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

Present day PET/CT: a dual-imaging modality in oncology

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Clinically, PET/CT has become an integral part of patient management in oncology, neurology and cardiology. By far, oncology accounts for most PET/CT applications.

Dual-modality: PET and CT

Many might think that PET and CT were originally incorporated together as we know them today only to help nuclear physicians in accurately localizing the origin of tracer accumulation, hence giving doctors and patients a more definitive report. In actual fact, it was a physicist and an engineer (Townsend and Nutt) who implemented dual-modality in order to overcome one of the major sources of artefacts in PET: attenuation. This is a process by which a beam of radiation is reduced in amplitude and intensity when passing through a material, in this case the radioactive signal emitted from a point source within the body and passing through patient tissues. Attenuation is caused by a combination of absorption and scattering processes. The deeper within the body the source of radiation is, or the denser the tissues, the more the attenuation. To correct for attenuation, transmission (as opposed to emission) images derived from an external positron-emitting source or an external radioactive source, which decays by emission of single events, started being used. This required a blank scan and another transmission scan of the patient. These methods have been used successfully for many years, but were very time-consuming and the radioactive source caused noisy transmission images propagated into PET images. A breakthrough occurred when high resolution, low noise CT transmission maps started being used for attenuation correction. Besides better quality attenuation correction of PET images and significantly shorter scan times, the superimposition of PET and CT improved the interpretation of PET images because anatomic and structural characteristics of tissue were added to the physiologically mediated distribution of the tracer. PET/CT scanners can produce functional PET and anatomical CT data in one session, without moving the patient and with minimal delay between reconstruction and fusion of the two image data sets[1]. Hitting two birds with one stone!

Applications in oncology

Cancerous cells have high metabolic rates. They use more glucose than normal cells. The most widely available PET/CT radiopharmaceutical today is an analogue of glucose labelled with ^{18}F, fluoro-2-deoxy-D-glucose (^{18}F-FDG) which has a half-life of 110 minutes. It was first used in neuro-oncology by a team led by Di Chiro in the 1980s[2] and then in the detection of lung cancer in the 1990s. ^{18}F-FDG is injected into the bloodstream, then transported into the interstitial space from where specific glucose transporters carry it into cells. Malignant transformation is associated with increasing energy demands and upregulation of these glucose transporters (especially GLUT-1). Like glucose, ^{18}F-FDG is phosphorylated by hexokinase to ^{18}F-FDG-6-phosphate. Unlike glucose though, ^{18}F-FDG lacks a hydroxyl group on the 2-position and its metabolite ^{18}F-FDG-6-phosphate cannot act as a substrate for glycolysis. Therefore the positron-emitting tracer is 'trapped' in the cell without being further metabolized, and dephosphorylation is slow. Another advantage of this tracer is that ^{18}F FDG is eliminated via the kidneys and very little is reabsorbed in the renal tubules, leaving low ^{18}F-FDG levels in blood.

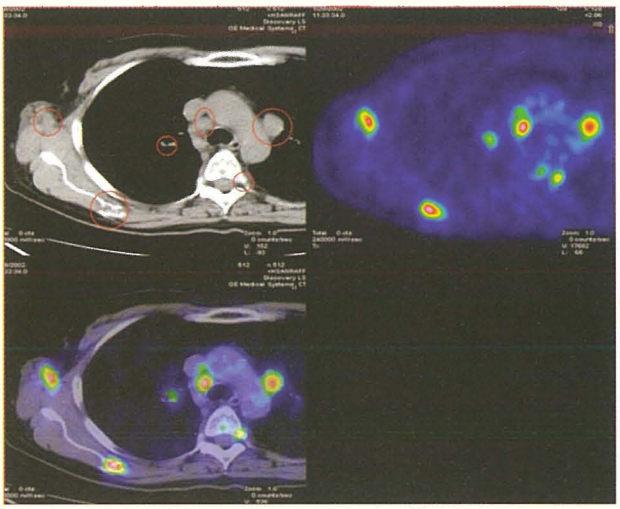

Figure 1: *Staging and re-staging using ^{18}F-FDG. Metabolic PET image superimposed on CT image helps the nuclear physician to report with confidence (Images courtesy of HSR, Milano)*

Clinical scenarios

^{18}F-FDG PET/CT has become an established technique for staging, detection of residual and/or recurrent cancer, significantly for planning therapy, and sometimes for diagnosis. Numerous studies demonstrate how PET/CT is essential in staging and restaging of most cancers including breast, cervical, colorectal, gastric, oesophageal, head and neck, lymphoma, lung, ovarian, uterine, thyroid, testicular, pancreatic, gall bladder and bile duct, renal, bladder, melanoma and sarcoma.

To illustrate further the clinical utility of ^{18}FDG PET/CT and to highlight the fact that many times this imaging technique is indispensable, some representative and common clinical situations are illustrated below:

A. In patients with 'radiologically indeterminate' pulmonary nodules, doctors may opt for a risky 'wait-and-see' or an invasive biopsy which could be marred by complications or false negatives, especially when nodules are in hard-to-reach locations and in cases of inadequate tissue collection. PET/CT has a very high negative predicative value. When negative, a biopsy can be avoided.

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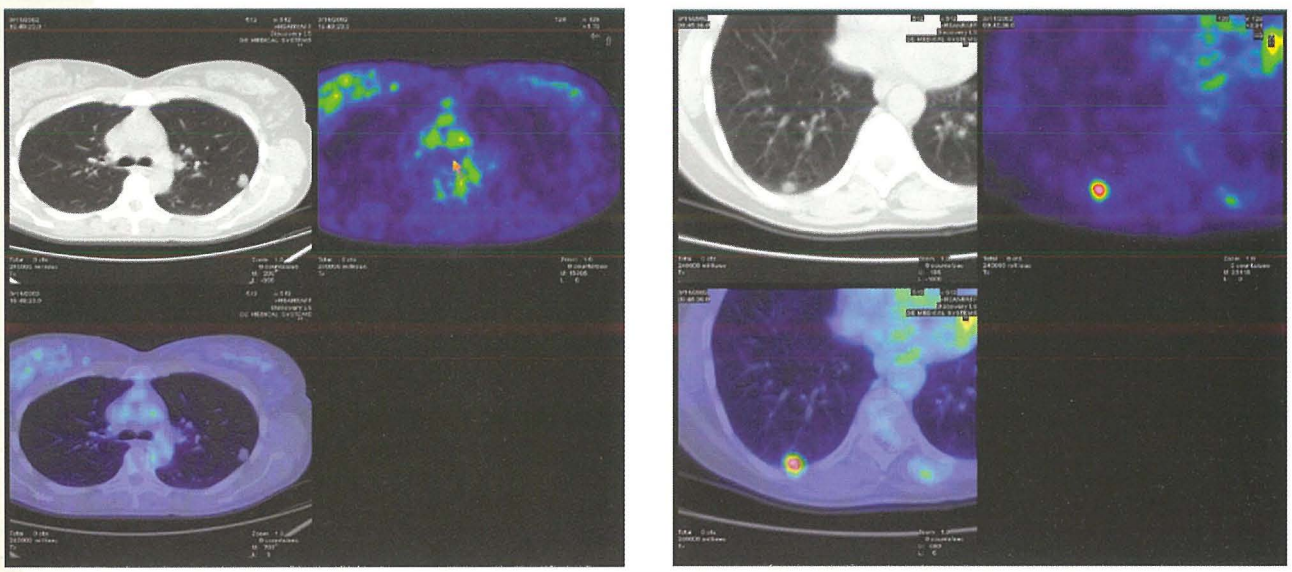

Figure 2: *Two patients presenting with a pulmonary nodule. In one patient (above left), the nodule showed no tracer uptake, and a biopsy was avoided. In the other patient (above right), the nodule showed avid tracer uptake. Moreover, whole-body PET/CT allowed immediate staging of the patient with the very suspicious lung lesion. Metabolic characterisation of pulmonary nodules is also very important when these are located in areas which are impossible to reach by a biopsy needle (Images courtesy of HSR, Milan)*

B. PET/CT is more sensitive than CT in pre-operative staging of most carcinomas; for example, many studies show that in oesophageal carcinomas, a significant number of patients deemed operable by CT may have unsuspected metastases which can be identified by PET/CT, hence drastically altering management[3].

C. A drawback of 'conventional' imaging techniques is their reliance on size criteria to define disease such as in the case of lymph nodes, with the consequent failure to detect disease in small lymph nodes and to exclude disease in larger lymph nodes. ^{18}F-FDG often permits distinction of suspicious lymph nodes as malignant or disease-free, also avoiding unnecessary procedures such as biopsies or mediastinoscopies. PET/CT staging and restaging (assessment of therapy) of Hodgkin's and non-Hodgkin's lymphoma is superior to stand alone CT and gallium scintigraphy[4].

D. In some carcinomas it is possible to follow-up using tumour markers (e.g. colorectal, ovarian, breast and pancreatic carcinomas). PET/CT is an asset in patients presenting with rising tumour markers during follow-up and with negative conventional morphological imaging. PET/CT allows the addition of early metabolic change data to the morphological images, potentially determining the cause of tumour marker rise. FDG-PET is also a valuable diagnostic tool in patients with cancer of unknown primary (which conventional imaging modalities fail to detect). These patients would initially present with metastasic lesions (e.g. bone, lymph nodes, lung)[5].

E. Increased tumour uptake is a function of proliferative activity and is also related to viable tumour cell number. Hence, if ^{18}F-FDG is related to tumour cell viability, then reduction in uptake (with effective chemotherapy) should reflect increased tumour cell killing rate. Clinical trials have demonstrated uptake of ^{18}F-FDG as an early and sensitive pharmacodynamic marker of the anti-tumoral effect of chemotherapy, even as early as the first cycle of chemotherapy[6]. The oncologist can consider changing a chemotherapy regime early on, avoiding extra costs in suboptimal therapies and saving the patient from side-effects.

F. When a patient presents with a tumour (as in lung carcinoma) with surrounding oedema, PET/CT permits the evaluation of the exact extent of the lesion, thus allowing better radiotherapy planning. Nowadays, PET images are used directly for radiotherapy purposes. Post-radiotherapy PET/CT helps determine whether any residual viable tumour is still present. This is difficult to distinguish on CT because both scar tissue (radiotherapy changes) and disease can alter anatomy.

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