POSITRON EMISSION TOMOGRAPHY: A REVIEW

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H.T. Turoğlu, M.D.*

* *Research Assistant, Department of Nuclear Medicine, Faculty of Medicine, Marmara University, Istanbul, Turkey.*

SUMMARY

The origin of most medical problems is biochemical in nature. Positron emission tomography (PET) is a powerful tool to enlighten the underlying biochemical disorder in human disease. Therefore, the biochemical information obtained by PET allows an understanding of the fundamental nature of human disease and provides diagnosting examinations with a high sensitivity coupled with a high specificity. Moreover PET can assist in the selection and monitoring of therapeutic correction. Initially PET was available only for research rather than clinical practice since it was an expensive and complex technology that necessitated an on-site cyclotron. However, the current trend shows a transition from research to clinical practice as a result of development of new radiopharmaceuticals, improving technology, commercially available "baby" cyclotrons and generator-produced radionuclides and automated radiochemistry systems. Already there are three established clinical applications: detecting coronary artery disease and myocardial viability, lateralizing the seizure focus in focal epilepsy and the diagnosis/localization as well as grading of brain tumors. Academic and commercial programs are being carried out in over 80 academic PET research centers and over 20 commercial companies all over the world. Academic programs are developing new radiopharmaceuticals, new procedures and new uses of PET. In the mean time academic and commercial programs are trying to lower the complexity and cost of the clinical applications of the technology. Recently the best resolution so far was achieved by the designers of the Donner-600 crystal PET scanner, the intrinsic resolution being 2.6 mm. Another major development was a new computer software system that enabled combined display of PET and three-dimensional brain magnetic resonance (MR) image, Therefore, it will be possible to correlate on the same video screen PET images with other imaging modalities such as CT and MR. This will enable to integrate biochemical/physiologic information with complementary anatomic data. Taking into account the enormous scope in diagnostic imaging, clinical research and consequent clinical applications PET has the potential to be the modality of choice in functional imaging. It seems that it is time for Turkey to plan her policy regarding when and how to start this sophisticated and expensive imaging modality that has opened new frontiers in medical imaging.

Key Words: Emission Computed Tomography, Brain Diseases, Coronary Disease, Clinical Research, Economics, Review.

INTRODUCTION

Positron emission tomography (PET) is an imaging modality that provides quantitative, regional measurements of biochemical and physiologic processes in living humans and animals. Biochemical changes occur prior to anatomic changes in most diseases and PET can detect these specific biochemical transformations before the anatomic changes have occurred. PET permits noninvasive in vivo measurement of the concentration of radioactivity in a volume of tissue which provides regional and global information about biologic and/or chemical processes within various organs.

PET scanners utilize certain radionuclides that decay through the emission of positrons. Positron emitting radionuclides are generated in a cyclotron by bombarding the target with protons. The proton displaces a neutron in the nucleus. The nucleus of the resulting atom has an excess of protons which makes it unstable. The proton in the nucleus is transformed into a neutron and a positively charged electron called positron. The positron and a neutrino are ejected from the nucleus. A positron is the antiparticle of an ordinary electron. After ejection from the nucleus positron loses its kinetic energy through interactions with the surrounding matter and comes to rest. The positron then combines with an electron in an annihilation reaction as a result of which the masses of the two particles are converted into energy. This energy is emitted in the form of two 0.511 MeV annihilation photons which travel 180 degrees apart. The annihilation radiation may be detected by two PET detectors at 180 degrees to each other that are designed to measure the simultaneous emission of these two photons. A coincidence circuit records only a pair of 0.511 MeV annihilation photons detected simultaneously by two PET detectors oriented at 180 degrees to each other. Events registered in only one

detector are rejected electronically. The point at which the annihilation reaction leading to positron emission took place has to lie along a hypothetical line joining the two detection points (the line of coincidence). The positron can travel a short distance on the order of millimeters before annihilation; consequently the spatial resolution of PET imaging is limited to theoretic maximum of 1 to 2 mm.

Positron emitters produced in cyclotrons are the radioisotopes of the fundamental building blocks of biological systems such as oxygen, nitrogen, and carbon. Over 500 compounds have been labeled with 0-15, N-13, C-11 and F-18 by radiochemists for PET imaging. These compounds consist of simple labeled molecules such as water, carbon monoxide and oxygen; sugars, amino acids, fatty acids, carboxylic acids, alcohols, numerous substrates, analogs and drugs make up the complex molecules available for PET scanning. The basic biomolecules such as glucose, amino acids, and thymidine can be traced to evaluate metabolism of carbohydrates and synthesis of proteins and DNA by virtue of the positron emitters.

TECHNOLOGY OF PET IMAGING

A- Cyclotron

The value of PET is based on the availability of positron-emitting radionuclides of carbon, oxygen and nitrogen. This increases the expense involved because owing to short half-lives of carbon-11 (20 min), oxygen-15 (2 min) and nitrogen-13 (10 min) an on-site cyclotron (i.e. close to the PET camera) is necessary. The cyclotron is a device that accelerates protons to high energies so that when they collide with the heavier nuclei of the target these protons displace the neutrons in the nuclei. Consequently unstable nuclei that decay by positron emission are created. The physics principle utilized in the cyclotron is the fact that a charged particle gains velocity and therefore energy, when attracted to an oppositely charged metal. This opposite charge is supplied by a high voltage supply. If the particle follows a circular path around the high voltage region that crosses this region in a repeated fashion, it would gain more energy in each circle. A magnet is used in a cyclotron to make the path of the charged particle circular. In a negative-ion cyclotron there are a pair of hollow, semicircular metal electrodes the so-called "D" electrodes that are positioned between the poles of an electromagnet. The D electrodes are separated from each other by a narrow gap. During the operation, protons are generated in bursts by ionizing hydrogen gas in the ion source at the center of the machine while a high voltage is generated by a high-frequency oscillator that is applied across the D electrodes. The negatively charged hydrogen ions are directed into the gap and immediately accelerated toward the positively charged D electrode by the electric field generated by the applied voltage. The alternating current voltage across the D electrode is such that the ions arrive at the gap just as the voltage across the D reaches its peak value in the opposite direction (i.e. contrary electric charge). Each time the negative hydrogen atoms cross the gap they gain energy and velocity and then follow their circular path in the opposite D electrode (1).

B-PET Camera

PET scanners have a ring of scintillation crystals made of Bismuth Germanate Oxide (BGO) crystals most of the time. As a scintillation crystal BGO has higher density and average atomic number compared to sodium iodide which results in a higher stopping power for the annihilation photons. Consequently, utilization of smaller individual detectors becomes possible which in turn provide better image resolution. The scintillation crystals are coupled to photomultiplier tubes for detection of the gamma rays. In order to have fewer photomultiplier tubes (PMT's) the BGO detectors are arranged either as modular detector systems or detector blocks. The block detector module used in many state-of-the-art PET scanners consists of a block of BGO scintillating crystal with cuts of different depth acting as light guides. This crystal is optically connected to a certain number of PMT's. From the ratio of light detected by each PMT, the independent detector formed by cuts of different lengths is identified. There is a circuit for each block that identifies which detector has received the gamma ray by looking at the ratio of signals from different PMT's. The position logic used in the Anger camera holds true for the PET camera too. The detector blocks utilized are arranged in a circular array to form the detection system. It is possible to add other circular arrays in order to increase the organ coverage and the efficiency obtained with a single circular array. Each row of detector elements in the circumferential array form a single image plane (2). The number of rows defines the number of image planes. The image plane formed from detectors of each row is the so-called "direct plane" whereas the plane formed from coincidence of detectors of two adjacent rows is the "cross plane" image. Cross planes are utilized to increase the efficiency and sampling in the axial direction.

Image reconstruction is accomplished via filtered backprojection following the same basic principles used in CT (x-ray computed tomograpy), MRI (magnetic resonance imaging), and SPECT (single-photon emission computed tomography). Tomographic image reconstruction is the art of producing a sectional (slice) image from measured count profiles or projection images. The backprojections of scan profiles at different angles are then added together by means of linear superposition to yield an approximation of the original distribution of the radionuclide. Then a mathematical operation called filtering is performed to

get rid of the blurring induced by the backprojection process.

PET VERSUS SPECT

PET imaging has some unique properties which make it the modality of choice in functional imaging rather than SPECT, due to the following advantages:

1. A reliable way of attenuation correction can be achieved in PET imaging whereas a limited one is possible with SPECT. Therefore an accurate measurement of local radioisotope concentration is possible with PET imaging.
2. The efficiency of PET imaging is much higher than that of SPECT. There are no collimators in front of the PET detectors; consequently unlike SPECT, PET imaging does not suffer from loss of more than 99% of the emitted gamma rays due to absorption or scatter by the collimators.
3. The use of short-lived positron emitting radionuclides in PET imaging results in lower radiation doses to the patients and the possibility of early repeat studies. Also because of the short half-life of the positron emitters radioactive contamination issues are reduced.
4. In comparison with SPECT, PET provides superior spatial resolution.
5. PET reflects physiologic and biochemical properties accurately since it uses the radioisotopes of the important organic chemicals found in the body such as C-11, 0-15, N-13. Since none of these elements have any radioisotope suitable for SPECT imaging, biochemical properties are not reflected with SPECT. Also SPECT cannot provide the quantitative information obtained with PET due to attenuation correction problems.

On the other hand there are some advantages of SPECT over PET which may be summarized as follows:

1. A SPECT facility costs much less than a PET facility. Not only is the price of the camera less, but also an on-site cyclotron installation and maintenance cost does not exist.
2. The radionuclides used in SPECT are cheaper and more easily available than their PET counterparts that are cyclotron-dependent.
3. The principle that PET successes are eventually translated into SPECT applications holds true in many cases.
4. The gamma rays used for SPECT are less penetrating than the annihilation radiation-the byproduct of positron emitters- therefore, the extra radiation safety measures such as thicker shielding are not necessary.

Briefly, PET is advantageous over SPECT because it provides superior spatial resolution, a 100-fold detection efficiency leading to high count rates, and quantitative information about regional metabolism. Accurate quantitation of tissue activity can be achieved with PET, because accurate attenuation correction is possible. The availability of positron emitting isotopes of carbon, oxygen, nitrogen and fluorine provides advantages over less biologically relevant elements used in SPECT such as technetium end thallium. These positron emitters make feasible the in vivo measurement of regional metabolism by tracing the dynamic behavior of basic biomolecules such as glucose, amino acids and thymidine to evaluate metabolism of carbohydrates and synthesis of proteins and DNA (3).

CURRENT CLINICAL PET APPLICATIONS

A. Heart Disease

Investigators have shown a high accuracy of PET for detecting coronary artery disease (CAD) with both sensitivity and specificity to be approximately 95% when compared with coronary arteriography (4-7). These PET studies have been performed by using rubidium-82 and N-13 labeled ammonia an analog of potassium and a blood flow marker, respectively. PET imaging also allows an insight into myocardial metabolism. In the ischemic myocardium the reduced oxygen supply causes a reduction in the oxidation of free fatty acids and an increase in glucose utilization and anaerobic glycolysis. F-18 fluorodeoxyglucose (FDG), an analog of glucose, mimics glucose uptake in the myocardial tissue. Therefore FDG shows increased uptake in ischemic myocardium while it is not taken up in necrotic myocardium. Similarly carbon-11 palmitate may be used to detect ischemic myocardium by depicting decreased fatty acid metabolism. Combined use of myocardial perfusion markers and glucose metabolism assists in distinguishing reversible from irreversible damage to the myocardium (8-10). The combination of PET perfusion and metabolism studies are of great value in establishing myocardial viability, in other words the myocardial tissue that is still alive.

In approximately 40% of patients who are considered to have irreversibly damaged myocardium by persistent (fixed) defects on exercise and redistribution SPECT thallium imaging there is viable myocardium detectable only by PET imaging. This "hidden" viable myocardium may return to normal function following revascularization procedures such as percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafts (CABG) (11, 12). An estimated 20 to 40% of more than 100.000 Americans undergoing CABG surgery do not benefit from it. PET can help select patients who would benefit from bypass surgery or angioplasty by showing accumulation of glucose in regions of decreased blood flow. PET can also indicate whether a complete heart transplant is necessary instead of a revascularization procedure. Following a heart transplant PET can ascertain

myocardial viability. Similarly PET can document both the revascularization and the return to normal metabolism expected to occur following successful PTCA or CABG. In conclusion, PET is an accurate noninvasive method for detecting the presence and severity of CAD, evaluating myocardial viability and the efficacy of therapeutic interventions and determining prognosis in CAD.

B. Brain Diseases

1. Epilepsy

PET has been reported to be clinically useful in the selection of patients for surgical treatment of some types of epilepsy. Approximately 20% of patients with complex partial seizures are not adequately controlled by medical theraphy. Such patients may benefit from surgical therapy if the epileptogenic focus can be located. Thus in focal epilepsy PET is used to lateralize the seizure focus in patients without CT or MRI abnormalities, who are being studied for complex partial seizures. About 60.000 patients in the U.S.A. would benefit annually from the work-up of such seizure cases. PET noninvasively identifies the precise location of the epileptic focus thus eliminating the need for invasive techniques such as intraoperative electrocorticography and dept electrodes. Sensitivity of PET during the interictal period is 70% with epileptogenic focus appearing as an area of hypometabolism (13-15).

PET and electroencephalography (EEG) play a complementary role in complex seizures unresponsive to medication. EEG serves to identify the seizure phenomenon while PET provides accurate spatial localization for surgical resection.

2. Cerebrovascular disease

PET can distinguish irreversible infarction from reversible ischemia by measuring oxygen metabolism and brain blood flow, which are disassociated in stroke patients as a result of increased oxygen extraction. The major challenge is the identification of viable brain tissue following stroke, as a guide to the use of thrombolytic therapy. Because of the rapid onset of brain infarction after stroke on the order of minutes, the goal of the intervention is salvage of jeopardized cerebral tissue. Studies show that the metabolism of oxygen in the brain can be preserved even when the blood flow is reduced to 55% of normal, infarction occurs when flow is less than 45%, in between is ischemia. Hence quantitative measurement of regional brain perfusion can be predictive and indicative of efficacy of treatment. Oxygen extraction ratio is elevated in ischemic brain but subnormal in tissue going on to infarction. Another parameter is the ratio of cerebral metabolic rates for oxygen and glucose which falls in ischemic brain as a result of anaerobic glycolysis. The decreases in blood flow, glucose, or oxygen metabolism signal that functional impairment is beginning, before structural abnormalities are detectable on CT and MRI.

3. Dementia

In Alzheimer's disease there is decreased cerebral blood flow and glucose metabolism involving the posterior temporal and parietal cortices. PET provides an accurate diagnosis of early Alzheimer's disease, whereas CT and MRI provide information to eliminate other possible causes of dementia. Patients with multi-infarct dementia have multifocal defects with high contrast between normal and abnormal areas of brain (16). Patients with Huntington's disease have abnormal metabolism and blood flow in the caudate and putamen even in the presence of normal CT scans (17). The characteristic patterns of glucose metabolism in Alzheimer's disease and in multi-infarct dementia are demonstrated by PET (18, 19). Therefore, correlation of PET imaging with CT and/or MRI makes feasible the differential diagnosis of Alzheimer's disease from multi-infarct dementia, depression or drug intoxication. In the U.S.A., 5% of the population older than 65 years of age suffer from dementia (20), and this figure increases to about 20% at age 85 years (21). Pathologic studies have shown evidence of Alzheimer's disease in about half of these patients (21), which is often misdiagnosed by clinical criteria. PET provides an early and accurate diagnosis of Alzheimer's disease.

4. Brain tumors

PET studies have shown a correlation between the glucose accumulation by the tumor and the degree of malignancy based on histologic grade of the brain tumor (22). In additon PET can be used to separate residual or recurrent tumor from radiation necrosis (23). Prognosis becomes worse as F-18 fluorodeoxyglucose (FDG) accumulation is increased (22, 24).

FUTURE OF CLINICAL PET IMAGING

A. Tumor Imaging

PET has the potential to develop analytic methods for assessing regional glucose metabolism (via F-18), protein synthesis (via C-11 and N-13 labeled amino acid metabolism), DNA synthesis and other processes distinctive to tumor. In comparison with their original tissues tumors have an accelerated intermediary metabolism that may be used to show tumor malignancy and response to specific antineoplastic drug.

Based on the generalization of the successful brain tumor studies it may be said that PET imaging of other tumors is likely to provide information regarding the following areas: tumor aggressiveness, patient prognosis, response to radiotherapy and chemotherapy, choise of an optimal biopsy site (to

obtain a representative sample of tumor), separation of residual and recurrent tumor from the response of normal tissue to guide treatment (25).

Another possible application of PET will be the use of labeled monoclonal antibodies which combine the disease-specific property of the agent with a high-resolution and high-sensitivity PET camera (26). Also, the quantitative nature of PET allows improved dosimetry estimates for radioimmunotherapy planinng.

B. Neurotransmitters and Receptors

Fluorodopa, labeled with fluorine 18, has been used to grade decreases in dopamin synthesis in the putamen and caudate of patients with Parkinson's disease. In addition F-18 fluorodopa may be used to look at patients who are undergoing adrenal transplants or fetus tissue transplants to basal ganglia to assess central dopaminergic functions.

PET is used in evaluating receptor density in a variety of conditions. PET scanning can yield information about both distribution and number of receptors. Most work with PET has been in the brain: Patients with temporal lobe epilepsy demonstrate increased opiate receptors in the temporal lobe at the site of hypometabolism. The role of D-1 and D-2 dopamine receptor assays in several psychiatric diseases is being evaluated for the detection of disease and for monitoring drug therapies. In the heart labeling of muscarinic cholinergic, beta adrenergic, benzodiazepine, and dopamine receptors is already accomplished (27).

C. Pharmacology

PET can show the regional distribution and time course of the therapeutic drug in the body noninvasively. Therefore, it makes feasible demonstration of drug kinetics as well as monitoring drug treatment. Antineoplastic drug kinetics are shown by F-18 labeled 5-fluoruracil, N-13 labeled BCNU and C-11 labeled BCNU and CCNU.

F-18 labeled captopril can effectively probe angiotensin converting enzyme (ACE) in rats. After administering the drug, researchers used PET and found high uptake in areas known to have elevated concentrations of ACE such as the lungs, kidneys and aortae (28).

Radiolabeled narcoleptics such as C-11 labeled spiperone are used for labeling of neurotransmitter receptors in the human brain.

RECENT ADVANCES IN PET IMAGING

Advances in PET imaging are achieved either by the development of new radionuclides/radiopharmaceuticals or by improvements in the PET camera leading to higher resolution. Another option is the development of new versions or modifications in the sources of positron emitters.

The continuous development of new radiopharmaceuticals is contributing to the expansion of the field by introducing new procedures and new uses of PET which in turn accelerate the transition from research to clinical practice. Some examples are already covered under the heading of "Future of Clinical PET Imaging" in the text. The pharmaceutical companies are realizing the impact of PET on clinical pharmacology after the labeling of neurotransmitter receptors in the human brain with radiolabeled narcoleptics and labeling of beta adrenergic receptors in the lung (29). The high uptake of F-18 labeled captopril in regions of elevated ACE concentration may lead to monitoring of therapeutic drug treatment in hypertension (28).

Important advances have occurred in the development of cyclotrons for medical applications (30). Several companies now provide small cyclotrons that are appropriate for clinical studies and can be installed in the hospital grounds. The operation of these "baby cyclotrons" is simpler and their cost is cheaper than the conventional cyclotrons. These "baby cyclotrons" occupy smaller place and are easily shielded. Recently, commercially available automated radiochemistry systems have been introduced. These take the radionuclides straight from the producing cyclotron and rapidly provide the radiopharmaceuticals needed on a routine basis in clinical practice.

Dedicated linear accelerators and superconducting magnet-based cyclotrons are being developed for production of positron emitters. Science Research Laboratories (SRL) is developing an accelerator exclusively for PET that will weigh and cost one-fourth and require only one-sixth the electrical power used in conventional cyclotrons (31). Several other companies are developing new accelerators exclusively for PET that can be installed in a hospital's imaging department.

Recently a high-resolution PET system designed for studies of brain metabolism and physiology was introduced. The intrinsic resolution of the Donner 600-crystal positron emission tomograph (PET 600) is 2.6 mm full width at half maximum (FWHM) in-plane and 6 mm FWHM axially. The clinical evaluation has confirmed the clinical and technologic practicality of high-resolution (2.6 mm) PET scan of the brain. The study showed that increased resolution improves image quality, allows more accurate quantitation of tissue isotope concentration, and increases clinical diagnostic efficacy (32).

ECONOMICS

The radionuclides used in PET imaging are cyclotron-produced and they have short half-lives. Consequently, the radiochemistry laboratory must be on-line between the cyclotron and the PET camera. Therefore, both an on-site cyclotron and sophisticated radiochemistry are needed to operate a PET facility efficiently.

A dedicated team working on a full-time basis is required to run a PET facility. For an academic institution planning to utilize cyclotron-produced radiopharmaceuticals, minimum staffing includes a physicist, a radiochemist and radiopharmacist, a full-time PET nuclear medicine physician, and 3 to 5 technologists and secretaries.

PET centers are expensive to construct, equip and operate. That is why PET is presently available in only 50 large hospitals and medical centers and a few small hospitals in the U.S.A. PET scanners are still undergoing development and new models are introduced nearly every year at costs of 0.9 to 2.8 million U.S. dollars. Average life expectancy for the PET scanner is 5 to 7 years whereas the lifespan of a cyclotron is 30 to 40 years. A dedicated cyclotron costs 1.0 to 2.0 million U.S. dollars. The space requirement for a PET scanner is similar to that of a CT scanner. The space needed for a cyclotron (that can weigh up to 40 tons) and radiopharmaceutical production is similar to the space needed for the PET scanner (25). The estimated installation cost including the building, PET system, cyclotron and ancillary equipment is more than 6 million U.S. dollars. This may increase up to 8 million U.S. dollars for a new academic PET center by adding personnel training and state-of-the-art equipment. The annual operating cost for a cyclotron/PET facility is about one million U.S. dollars (33). The estimated procedure cost varies from 1500 to 2000 U.S. dollars (33). The Task Force on Clinical PET is more optimistic about the costs involved. They predict that the operating costs for the PET scanner and cyclotron vary between $ 400.000 and $ 1.000.000 per year (based on lifespans of 5 to 7 years for the scanner and 30 to 40 years for the cyclotron). For the patients, this results in per scan charges ranging from $600 to $2.500, depending upon the complexity of the scan, the use of the cyclotron, the number of procedures per day per facility (34).

Unlike the academic and research centers, small medical centers can depend on generators and/or central radiopharmacies to supply the radiopharmaceuticals instead of a cyclotron. New cyclotron/PET centers can be operated as a consortium of local hospitals sharing the expense of a cyclotron (34). In-house generators can provide radionuclides such as gallium-68, rubidium-82 and copper-62. The availability of positron emitters is going to be easier and cheaper as a result of the introduction of commercially available "baby cyclotrons" and in-house generators and the recently developed dedicated linear accelerators, since all of them can replace the conventional cyclotrons. The need for specially trained physicists and chemists in clinical PET centers has been removed by the recent developments in automated radiopharmaceutical synthesis and PET scanners (25).

The transition of PET imaging from research oriented to clinical oriented practice has been marked by the evolution of new technologies to provide its metabolic/biochemical imaging capabilities in a way and cost appropriate for clinical practice. The effort to lower the complexity and cost of the clinical versions of the PET technology are carried out by the academic programs in over 80 academic PET research centers and commercial programs in over 20 commercial companies (1). Academic programs are continually developing new radiopharmaceuticals, new technology and computer software. Recently, a new computer software system was developed which enabled combined display of PET and three-dimentional (3-D) brain MR image (35). This was a major breakthrough since it will make possible to correlate, on the same video screen, PET images with other imaging modalities such as CT and MRI. Thus the integration of biochemical/physiologic information with complementary anatomic data will be possible. As demonstrated by this example, there is tremendous research going on with the potential to be converted into clinical PET practice. Research with positron emitters and positron emission tomography totaled $20.5 million (36).

At present, many of the PET facilities in the U.S.A. are supported by funded research. Routine clinical applications of PET imaging are being done in the U.S. despite lack of reliable reimbursement for these examinations. In March 1989 HCFA initiated the evaluation process which may lead to national Medicare coverage (in the U.S.) for certain PET procedures. Procedures aimed at consist of myocardial viability, patient selection for surgical treatment of seizure disorders (intractable complex partial seizures), and tumor grading, assessing prognosis and detecting recurrence in glioma patients (34).

CONCLUSION

Most of the medical problems are biochemical in nature. PET permits noninvasive in vivo examination of global and regional biochemistry that provides a biochemical description of disease. The biochemical information obtained allows understanding of the fundamental nature of human disease and provides diagnostic

examinations with high accuracy. It can improve the selection and monitoring of therapy.

At present the clinical applications of PET include the following:

1. Detection of coronary artery disease (new gold standard?)
2. Determination of myocardial viability for selection of patients who will benefit from revascularization procedures.
3. Grading of gliomas and detection of recurrence after therapy.
4. Selection of patients for surgical treatment of complex partial seizures.
5. Differential diagnosis of dementia.

In the future tumor imaging, neurotransmitter receptor labeling, and drug labeling (to demonstrate kinetics and to monitor drug treatment) may become part of the clinical PET imaging.

The challenge currently facing PET imaging is to expand its availability beyond the large centers by lowering the cost and complexity of the technology.

First, the new high-resolution that require less technical support than the previous systems should be more easily available at a cheaper price.

Second, the positron emitting radionuclides must be widely available at a cheaper price. This may be achieved by the purchase of a "baby" cyclotron, utilization of in-house generators or shipment of relatively longerlived radionuclides. Small medical centers can be operated as a consortium of local hospitals sharing the expense of a cyclotron.

Third, the transition of PET from research to clinical practice should be accelerated. The information provided should be cost effective for clinical care. It must be proven that diagnoses are being made that would be impossible otherwise.

The computer software systems should be improved: the length of data processing should be modified, the combined display of PET and 3-D MR should be commercially available. This is the fourth goal to achieve to overcome the challenge.

Fifth, is to provide reliable reimbursement by persuading the third party payers all over the world.

In addition to these general challenges, there is a special challenge our country has to face. What is Turkey's policy concerning PET technology? Taking into account the enormous scope in clinical research and consequent clinical applications, PET may become the modality of choise in functional imaging. A cyclotron and PET center will have great contributions to fields such as physics, chemistry, biochemistry, biophysics, engineering, nuclear medicine, radiopharmacy. It will be possible to perform research, to provide on the job training for the students and professionals in the related fields. As a country intending to become a member of the European Community, Turkey cannot underestimate the benefits and potential of this technology.

A pragmatic solution could be to prepare the future staff by sending them to an established cyclotron/PET center abroad. Once the team is ready, the project may be initiated via a pioneering academic institution (in Turkey) consisting of a PET scanner and a cyclotron. This pioneering institution eventually will be converted into a research and training center, where scientists, physicists, radiopharmacits and PET nuclear physicians of the future can learn and apply this sophisticated and expensive technology.

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