

PET-CT: principles and practices

Key words: positron emission tomography (PET); x-ray computed tomography (CT); image co-registration; attenuation correction; ^{18}F -labelled fluorodeoxyglucose (FDG); lung neoplasms; lymphoma; colorectal cancer

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Abstract

Positron emission tomography-computed tomography (PET-CT) is the fastest-growing imaging modality worldwide. Integration of a PET scanner and CT scanner to provide co-registered images combines the high spatial resolution and anatomical detail of CT with the molecular, quantifiable images obtained by PET. Moreover, attenuation correction of PET images using the CT data enables PET-CT to be faster than PET alone, thereby improving imaging efficiency and patient throughput. PET-CT has been proven to be the most sensitive and specific examination for tumour staging through the complementary nature of the two systems in many tumours. PET is highly sensitive for identification of lesions, whilst CT localisation of foci in co-registered images increases the specificity of these findings and can show pathology not resolved by PET alone. The current most frequent indications for PET-CT are non-small-cell lung cancer, lymphoma and suspected recurrence of colorectal cancer, where PET-CT data are valuable for staging, therapy/surgery planning and prognosis. The spectrum of successful applications for PET-CT is increasing, and emerging indications include imaging of inflammation, and the potential for combining CT coronary angiography with PET imaging of rest and stress perfusion to enable a full 'one-stop' cardiac examination. PET-CT currently represents the best of clinical molecular imaging and seems certain to develop further with advances in radiotracer and scanner technology.

Introduction

Positron emission tomography (PET) imaging in its new technological form of PET-CT (PET-computed tomography) is the fastest-growing imaging modality worldwide. The principal reason for this is that PET-CT is an excellent modality for tumour staging. Thus – using ^{18}F Fluorine (^{18}F)-labelled Fluorodeoxyglucose (F-18-FDG) – PET is able to demonstrate increased glucose uptake/metabolism as a molecular rather than an anatomic feature of the tumour.

The additional use of CT contributes an anatomical reference frame to the PET-imaged lesions, and helps to specify some of the findings. It is apparent that measuring changes in FDG uptake/metabolism is much more sensitive for detecting tumours and response to therapy than measuring morphological changes. With this attribute, PET-CT currently represents the best of clinical molecular imaging. This article outlines the principles of PET-CT imaging and presents the current and predicted future indications for this imaging modality.

Principles

PET imaging

PET is an imaging technique based on nuclear medicine principles. A radiolabelled tracer, typically the ^{18}F -labelled glucose analogue F-18-FDG, is injected into the patient and localises in the areas of high glucose uptake/metabolism. The ^{18}F isotope undergoes a Beta+ or positron decay with a half life of 110 minutes. The positron emitted is a particle of antimatter and, as such, it is not stable. As a result, it reacts with a nearby electron, typically within a distance of 1 mm from where the positron has been emitted. This annihilation reaction between the positron and electron results in the generation of two gamma rays, which travel almost exactly in opposite directions. It is the detection and analysis of these emitted gamma rays that enables the generation of PET images.

The PET scanner

The PET scanner is a system that is able to detect the gamma rays emitted from the annihilation reaction and then compute cross-sectional images of tracer distribution. This process produces emission images which depict the distribution of ^{18}F activity in the body. Typically, 200 to 300 axial images are acquired in batches of 30 to 50 from head to pelvic floor, thereby providing a survey of the most important body structures.

Limitations of PET

An unwanted effect in PET imaging is the attenuation of the emitted gamma rays by the patients' body tissues. As a result of this, positron decays from deep within the body appear attenuated relative to those occurring on the surface. In order to correct for this, transmission images, as well as the emission images, are acquired by the PET scanner. A mathematical algorithm using these transmission images is used to correct the emission images for attenuation (Figure 1). However, attenuation correction PET data acquisition represents around 30% of imaging time.

patient movement, the PET and CT images are perfectly co-registered. Thus, on these 'hardware co-registered' images, CT provides high spatial resolution of anatomical landmarks for the assessment of PET findings. Moreover, there is a synergistic benefit of integrating CT with PET imaging, as CT data can also be used for the attenuation correction described above, and imaging time is reduced.

For the correction of photon attenuation in the PET emission data, the CT data relating to the original acquisition energy of 70–140 keV are transformed

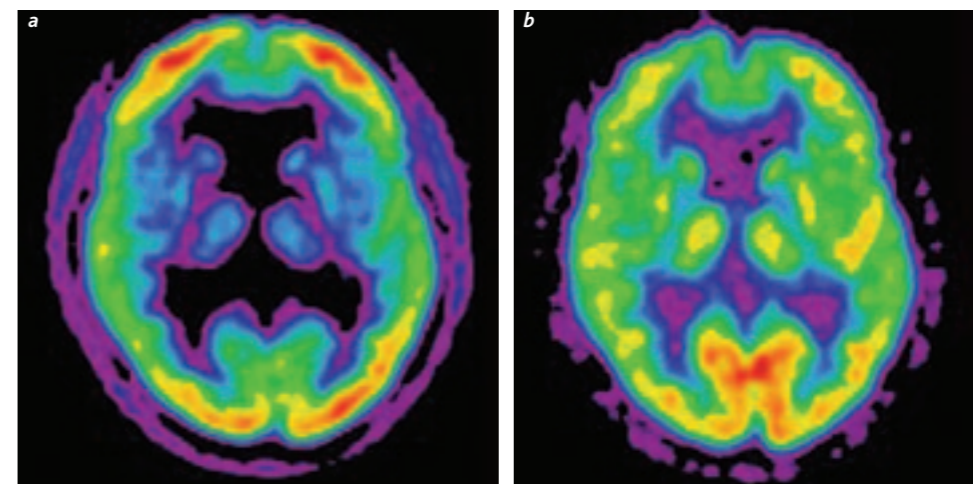


Figure 1. Axial FDG brain image: (a) without attenuation correction showing net attenuation of the important central cerebral structures (basal ganglia and thalamus) and giving the appearance of the patient having a hydrocephalus; and (b) after attenuation correction. These structures demonstrate FDG uptake comparable to the cortex.

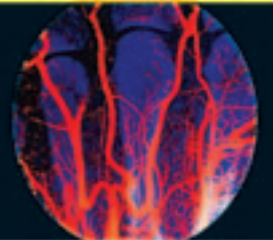
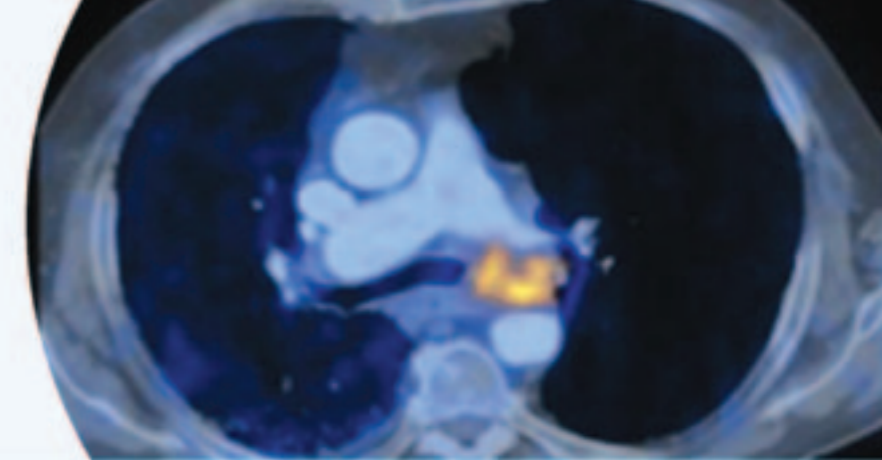
In addition, the anatomical detail provided by PET images is limited. PET scans have a limited spatial resolution in the range of 5–7 mm and also contain few anatomical landmarks for localising pathological F-18-FDG foci apparent on the scans. In order to deal with these drawbacks, integration of PET and CT into a single system has been proven to make eminent sense.

PET-CT in a single system

In integrated systems, a PET and a CT system are placed in line and close together (<60 cm). When data are acquired sequentially in both systems without

mathematically, and this correction provides attenuation maps at the PET gamma ray photon energy of 511 keV (Figure 2). Furthermore, as CT imaging is fast, taking a maximum of 30 seconds when scanning from head to pelvic floor, the imaging speed of a PET-CT scanner is typically 30% faster compared with a PET scanner. The resulting higher patient throughput also improves the efficiency of use of F-18-FDG.

There are some minor technical issues associated with the use of a combined system. They are mainly due to the fact that a CT scan is acquired while the patient is



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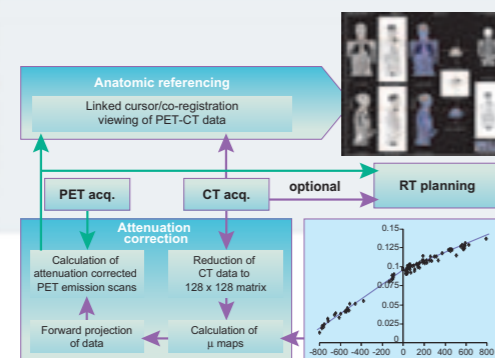


Figure 2. Data flow in PET-CT. CT data are acquired, reduced in matrix size, and corrected to 511 keV absorption maps (μ maps) using the plot in the lower right hand corner.¹ Then, the data are forward-projected and used in the calculation of the corrected PET emission scans. The PET and CT data are jointly viewed in an image viewer. The CT data can also be used for radiation therapy (RT) planning.

holding their breath, whereas PET scans are acquired during free breathing. However, appropriate precautions can minimise these problems, for example by the use of suitable respiration protocols during acquisition.²

Many validation studies have shown that PET images corrected for attenuation by CT images have similar properties compared with those corrected with PET transmission images. Moreover, the quantification of PET data is also possible.^{1,2}

Practices

PET-CT image acquisition

As stated earlier, PET-CT is currently used mostly for tumour staging and therapy control, and the dominant tracer used is F-18-FDG. Axial scans are acquired, stretching typically from the head to the pelvic floor. They are then represented to the reader not only in this format, but also as fused PET-CT images and as coronally and sagittally reformatted images. Imaging protocols developed so far use mostly low-dose CT scans following administration of bowel-delineating contrast material combined with injections of 340 to 510 MBq of F-18-FDG. Increasingly, additional intravenous contrast media-enhanced CT images are also acquired at the end of the imaging study (Figure 3).

The use of contrast-enhanced CT images for attenuation correction can cause some image artefacts if the contrast media density exceeds 200 Hounsfield units. This is due to the fact that X-ray contrast media provide contrast at the energies at which CT data are acquired, whereas at the much higher photon energies of the PET gamma rays, the attenuation characteristics of X-ray contrast material are virtually the same as those of soft tissues, i.e. they do not act as contrast material at these energies. Thus, if contrast-enhanced CT images are to be used for attenuation correction, contrast enhancement should be done with dilute material, and the use of images acquired after an intravenous bolus of X-ray contrast material is not recommended.³ Depending on the technical characteristics of the CT scanner, very sophisticated imaging protocols may be run, which can also provide angiographic information.

In fact very early results now exist on using PET-CT as a 'one-stop-shop' cardiac imaging modality (see the following Outlook).

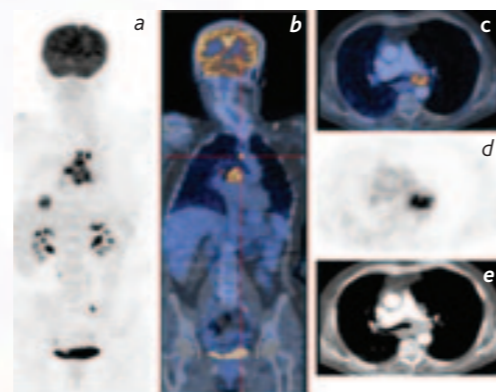
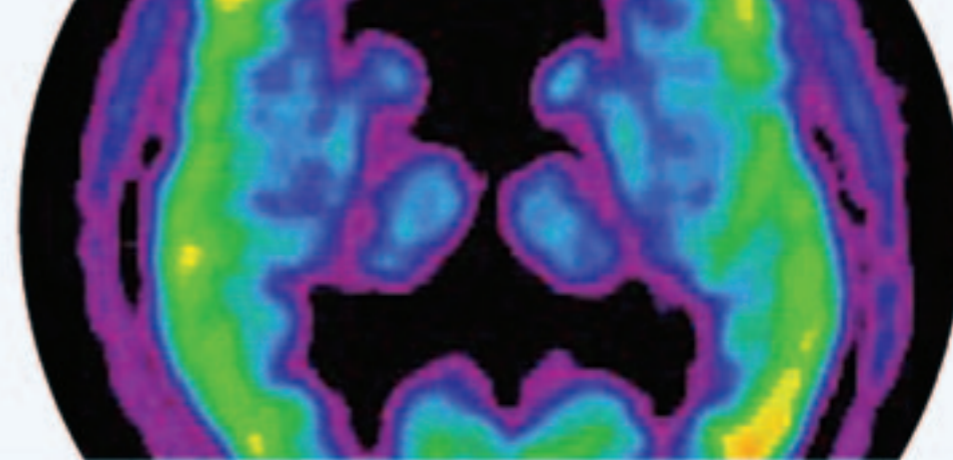


Figure 3. Patient with right-sided bronchial carcinoma and mediastinal lymph node metastases. In addition to these findings, the coronal FDG-PET scan (a) and the fused PET-CT scan (b) shows physiologic FDG-uptake into the brain, the renal collecting system and the bladder as well as some focal urinary FDG along the course of the ureters and weak liver and spleen uptake. In this scan also containing i.v. CT contrast (e), the axial images show the tumour to be separate from the vascular structures in the aorto-pulmonic window (fused PET-CT image (c), PET image (d), contrast-enhanced CT image (e)).



performance of PET-CT, some more specific statements regarding PET-CT for certain tumours can be made on the basis of our data and from other available literature.

The most frequent indication for PET-CT is non-small-cell lung cancer (NSCLC) (Figures 3 and 4). In Switzerland, over 20% of all PET scans performed in 2003 were for this indication. In this disease, PET-CT is the best imaging modality for N and M staging, and early results suggest that PET-CT is better than PET alone, CT alone, and PET and CT read next to each other, even in T staging where PET has so far played no role.⁷

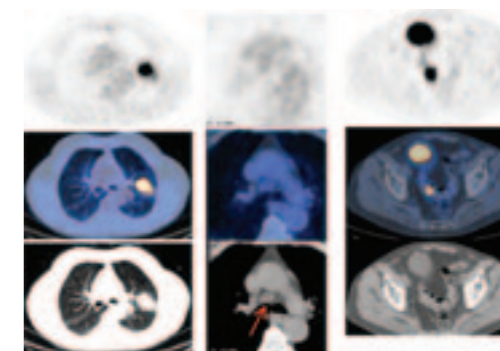


Figure 4. Patient with right-sided bronchial carcinoma. An enlarged lymph node seen on CT (all CT images in bottom row) is unequivocally defined as benign on the PET scan (all PET scans in top row), as there is no FDG uptake. Fused PET-CT images are shown in the middle row. In addition, there is an FDG-containing focus which is localised into the large bowel on CT. The latter lesion was found to be a villous adenoma. In an extended review of over 3000 PET-CT scans we found that in 3% of all patients referred for tumor imaging, a second malignancy or pre-malignancy was present in the large bowel.

FDG-PET scans show little glucose accumulation in the body of patients kept nil by mouth for >4 hours. Organs strongly accumulating FDG are the brain, which is an obligatory glucose user, the renal collecting system and the bladder and sometimes the myocardium, with weaker accumulation in the liver (Figure 3). Additional 'normal' glucose uptake occurs in strained or very recently exercised muscles⁴ and, in around 3% of patients, into fatty tissues⁵ mainly in the shoulder girdle region, which is believed to be brown fat.

Most tumours avidly take up FDG, the most notable exception being prostate cancer, which will do so only in its most malignant forms. There is increasing evidence that the use of PET-CT in assessing these tumours yields better staging information than other imaging modalities. One of the most evident facts in clinical practice is the complementary nature of PET and CT. PET tends to identify the lesions easily and thus is highly sensitive. However, FDG foci, which can represent false positives with regards to tumour staging, include inflammation, focal muscle uptake and focal urine activity (Figure 3). Localisation using CT helps to reduce these false positives drastically – probably by around 50%⁶ – and this in turn results in an increase in specificity without loss of sensitivity. In addition, CT is able to show pathology that adds to the sensitivity of the examination, but which is not seen on PET, for example: bronchial carcinomas that are not FDG avid; small lung foci, which represent metastases but are too small to show FDG uptake; and relevant calcifications such as silent kidney stones or lymph node calcifications. This leads to PET-CT being the most sensitive and specific technique currently available for tumour staging and follow-up examination.

Key indications for PET-CT

Our group has scanned in excess of 5000 patients with PET-CT to date and analysed several patient subsets. In addition to the general findings with regards to the

Almost all patients going to surgery in our institution for NSCLC undergo PET-CT. There is still debate regarding the settings in which PET-CT in NSCLC should be performed with intravenous CT contrast material (Figure 3), but it is likely to be necessary only with substantial central tumours, where delineation from vascular structures is necessary. In addition, PET-CT appears to be of value in patients with small cell lung cancer, as it is able to classify patients with limited and

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those with extended disease, and in patients with mesothelioma, where PET-CT can indicate to the surgeon which of the plaques seen on CT are malignant and which are fibrous.

The second most frequent indication for PET-CT is lymphoma. While initial staging of lymphoma may not require PET-CT, with CT alone being adequate, therapy follow-up is of major importance in this disease entity, particularly because of the bulk lesions remaining after therapy. On CT, only slow regression of the size of these lesions over extended periods will be evident, while the additional PET information has relevant prognostic value. Patients without FDG accumulation in remaining tissue bulks do much better than those with FDG accumulation.⁸ Recent data from our group suggest that in the follow-up scans of these patients, FDG-PET-CT without intravenous contrast media is sufficient.⁹

The third most frequent indication for PET-CT is in the suspected recurrence of colorectal cancer. The critical information required is whether patients have metastatic disease to the liver only, or whether there is more extensive involvement. Here again, FDG-PET-CT enables better triage to surgery (Figure 4).¹⁰

Many other patients with malignant tumours are currently undergoing PET-CT with F-18-FDG and further information on the advantages of the technique is rapidly emerging. Another very relevant application is the use of PET-CT in the process of radiation therapy planning. The CT data acquired with proper patient positioning can be directly used for the planning process, and early results indicate that defining the relevant tumour volumes for therapy can be performed with higher precision using PET-CT rather than PET alone.¹¹

Outlook

In a short time, PET-CT has proven to be a very successful imaging technique in many malignant diseases. Although in some tumours, such as prostate cancer, FDG is a poor marker of disease, other markers such as F-18-choline seem to be able to identify prostate cancer lesions successfully. In general, development of alternative radiotracers is bound to increase the spectrum of successful application of PET-CT. New applications are also emerging. For example, FDG is also avidly taken up into macrophages and granulocytes, which are activated when fighting inflammation. Good indications for PET-CT are emerging here, although the field is less developed than that of tumour imaging.¹²

Finally, in the near future one can expect CT developments which will permit CT coronary angiography. Integrating such CT scanners with PET scanners may finally yield the cardiac 'one-stop-shop' examination, with CT providing anatomic information on the coronary arteries and possibly wall motion, while PET can provide rest and stress perfusion, the latter being done with radioactive ammonia, water or rubidium (Figure 5). Whether such systems will be of interest and competitive to other modalities will have to be demonstrated, but this is certainly a very interesting area of research.¹³

Conclusions

PET-CT currently offers the best of clinical molecular imaging. Combining the two imaging modalities to produce co-registered images has enabled the detailed differentiation and characterisation of tissue alterations. The value of this technique has been proven in tumour imaging and new applications are emerging rapidly. New developments and indications for PET-CT, particularly associated with advances in radiotracer and scanner technology, is an exciting prospect.

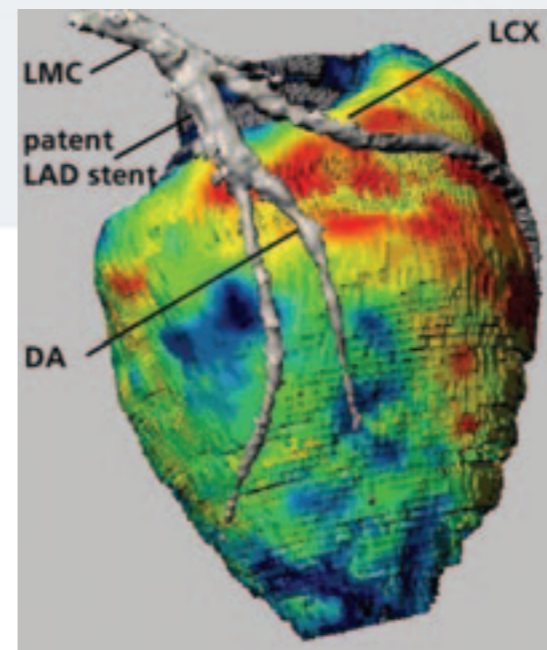
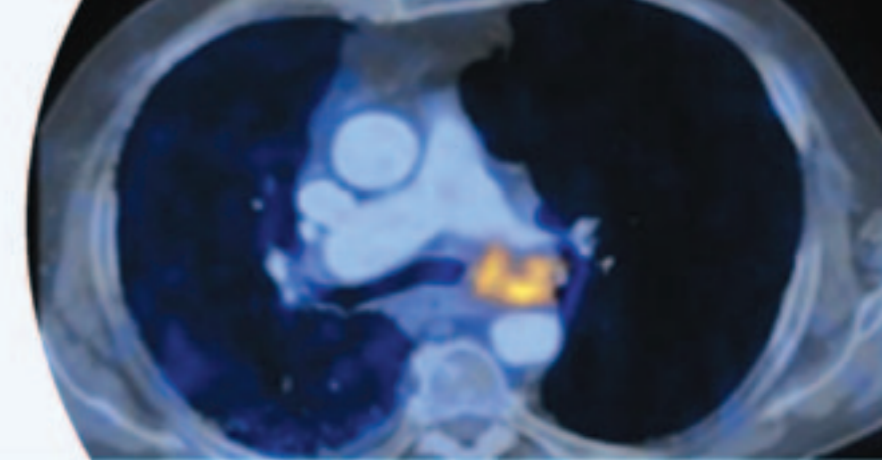


Figure 5. Experimental use of a 4 row, 0.5 sec CT scanner within a PET-CT scanner to produce cardiac 'one-stop-shop' images. The coronary angiogram was acquired using this CT, while the surface of the myocardium is coloured using the data of the ammonia PET stress perfusion scan done during the PET-CT examination. The quality of the coronary arteries is still suboptimal (due to the lack of appropriate rendering software rather than poor imaging data), but it can be clearly seen that territories in the distal LAD region are blue, which signifies reduced stress perfusion.

Key Learning

- PET (positron emission tomography) demonstrates glucose uptake/metabolism as a molecular feature of tissues, but proper reconstruction of PET images requires additional attenuation correction and PET offers limited spatial resolution
- CT (computed tomography) provides high spatial resolution and the data can be used for the attenuation correction of PET images
- PET and CT in an integrated system enable co-registered images that provide excellent anatomical resolution for assessing findings shown by PET
- PET-CT is the most sensitive and specific examination for tumour staging in many tumours, the most frequent indications being non-small-cell lung cancer, lymphoma and recurrent colorectal cancer
- PET-CT is the fastest-growing imaging modality worldwide; new indications are emerging rapidly, including the development of combined molecular and angiographic imaging to provide a detailed cardiac examination in a single procedure

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