NUCLEAR MEDICINE

A case for the provision of positron emission tomography (PET) in South African public hospitals

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Nuclear medicine is expanding into new areas of clinical practice, of which positron emission tomography (PET) is an example. As in new treatments with labelled monoclonal antibodies, especially for lymphoma, the wide introduction of PET into health care in South Africa presents benefits and challenges to patients, doctors, and funders.

PET is an imaging modality that has been available in specialised centres in the developed world since the 1970s. It was initially used as a research tool to image organ function *in vivo*. The development of the radiopharmaceutical F-18-fluorodeoxyglucose (FDG), a glucose analogue taken up avidly by the majority of tumours, has resulted in PET now being used routinely in the management of many cancer patients in centres with access to it. There has been rapid growth of PET in the developed world and it has also been introduced into developing countries, including Egypt. We welcome government initiatives to establish PET imaging in South Africa, as evidenced by the provision of cyclotrons in Gauteng and Cape Town.

The principle of PET

PET is a functional imaging method that is sensitive and specific and allows the metabolic mapping of normal processes and disease *in vivo*. Tracer amounts of radiolabelled compounds are injected; these are handled biochemically in a manner similar to that of their normal or 'cold' biochemical equivalents. Positron-emitting isotopes such as F-18, C-11, N-13, and O-15 are incorporated into organic compounds without altering their properties. The flexible chemistry afforded by PET radionuclides provides a vast range of radiotracers with the potential to investigate physiological processes and tumour biology. There is an extensive literature on the use of radiolabelled carbohydrates, amino acids, neurotransmitters and drugs, among others. Imaging of glucose utilisation with FDG is an established, clinically useful tool. There is a rapidly growing literature on the imaging of cellular proliferation, hypoxia, neo-angiogenesis and apoptosis.[1]

After injection of the radiopharmaceutical the radionuclide incorporated in the molecule undergoes decay *in vivo* with the emission of a positron. The positron travels a short distance within tissue before interacting with an electron, undergoing annihilation and releasing two gamma rays in opposite directions. A ring of detectors, which determine the biodistribution of the radiolabelled compound, detects these gamma rays leaving the patient. This is represented as a three-dimensional image, similar to those of computed tomography (CT) or magnetic resonance imaging (MRI).

PET/CT

PET and CT scanners have recently been combined into a single hybrid imaging device that performs the two separate scans in the same imaging session, allowing accurate fusion of the two image types. PET/CT combines the strengths of the two imaging modalities, namely the anatomical detail of CT and the functional information of PET. The enhanced localisation of PET lesions using CT improves the accuracy of interpretation of the study.[2] The advantages of combining PET and CT include: (*i*) superior lesion localisation from accurate anatomical/functional registration with fewer motion artefacts; (*ii*) better distinction between physiological uptake and pathological uptake; (*iii*) consolidation of a patient's imaging studies; and (*iv*) significantly shorter scan time by using CT for attenuation correction – this enhances patient comfort and minimises problems with claustrophobia.

PET is a nuclear medicine imaging procedure that uses open sources of radioactivity, and 18F-FDG and other positron-emitting radiopharmaceuticals are not sophisticated 'contrast agents'. The introduction of the combined technique has resulted in a debate about the respective roles of the two specialties, nuclear medicine and radiology, although recommendations exist in this regard.[3]

Clinical indications

While there are established indications in neurology and cardiology, the vast majority of the PET studies performed today are in the field of oncology. PET provides unique information to characterise lesions, stage and restage cancers,

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predict patient prognosis, and monitor the effectiveness of cancer therapies. PET has a particular role in tumours of the head and neck, lung, oesophagus, breast and colon, as well as in lymphoma and melanoma. Radiation therapy treatment planning and infection imaging (fever of unknown origin) are promising areas for its utilisation in the future.[4,5] It is also useful in the management of AIDS patients with central nervous system (CNS) lesions since high FDG uptake probably represents a malignant process, which should be biopsied for confirmation rather than treated presumptively as infection.[6]

The diagnostic accuracy and cost-effectiveness of any new method depends in part on the prevalence of the disease in the population under investigation. Therefore a simple extrapolation of data from other populations may not be accurate for the majority of the South African population and must be taken into account in considering and adapting the clinical utility of the technique in our country. To avoid inappropriate and costly utilisation of the modality, the clinical indications should be limited to those already scientifically accepted. The only acceptable exception is in conducting rigorously constructed research for new indications.

PET in public sector hospitals

South Africa has lagged in the practical implementation of technological developments. This has been more marked in the public sector. Recently the first PET scans in South Africa were performed in a private hospital and it is likely that the modality will proliferate in other private hospitals. Historically, novel imaging modalities have followed a similar pattern in South Africa, with initial introduction largely taking place in private hospitals. The latter sometimes sold the services to state facilities, with the technology only becoming available much later in academic hospitals.

So far it appears that PET is following this pattern. However, 4 years ago the Department of Health conducted a process of 'modernisation of tertiary services' in South African public hospitals. Its objective was to anticipate and put plans in place to address the needs of each specialty over the following decade. Nuclear medicine and radiology made provision for PET in the plans. Increasingly efficient revenue collection is now providing the financial means to make the acquisition of such equipment possible.

Having PET initially only available in the private sector may not be the most cost-effective way of introducing a new technology into the country. A proliferation of private facilities may not only be costly to private funders, but the provision of services to state hospitals by private facilities is also expected to be too costly. It can be argued that the late arrival of CT and MRI in the public sector resulted in additional costs being incurred. A comprehensive review,[7] published in 2001, of F-18 FDG PET oncology literature documented its impressive performance in the diagnosis, staging, re-staging and monitoring of therapy for most malignant tumours. This should serve as a reminder not to repeat previous mistakes with the introduction of PET.

It needs to be asked whether the absence of public PET facilities is appropriate for the training of nuclear medicine physicians, radiologists, radiographers, medical physicists, and other medical scientists. Until academic hospitals have these facilities available, training will have to occur on a piecemeal basis at overseas facilities, or within local private facilities. This will be less efficient and less effective than when placed within the training facility.

Finally, and perhaps most importantly, the exclusive availability of PET in private facilities will not provide equitable access to the benefits of this technique by all South Africans.

The public sector is best positioned to perform much-needed research to determine the usefulness of PET in our context. The diagnostic sensitivity, specificity and accuracy of a method depends in part on the prevalence of diseases, including those that may lead to false-positive or false-negative results. Therefore an extrapolation of results particularly from high-income countries to South Africa may be misleading. Locally relevant research is required to reconsider the clinical utility of the technique, including other applications, and to make the necessary adaptations for South Africa.

PET is a multidisciplinary modality involving nuclear medicine, radiology, oncology, cardiothoracic surgery, general surgery, and related disciplines such as radiography, medical physics and radiopharmacy. The availability of PET is likely to play a crucial role in facilitating the recruitment and retention of these personnel in the public sector, thus assisting in reducing the brain drain. Because the UK was well behind its economic peers in terms of PET availability, a plan for the roll out of PET in the UK was drawn up in 2003.[8] Although these recommendations are unlikely to be wholly applicable to South Africa, they provide a useful departure point.

Cost-effectiveness

The cost-effectiveness of any procedure involves measuring its cost against its financial impact on patient management. For each indication these depend on the local cost of the procedure, and the local cost of available alternative diagnostic and therapeutic strategies. While the cost-effectiveness of PET in South Africa must be evaluated, a growing literature demonstrates that PET is cost-effective for a variety of indications and evidence suggests that, used appropriately, PET will reduce costs. This may be through the avoidance of expensive invasive diagnostic procedures, the minimisation of futile surgery, and the early cessation of ineffective chemotherapeutic regimens. Studies of lung cancers have shown that when PET imaging was done patients being assessed for major surgery had their staging changed;[9] there were major changes in treatment in a significant number of

cases, including cancellation of surgery; unnecessary surgery was avoided in 1 out of 5 patients with suspected non-small cell lung cancer;[10,11] and the number of 'futile' chest operations was halved.[9]

Unlike anatomical imaging, PET predicts the efficacy of chemotherapeutic regimens early in the course of therapy, enabling costly ineffective therapy to be altered early, with benefits to patients and costs.[12]

Conclusion

We welcome the arrival of PET in South Africa, as it will undoubtedly contribute to the better care of our patients and to the growth of nuclear medicine as a specialty. Clinical PET imaging is developing rapidly and many more radiopharmaceuticals are being developed to evaluate tumour biology, some of which will have advantages over FDG in specific clinical situations. Some will be more tumour-specific with little or no uptake within normal organs, thereby increasing the need for the anatomical correlation that combined PET/CT provides.

Accompanying the potential benefits of the arrival of PET in South Africa are a number of important challenges that need to be met. These include: (*i*) ensuring equitable access to PET for all South Africans; (*ii*) validation of PET by local nuclear medicine facilities, rather than simply extrapolating international data; (*iii*) communicating the strengths and weaknesses of PET to oncologists and other clinicians by the nuclear medicine community; (*iv*) reaching consensus on guidelines for the local training of nuclear medicine physicians, radiologists, radiographers, medical physicists, and radiopharmacists; (*v*) reaching consensus on guidelines for the indications of PET studies; and (*vi*) establishing the role of radiology in PET/CT, and achieving co-operation and cross-education of physicians and technologists.

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