brain lesion.

Other technological improvements requested include improved reconstruction algorithms, simultaneous acquisition and reconstruction, and improved methods for attenuation correction.

Functional and anatomical image fusion

Oncology evaluations typically begin with a CT or MRI study that defines the anatomy, and often reveals a mass lesion that is suspicious for cancer. PET imaging is then performed to determine whether the suspicious mass lesion has metabolic function, indicating a cancerous lesion. It is imperative that the anatomical information be correctly matched with the metabolic images. This process of accurately registering anatomic information with metabolic function is referred to as Image Fusion (Figure 6).

There are several approaches to obtaining fused images: mental fusion, anatomical markers, and hybrid systems. In mental fusion, the physician views both the anatomical images and the PET images. He/she determines the locations of the lesions on both scans to determine if there is a match.

Alternatively, anatomical markers can be placed on the patient prior to the anatomical exam to create a registration locater. The same markers are then imaged during the PET study. The markers are used in a computer system to overlay the sets of images for diagnostic purposes. While this is a better approach than visual matching, there are still several potential sources of error, including inadvertent movement of the markers and patient motion. A third approach is the use of a hybrid system that

integrates a CT system with a PET imaging system. This system has a common patient bed and both modalities are used to image the patient. Electronic markers are used to co-register images obtained with each modality. However, there are still problems due to motion of the lungs and intestine between the studies. Several manufacturers have introduced combined PET/CT systems, and Philips Adac is developing a new system called the Gemini. While these systems have major advantages for Fusion Imaging, this approach raises certain issues.

The first problem relates to patient throughput and the financial consideration of the number of patients that may be imaged on each system. The throughput for a CT scanner can be 15-20 patients per day, whereas a PET system can perform only 6-8 studies per day. Thus, the expensive CT scanner will have significant dead time. The overall cost of an integrated PET/CT system is significantly higher than a stand-alone PET system.

The second problem relates to the order of the studies and the ability to obtain payment for the CT portion of the imaging procedure. In the United States, third parties and Medicare often require the CT or MRI study to be performed prior to the PET study to identify a suspicious malignancy. Patients with abnormal CT studies can then be referred for a PET scan for staging. In this case, both CT and PET studies would be reimbursed. In a scenario where the patient has a CT study performed prior to the combined PET/CT procedure, the second CT procedure will probably not be reimbursed, and the patient receives extra radiation exposure. This can present a financial enigma for a CT/PET owner, in that the cost of the CT component of the system could not easily be recovered.

A third issue relates to the frequency with which Fusion Imaging is required. First of all, not all CT or MRI studies will reveal a suspicious lesion. It is estimated, however, that 20-25% of all CT or MRI studies performed for oncology applications will contain one or more suspicious areas in the lung, liver or abdomen. In such cases, PET imaging is useful in clarifying the diagnosis, and Fusion Imaging is therefore valuable. The question remains as to whether the expensive, combined PET/CT system can be justified, or whether visual registration or possibly a flexible alternative, which allows DICOM connectivity between a dedicated PET and a stand-alone CT or MRI, would be more cost effective. The answer to this question will certainly be defined as more experience is gained with the combined CT/PET system. It will be interesting to determine whether the prediction made by Henry Wagner, MD, one of the leaders of nuclear medicine, will come true. He predicted at the SNM 2000 meeting of the Society of Nuclear Medicine, 'Within five to ten years, 60% of all imaging studies will be fused images'.

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CONCLUSION

For PET, the future is finally here, and the application for oncology is growing at a rapid rate. The future for PET beyond oncology is even more exciting as we enter the era of Molecular Imaging. Example applications include PET being used to examine behavioral abnormalities, or for new therapeutic applications. In addition, Molecular Imaging will use unique molecular substances to track and monitor their diagnostic or therapeutic effect in neurological diseases, or for genetic disorders. Since all biological molecules contain nitrogen, oxygen and carbon, and all have positron-emitting isotopes, the molecular substances concerned can be labeled with positron emitters. This will allow their metabolic or physiologic actions to be tracked with PET scanners. Thus, the next applications will further secure the future of PET imaging.

PET offers potential in molecular imaging.

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