

Recommendations for cross-sectional imaging in cancer management, Second edition

Positron emission tomography CT (PET-CT)

Faculty of Clinical Radiology

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Positron emission tomography CT (PET-CT)

Derangement in chemical processes is one of the first indicators of cancer and this precedes changes in morphology. PET-CT provides unique information about metabolic processes within tissue and precisely identifies where areas of deranged metabolism are occurring. The majority of cancers have increased glucose metabolism compared with normal tissue. In clinical practice, ¹⁸Fluorine fluoro-deoxyglucose (FDG) is the most widely used radiotracer with PET-CT in clinical practice. FDG PET-CT identifies the difference and increase in glucose metabolism of cancer cells compared with normal cells. FDG PET-CT is now recognised as a key investigation for optimum management in an increasing number of malignancies. Depending on the tumour type, FDG PET-CT can be highly effective for primary tumour staging, assessing treatment response and for detecting disease recurrence.¹ These applications of FDG PET-CT have been shown to alter patient management in approximately one-third of patients with cancer. The current document makes reference to the use of FDG PET-CT in specific tumours where best evidence supports its use in routine clinical practice and its limitations in other tumours are also addressed in the appropriate disease sections.

Drawing from new evidence, the use of FDG PET-CT in our cancer patients continues to be refined and expanded. The role of FDG PET-CT for radiotherapy planning and monitoring early response to neoadjuvant chemotherapy treatment are two areas which are currently attracting considerable research attention. Radiotracers other than FDG are being studied; included are fluoro-thymidine which provides an index of cell proliferation and fluoro-ethyl and fluoro-methyl choline which measure cell membrane turnover.

Patient preparation

All patients should receive written confirmation regarding the timing of their appointment along with information about what the scan involves, how long it will take and how the results will be communicated to their clinician. To reduce the risk of wasted FDG and appointment times, patients should be asked to confirm that they will

be attending for their appointment at which point the importance of arriving on time should be stressed. The information sheet should request that patients inform the department if they are diabetic, claustrophobic, pregnant, breast feeding, have difficulty lying flat on their back for at least 30 minutes or if they are scheduled for any other hospital appointments on the same day as their PET-CT scan. At the time of booking, patients should also be advised that it is recommended that they have minimal close contact with pregnant women or young children for the remainder of the day following their scan. For patients who are claustrophobic or have difficulty lying down it is recommended that they visit the department prior to their appointment to look at the scanner and discuss whether they think they will be able to tolerate the scan. Depending on the referral indication and local experience, imaging protocols will vary slightly and specific information should be provided where possible.

Patients are asked to abstain from food and drink, other than water, for at least four to six hours before the scan. Patients should be encouraged to drink plenty of water but should be told that they can void as often as required and do not need to have a full bladder. Insulin-dependent diabetic patients should not be asked to fast and should be instructed to eat and take their medication as usual. Their appointment should be scheduled so that their FDG injection is given as long after their last meal as possible, while preserving their normal routine. For patients with poorly controlled diabetes, a discussion between the Administration of Radioactive Substances Advisory Committee (ARSAC) certificate holder and the patient's referrer prior to booking will reduce the likelihood of an uninterpretable scan.

Patients with stomas following bowel surgery should be asked to bring fresh stoma bags with them so that, if required, the bag can be changed immediately prior to scanning.

To reduce the risk of false-positive or false-negative results, when scheduling the patient's appointment, consideration should be given to

the timing of the appointment in relation to concurrent or recently completed chemo and radiotherapy. Guidance should be sought from the ARSAC certificate holder as to the optimal time for scanning.

For patients who will be receiving contrast media as part of their PET-CT scan, please refer to the information provided in the CT section of this document.

On arrival in the department, it is important that the procedure is clearly explained to the patient and that the patient is allowed an opportunity to ask questions so that they are as relaxed as possible. It is important to take a clear clinical history from the patient including details regarding recent treatment and to measure and record the patient's height and weight. Where appropriate, last menstrual period (LMP) dates should be requested and recorded and, if necessary, pregnancy status should be established with local protocols followed ensuring compliance with *The Ionising Radiations Regulations 1999*² and the *Ionising Radiation (Medical Exposure) Regulations 2000*.³ For these reasons appointment times should ideally include a pre-injection period of at least 20 minutes.

The patient should be comfortably warm before the scan to aid relaxation and reduce normal physiological muscle and brown fat FDG uptake. It is important to diminish physiological uptake by brown fat and muscle because this can lead to errors in interpretation of the scan.

Normal physiological uptake of FDG into the intrinsic laryngeal muscles is demonstrated in patients who speak before, during or after tracer injection and this can cause confusion. For this reason, it is recommended that patients, and especially those with conditions involving the head and neck, such as head and neck cancer, observe a silence protocol with no talking for 20 minutes prior to the injection, during the injection period and for the majority of the uptake period (the first 30 minutes after injection being the most important period). These patients should, therefore, be asked to arrive for their appointment at least 40 minutes before their scheduled injection time.

Hyperglycaemia

All patients must have their blood glucose measured and recorded prior to FDG injection. The finger prick blood test is, as a rule, avoided and instead a drop of blood is taken during cannulation.

Considerations for a non-diabetic patient with high blood glucose

The patient's blood glucose is usually high because they have not fasted as instructed. If so, the patient is invited to drink 3–4 glasses of water and the blood glucose is repeated about two hours later. The blood glucose is then ordinarily normal.

If the blood glucose remains high, it is usually due to a concurrent infection. If this is the case most centres would consider postponing the scan and inviting the patient to visit their GP.

Considerations for a diabetic patient

- Tablet controlled: The patient is usually invited to attend an early morning appointment and asked to refrain from breakfast and their diabetic medication, or invited to attend a middle of the day appointment having eaten a light breakfast at 6 am and taken all their medication including diabetic medication at the time of breakfast.
- Insulin controlled: In general, the patient is invited to attend a middle of the day appointment having eaten a light breakfast at 6 am and taken all their medication at the time of breakfast, including their insulin injection. However, each patient is advised on an individual basis and factors such as the time of the insulin injection will influence their appointment.

Patients with diabetes mellitus (DM) are asked to drink plenty of water in the six hours leading up to the scan appointment (about a litre). Depending on the nature of the DM and the preparation instructions that have been given, they are advised to bring their food/tablets/insulin with them to be taken immediately after their scan. Advice given is guided by the patient's recent blood glucose levels and, for follow-up FDG PET-CTs, advice is also influenced by the blood glucose level of previous scans. In patients with blood glucose of more than 12 mmol/litre, it is

usually appropriate to consider deferring the FDG PET-CT, as it can result in false-negative results. However, each patient is advised on an individual basis and with all relevant factors taken into consideration.

Injection site

It is advisable to allow the patient to relax for a couple of minutes between the cannulation and the administration of the FDG. This also ensures that the integrity of the line can be adequately checked and will reduce the risk of extravasation. It is critical that the member of staff performing the cannulation and injection (usually the nuclear medicine technologist or radiographer) is well trained and well practised as a precise technique is critical. Local extravasation results in a local radiation dose and can cause problems with scan interpretation, particularly as extravasated radiotracer drains into the lymphatic system and therefore FDG uptake may be observed within axillary lymph nodes on the scan. It is for this reason that, in patients with breast cancer, the radiotracer injection should be given on the side not affected by breast cancer if at all possible. Where there is any concern regarding the quality of the injection, care should be taken to make sure that a quick image of the injection site is acquired and available for the reporting clinician so that they can report with confidence.

Scanning

Imaging is usually commenced 60–90 minutes post-FDG injection. Patients are routinely imaged with their arms raised above their head. This is important as it prevents beam hardening artefacts on the CT component of the study. In patients with head and neck cancers, however, imaging is done with their arms straight and crossed over the front of their abdomen to reduce the impact of beam hardening artefacts in the area of most interest. Some centres acquire two separate datasets for head and neck patients; a scan with the arms up from the clavicles to the mid-thighs and a separate scan including only the head and neck with arms down to the sides. Whichever positioning is used, it is essential to provide the patient with sufficient immobilisation support to ensure that they will be able to remain still for the duration of the scan, as this will reduce the risk of movement which would lead to mis-registration and attenuation artefacts.

Depending on local practice, some centres routinely include the cranial cavity and others start scanning from the skull base. With modern scanners, it usually takes about 30 minutes to obtain an FDG PET-CT from skull base to mid-thighs.

Most centres in the UK do not give IV contrast as part of the FDG PET-CT examination. If IV contrast CT is required, this is usually obtained immediately after the PET-CT applying standard CT technique and in the same scanner.

Standardised uptake value (SUV)

The maximum SUV (SUV_{max}) of a lesion is the most commonly used measure of FDG uptake and may be used to measure response during therapy and, in some cases, provide information relating to the grade of a tumour. There are many factors that critically influence SUV_{max}, including time of imaging post-injection (uptake period) and the blood glucose value at the time of injection. To enable reliable comparison between patients, standardisation of protocols and meticulous attention to technique is imperative. For meaningful comparison of SUV_{max} in interval scans in the same patient, it is essential that their scans are performed on the same scanner and in the same way at each visit. Ideally this includes scheduling the appointments at a similar time of day and ensuring that the uptake period is the same for each scan. Where variations to protocol have been applied, this latter consideration should take priority.

Radiation protection

UK regulations^{2–4} governing exposure of ionising radiation require radiation protection advisers (RPA), radioactive waste advisers (RWA), medical physics experts (MPE) and radiation protection supervisors (RPS) to provide radiation protection guidance in nuclear medicine procedures. As key members of the PET-CT team, they play a pivotal role in the protection of staff, patients, comforters, carers and the general public from unnecessary exposure to radiation. They facilitate good design of PET-CT centres with 'hot' and 'cold' areas well separated and ensure the department applies the well-understood tenets of radiation protection; that is, shielding, time and distance to comply with regulatory requirements. In addition to enforcing

that all equipment and all personnel involved in PET-CT are 'fit for function', legislation ensures that risk assessments and audits are performed, patient doses are optimised; that is, as low as reasonably practicable (ALARP) and that radioactive waste is managed safely.

Responsibility for FDG administration to each patient is taken by a suitably qualified clinician,⁵ with guidance provided for diagnostic reference levels (DRL) of injected activity (18FDG adult DRL is 400 MBq ~ 8 mSv effective dose).

FDG has a relatively short half-life of approximately 110 minutes, compared with Technetium-99m (Tc-99m) which is six hours. Following a FDG PET-CT with a 60–90-minute uptake period and a 30-minute scan (the typical duration of a scan), the patient can travel on public transport with no need for any restrictions. Nevertheless, many centres recommend maintaining some distance and avoiding close contact with pregnant women and children for a number of hours following an FDG PET-CT scan.

On average, background radiation accounts for about 2.4 mSv per year and the dose limit to members of the public from artificial sources is 1 mSv per year.⁶ The dose limit for adult radiation workers is 20 mSv per year (averaged over five years) but it is desirable for PET-CT staff to be non-classified; that is, to receive an effective dose <6 mSv per year. For pregnant women, the fetus should receive no more than 1 mSv during the declared term of the pregnancy and systems of work must be set in place to identify potential mothers-to-be. The dose to the abdomen of a woman of reproductive capability shall be limited to 13 mSv in any consecutive period of three months. Others who deal with patients regularly also need radiation protection consideration, training and risk assessment, such as healthcare workers, drivers, helpers, carers, and so on.

At major transport centres such as airports, very sensitive state-of-the-art radiation detectors may be installed and these may be triggered by nuclear medicine imaging and therapy agents. If a patient intends travelling through such a hub, particularly immediately after a PET-CT, it may be prudent to advise the patient to take evidence that they have had a recent PET-CT or alternatively to delay travel for 24 hours as a precaution.⁷

Recent developments about safety have been highlighted in the International Atomic Energy Authority (IAEA) *Radiation Protection in Newer Medical Imaging Techniques: PET/CT, Safety Report 58*.⁸

Radiation dose

The total PET-CT dose is a combination of PET emission scan dose and CT transmission scan dose. At the time of writing, the National Cancer Research Institute recommends typical 18FDG-injected activities for validated UK PET trials of between 150–400 MBq with an ARSAC certificate holder's permission required for administration above 400 MBq. This relates to an adult, whole-body, effective dose range of around 3–8 mSv; using 1.9×10^{-2} mSv/MBq conversion factor in Report 106 of the International Commission on Radiological Protection (ICRP).⁹ For image quality, longer scan time per bed is preferred to increased FDG activity for larger patients.

A relatively low-dose CT (~5 mSv) is acquired predominantly for attenuation correction and for anatomic localisation of FDG uptake. However, if detailed morphological analysis is required especially with liver and spleen, currently low-dose CT in PET-CT may be followed by standard contrast-enhanced CT (~16 mSv typical).¹⁰ CT scanning can account for around 50–80% of the combined PET-CT patient dose; however, automatic exposure control techniques have been used to reduce diagnostic CT doses (~ 8 mSv).¹¹ Accordingly protocol-dependent effective doses arising from whole-body PET-CT scanning may be represented typically in the range of 8–24 mSv.

The radiation burden from multiple radiological investigations can be substantial, leading to increased risk of potentially fatal interval cancers compared with the rest of the population. Consideration should be made for reducing radiation dose, whenever possible, without compromising diagnostic quality.¹² Scanning which routinely extends from the base of brain to top of thighs is recommended unless there is a reason to include imaging of the brain and lower limbs. In patients having a diagnostic CT scan following a PET-CT and in the same PET-CT scanner, replacing the low-dose CT with the diagnostic CT for attenuation correction may be advocated,¹³ providing attenuation correction is

uncompromised by presence of contrast. PET-CT scanners which include hardware developments such as PET Time-Of-Flight systems allow superior dose and signal/noise optimisation. Software innovations such as Adaptive Statistical

Iterative Reconstruction (ASIR)¹⁴ offer the promise of considerable CT dose savings of up to around 40%. Technological progress will result in further lowering of radiation dose in the future.

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