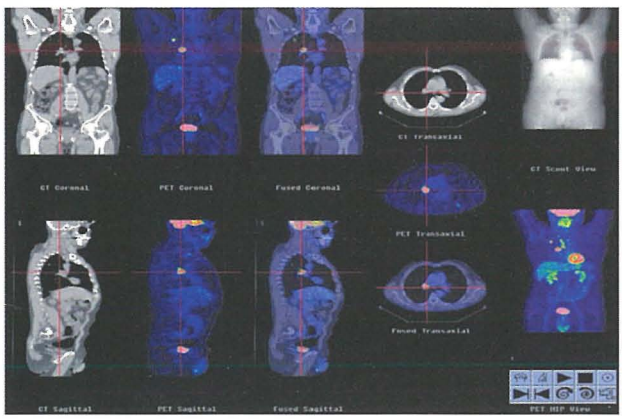
A practical and comprehensive overview of PET/CT – Part I

by **Mark Anthony Aquilina** *MD CCST*
Specialist in Nuclear Medicine
Nuclear Medicine and PET/CT Unit
San Raffaele Hospital, Milan, Italy
Email: aquilina.markanthony@gmail.com

Like other nuclear medicine procedures, positron emission tomography (PET) differs from other imaging modalities in that it demonstrates physiological function of the system being investigated rather than anatomy. Tracer distribution and concentration is followed, hence allowing doctors to monitor the various cellular and molecular events taking place. A nuclear physician has the advantage of being able to interpret the superimposed images of a PET and a computed tomography (CT) scan concomitantly. This gives specialists much more confidence in writing definitive PET/CT reports: adding metabolic to anatomic data is synergistic with obvious advantages over stand-alone CT, or even stand-alone PET.

PET/CT involves an intravenous injection of radioactive tracers labelled with a positron emitting isotope. A positron may be considered to be an elementary particle with the same mass and magnitude of charge of an electron but exhibiting a positive charge, or simply a positive electron. Contrary to what many might think, PET does not detect positrons directly. It uses important features of positron 'annihilation' to determine their spatial location (see below).

It is curious that CT was originally integrated with PET for another fundamental reason besides the obvious diagnostic gain, as explained in the second part of this article. More advances are in the pipeline. Improved detectors and technology, PET/MRI and new tracers are being developed. This three part scientific overview is representative and by no means exhaustive. PET/CT will be justified as a contemporary, upcoming and indispensable imaging modality.



Dual-modality: a nuclear physician has the advantage of being able to interpret a metabolic image of a PET scan concomitantly to the anatomic data from a CT scan (image courtesy of HSR, Milano).

PET/CT tracers: The basics

In the synthesis of an ideal tracer, chemists must take into consideration that the label should not significantly change the biological properties of the parent molecule (transport, affinity with target, elimination). In fact PET/CT tracers most often comprise Carbon-11 (^{11}C), Nitrogen-13 (^{13}N), Oxygen-15 (^{15}O), and Fluorine-18 (^{18}F), all radioactive isotopes of elements that are easily incorporated by direct substitution into naturally occurring biomolecules. Substitution of ^{11}C for ^{12}C does not alter reaction times or mechanisms of the molecule. A similar situation exists for ^{13}N and ^{15}O; ^{18}F can often be substituted for a hydroxyl group on a molecule, or placed in a position where its presence does not significantly alter the biological behaviour of the biomolecule.

The positron-emitting isotope chemically linked to the molecule of interest must not dissociate easily, otherwise it is the isotope that is 'followed' by PET/CT rather than the tracer. Moreover, these tracers have the 'advantage' of a relatively short half-life with a consequent decreased radiation exposure to patients. On the other hand, time is critical: tracers must be synthesized and imaged within a time frame compatible with the half-life of the isotope. Ideally the tracer must be eliminated rapidly from sites where there is no target molecule and from blood, so that a high contrast can be obtained between tumour and surrounding tissue.

History

PET has come a long way since researchers started working on the concept, due to the necessity of developing several elements that merged into the imaging modality we know today[1]. In the late 1950s the first successful transaxial emission tomography was developed. Early systems gave poor results because of inadequate reconstruction methods. The advancement of PET progressed slowly until the development of advanced reconstruction techniques that accompanied the development of CT. The driving force behind the use of positron emitters centered on the availability of radionuclides, surprisingly discovered more than 60 years ago. ^{11}C preceded ^{14}C by several years but had experimental limitations because of a very short half-life (20 minutes). Interest was rekindled some 20 years later when it was appreciated that their short half-lives and body-penetrating photons had potential to image biochemical transformations. The successful synthesis of ^{18}F-FDG (fluorodeoxglucose, a glucose analogue) by Wolf *et al* in the mid-1970s[2] and works in imaging glycolysis by Sokoloff *et al* in 1977[3] provided another impetus for PET development. Once the broad utility of this tracer was demonstrated, plus the concomitant creation of scanners as we know them today by a team which included physicists Michel Ter-Pogossian and Michael Phelps (Washington University School of Medicine, 1975)[4], the medical community became excited by the possibilities and began to clamour for more clinical applications[1].

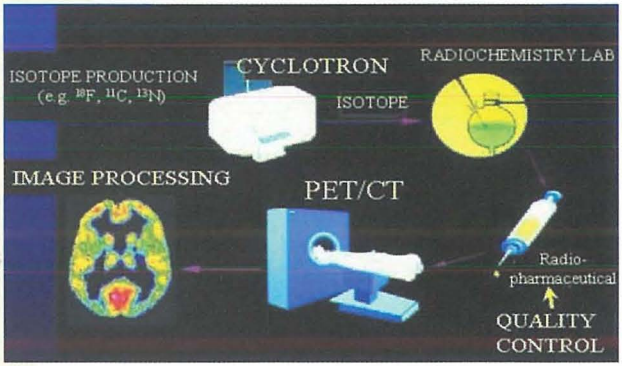
Radiotracer production and imaging

A cyclotron accelerates a beam of protons using high voltage electrodes and directs it towards the target nuclei, thereby incorporating an extra proton into them. This generates new radioactive isotopes with a neutron-to-proton ratio which by definition makes them energetically unstable. Isotopes are then coupled to the compound of interest, which will allow the incorporation of the radiotracer into the cellular-physiological processes of interest. To become stable, the radioactive part of the tracer will undergo a process of decay whereby the excess proton is usually converted into a positron, a neutron and a neutrino. The positron travels up to a range of a few millimetres in body tissue before 'colliding' with an electron along its path.

continues on page 6

A practical and comprehensive overview of PET/CT – Part I

continued from page 4



A summary of processes involved in PET/CT from tracer production to patient acquisition.

They together undergo an 'annihilation' process, producing energy in the form of two photons (gamma rays) of exactly equal energy (511 Kiloelectron Volts [KeV]), traveling in opposite directions (180 degrees of each other, starting from the same point). PET scanners contain several rings of hundreds of scintillation detector blocks (inorganic crystals) coupled to photomultiplier tubes. The pair of protons produced from a single annihilation will register simultaneously on opposing pairs of detectors as coincidence events. The paths of these two corresponding photons can thus be traced back (line of response). Detector rings register thousands of coincidence events emitted from the patient per second. For a coincidence event to be 'accepted' as correct, the photons must be registered within a very short time frame, otherwise it is discarded as a random event. Registered data is used to determine the source of positron annihilation at a given time. These data are then collected into 2D matrices (sinograms) which are then converted into tomographic 3D data using reconstruction software. PET/CT allows whole body imaging, hence imaging is not limited to any particular body district, especially in staging of oncology patients.

References

1. Schlyer D. PET tracers and radiochemistry. *Ann Acad Med Singapore* 2004; 33:146-54.
2. Ido T, Wan C, Casella V et al. Labelled 2-deoxy-D glucose analogs, ^{18}F-labeled 2-deoxy-2-fluoro-D-glucose, 2-deoxy-2-fluoro-D mannose and ^{14}C-deoxy-2-fluoro-D-glucose. *J Label Cmpds Radiopharm* 1977; 14:171-83.
3. Sokoloff L, Reivich M, Kennedy C et al. *J Neurochem* 1977; 28:897-916.
4. Phelps M, Hoffman E, Mullani M, Ter-Pogossian M. Application of annihilation co-incidence detection to trans-axial reconstruction tomography. *J Nucl Med* 1975; 16:210-24.