# 18F-FDG PET/CT in Oncology

Summary of EANM guidelines

## 1. Introduction

18F-FDG (FDG) PET imaging is a non-invasive diagnostic tool that provides tomographic images and can be used to obtain quantitative parameters concerning the metabolic activity of target tissues. 18F is a cyclotron-produced radioisotope of fluorine that emits positrons and has a short half-life (109,7 min). It allows labelling of numerous molecular tracers that can be imaged within a few hours (typically < 3 h) after injection. 18F-FDG is an analogue of glucose and is taken up by living cells via cell membrane glucose transporters and subsequently incorporated into the first step of the normal glycolytic pathway. PET is a tomographic technique that measures the three-dimensional distribution of positron-emitting labelled radiotracers.

PET allows non-invasive quantitative assessment of biochemical and functional processes. The most commonly used tracer at present is the 18F-labelled glucose analogue FDG. FDG accumulation in tissue is proportional to the amount of glucose utilization. Increased consumption of glucose is characteristic of most cancers and is in part related to overexpression of the GLUT glucose transporters and increased hexokinase activity. FDG PET has been proven as a sensitive imaging modality for detection, staging and restaging and therapy response assessment in oncology. FDG PET/CT provides essential information for radiation treatment planning, helping with critical decisions when delineating tumour volumes.

CT uses a combined X-ray transmission source and detector system rotating around the subject to generate tomographic images. CT allows not only attenuation correction but also the visualization of morphological and anatomical structures with a high spatial resolution. Anatomical and morphological information derived from CT can be used to improve the localization, extent and characterization of lesions detected by FDG PET. These guidelines focus on the use of FDG PET/CT in oncology, where PET/CT continues to gain importance.

Recently, combined or integrated PET and MRI systems (PET/MRI) have come onto the market. PET/MRI technology is, however, still in development and is not yet widely available. Therefore, this version of the guidelines does not address FDG PET/MRI. Currently the quantitative performance of FDG PET/MRI is being explored as a scientific project within EANM Research Limited (EARL).

## 2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

## 3. Indications

FDG PET/CT is a rapidly evolving imaging modality at both national and international

levels, with some striking differences between individual countries. FDG PET/CT has become one of the cornerstones of patient management in oncology.
Indications for FDG PET/CT include, but are not limited to, the following:

- Differentiation between benign and malignant lesions
- Searching for an unknown primary tumour when metastatic disease is discovered as the first manifestation of cancer or when the patient presents with a para-neoplastic syndrome.
- Staging patients with known malignancies.
- Monitoring the effect of therapy on known malignancies.
- Determining whether residual abnormalities detected on physical examination or on other imaging studies following treatment represent tumour or post-treatment fibrosis or necrosis.
- Detecting tumour recurrence, especially in the presence of elevated tumour markers.
- Selection of the region of tumour most likely to yield diagnostic information for biopsy.
- Guiding radiation therapy planning.

Other documents include further indications for FDG PET/CT. The clinical utility of this valuable technology continues to expand in oncology and therefore an exhaustive list of appropriate indications would not be possible and would not remain final for long.
FDG PET/CT also has an increasingly relevant role in inflammation and infection imaging, cardiology and neurology. In these areas the FDG PET/CT procedure may require specific elements not addressed in these guidelines.

**4. Relation to other diagnostic procedures**

Abnormalities on a PET scan must be correlated with the CT scan (if necessary, with the MRI). In many cases, these investigations will already be available (and of course, this is always the case in PET-CT scans). The aim of this correlation is to find an anatomical substrate (in particular of the clinically significant PET findings), mainly to reduce false positivity. In a direct sense, this is the case if the CT scan gives an obvious benign explanation for the FDG-positive focus. If the corresponding abnormality on the CT is indeed suspicious, the biopsy site can be accurately indicated to the referring physician. If no substrate is found on an adequate CT or MRI (technically adequate, suitable for the area to be assessed and carried out not too long ago) that abnormality must be regarded as a false-positive finding. Otherwise, this would prevent, at least at the primary stage, planned curative treatment being wrongly denied.

**5. Medical information for planning**

*Procedure/specification of the investigation*

*1. Request*

The request for the investigation should include sufficient medical information to demonstrate medical necessity and should at least include the diagnosis and questions to be answered. Furthermore, to guarantee adequate image quality, weight and length of the patient are needed for establishing the necessary dose and/or acquisition-time and factors influencing body clearance such as renal function impairment.

*2. Review of the medical history*

The medical record should be reviewed with a special focus on the diagnosis (type

of cancer and known sites), oncological history and relevant comorbidity (especially infection/ inflammation and diabetes mellitus, incl. oral antidiabetics). A short interview with the patient and/or family can help clarify some of these issues.
Relevant laboratory tests should be considered. The results of prior imaging studies should be available for review, including planar radiography, CT, MRI, bone scanning and FDG PET/ CT. Relevant prior studies should be directly compared with current imaging findings when possible. The following list shows all aspects that should be considered in any review of the request:

- Height and body weight (these must be determined precisely in the case of SUV measurements, see below). Weight must also be measured directly prior to each FDG PET/CT (also in the case of longitudinal studies) because body weight often changes during the course of disease.
- Full overview of current and recently used medication, especially (but not limited to) antidiabetic medication, corticosteroids, growth factors and sedatives. In the case of therapy evaluation: type and date of last therapeutic intervention.
- Results of other imaging tests (especially CT, MRI and previous PET/CT), including dates of acquisition, full reports and, if possible, DICOM data of the referred studies for comparison.
- Other investigations performed earlier on the same day as the PET/CT is scheduled. If intravenous contrast agent has been used or specific preparation followed in the 24-48 h prior to the FDG PET/CT examination, the situation should be evaluated and noted; if possible such circumstances should be avoided in patient scheduling.
- Allergy to contrast agents: If an FDG PET/CT with intravenous CT contrast agent is strictly necessary the relevant local premedication protocol to prepare the patient must be applied.
- Renal function: Creatinine and/or glomerular filtration should be evaluated, according to national guidelines, if intravenous contrast agent is to be used. If renal function is suboptimal and an FDG PET/CT with intravenous CT contrast agent is necessary, then the referring physician can initiate the protocol for prevention of nephrotoxicity (hydrate the patient and repeat the blood test, if necessary prescribe medication for prevention of nephrotoxicity).

The following list shows all aspects that should be considered for relevancy in the review of the request:

- Tumour type (if known) and known tumour sites.
- In diabetic patients the usual serum glucose levels and dosage scheme of oral anti-diabetics as well as insulin injections relevant to time of day of the scheduled investigation.
- Oncological history and relevant comorbidity (especially infection/inflammation and diabetes mellitus).
- Neurological or psychiatric clinical presentations, including suspected neurological para-neoplastic syndromes.

**6. Radiopharmaceutical**

Product: [18]F-fluoro-2-deoxyglucose (FDG)
Nuclide: Fluorine-18

Dosage/activity: Dependent on the system, time per bed position and the patient's weight
Administration: Intravenous
Synthesis and quality control: In accordance with the European Pharmacopoeia

**7. Radiation safety**

1. The radiation dose of FDG PET/CT is the combination of the radiation exposure from the radiopharmaceutical (Table 1) and the CT study. The radiation dose of a diagnostic CT is a matter of concern, particularly for paediatric investigations. The mean dose for a CT scan depends on applications, protocols and CT systems. Especially in children but also in adults it is important to optimize the radiation exposure with respect to the diagnostic question. Recent advances in technology have allowed the radiation doses to be significantly reduced relative to a conventional CT or PET.

| | Adult | 15 years | 10 years | 5 years | 1 year |
|---|---|---|---|---|---|
| **Recommended administered activity at nominal weight (MBq)** | See section 7 | 302 | 189 | 120 | 70 |
| **Nominal weight (kg)** | - | 55 | 32 | 19 | 10 |
| **Organ receiving highest dose** | Bladder | Bladder | Bladder | Bladder | Bladder |
| **Absorbed dose per unit activity at voiding interval (mGy/MBq)** | $1{,}3\times10^{-1}$ | $1{,}6\times10^{-1}$ | $2{,}5\times10^{-1}$ | $3{,}4\times10^{-1}$ | $4{,}7\times10^{-1}$ |
| **Voiding interval (h)** | 3,5 | 3,5 | 3,5 | 3,0 | 2,0 |
| **Effective dose (mSv/MBq)** | $1{,}9\times10^{-2}$ | $2{,}4\times10^{-2}$ | $3{,}7\times10^{-2}$ | $5{,}6\times10^{-2}$ | $9{,}5\times10^{-2}$ |

*Table 1*. Radiation dosimetry for FDG

2. The coefficient for effective dose from FDG in adults is $1{,}9\times10^{-2}$ mSv/MBq according to ICRP publication 106, i.e. about 3,5 mSv for an administered activity of 185 MBq. The radiation exposure related to a CT scan carried out as part of an FDG PET/CT study depends on the intended use of the CT study and may differ from patient to patient: the CT scan can be a very low-dose scan (with lower tube voltage and current) for attenuation correction only, or as a low-dose or intermediate-dose scan for attenuation correction and localization of PET lesions, or additionally a diagnostic CT scan can be indicated (in most cases with intravenous contrast agent administration and deep inspiration for chest CT) for a full diagnostic CT examination. The effective CT dose ranges from 1 to 20 mSv and may be even higher for a static high resolution diagnostic CT. Given the variety of CT systems and protocols, the

radiation exposure for an FDG PET/CT study should be estimated specifically for a given imaging system and protocol. Guidelines provided by European radiological societies should be consulted regarding effective dose from the CT.

3. The choice of imaging protocol strongly depends on the clinical question and must be considered for every single case. Paediatric studies require special attention. For the optimization of FDG PET/CT studies, dose reduction techniques should be considered.

*Pregnancy (suspected or confirmed)*

For any diagnostic procedure in a female patient known or suspected to be pregnant, a clinical decision is necessary in which the benefits are weighed against the possible harm. The International Commission on Radiological Protection (ICRP) reports that for an adult patient the administration of 259 MBq (7 mCi) of FDG results in an absorbed radiation dose of 4,7 mGy to the non-gravid uterus (i.e. $1{,}8\times10^{-2}$ mGy/MBq). Direct measurements of FDG uptake in a case study suggested somewhat higher doses than are currently provided in standard models. A pregnancy test may help with the decision, provided the 10-day post-ovulation blackout is understood.

In the event of doubt and in the absence of an emergency, the 10-day rule should be adopted. In Europe, national guidelines may apply.

*Breastfeeding*

The ICRP does not recommend interruption of breastfeeding after FDG administration since little FDG is excreted in the milk. However, as the lactating breast accumulates FDG, it is suggested that contact between mother and child be limited for 12 h after injection of FDG to reduce the radiation dose that the infant receives from external exposure to radiation emitted by the mother. It is recommended that the infant be breastfed just before injection, to maximize the time between the injection and the next feed. Breast milk may be expressed and fed to the infant via a bottle for 12 h to help minimize the interruption in close, prolonged contact between the infant and the mother.

**8. Patient preparation/essentials for procedure**

*Recommendations for FDG administered activity*

The minimum recommended administered FDG activity and PET acquisition duration for each bed position must be adjusted so that the product of the FDG activity and PET acquisition duration is equal to or greater than the specifications set out below. Therefore, one may decide to apply a higher activity and reduce the duration of the study or, preferably, to use a reduced activity and increase the study duration, thereby keeping ALARA principles in mind as well. In these guidelines two recommendations are provided for determining the minimum FDG administered dose in adults, which assume a linear and a quadratic relationship, respectively, between PET acquisition time per bed position, patient weight and recommended FDG activity. Compared with linear activity prescription, the quadratic scheme results in a slightly higher administered activity for patients >75 kg; this compensates for the lower signal to noise ratio (and hence degraded image quality) due to excessive attenuation, which occurs when linear activity prescription is applied.

The following specifications are given when imaging sites prefer the use of a linear relationship for pragmatic reasons (minimum acceptable administered activity recommendation):

1. For systems that apply a PET bed overlap of ≤30%, the minimum recommended administered activity is calculated as follows:
   FDG (MBq)=14 (MBq·min·bed-1·kg-1) × patient weight (kg)/emission acquisition duration per bed position (min·bed-1).
2. For systems that apply a PET bed overlap of >30%, the minimum FDG administered activity is calculated as follows:
   FDG (MBq)=7 (MBq·min·bed-1·kg-1) × patient weight (kg)/emission acquisition duration per bed position (min·bed-1).

*Alternative:* This alternative includes using a quadratic relationship between recommended administered FDG activity, weight and duration of emission acquisition. In this case use the above equations to determine the administered activity for a 75 kg patient. Next, multiply this activity by the square of the patient weight/75. This will provide the minimum administered activity.

1. For systems that apply a PET bed overlap of ≤30%, the minimum administered FDG activity is calculated as follows:
   FDG (MBq)=1,050 (MBq·min·bed-1·kg-2) × (patient weight (kg)/75)2/emission acquisition duration per bed position (min·bed-1).
2. For systems that apply a PET bed overlap of >30%, the minimum FDG activity is calculated as follows:
   FDG (MBq)=525 (MBq·min·bed-1·kg-2) × (patient weight (kg)/75)2/emission acquisition duration per bed position (min·bed-1).

Specific notes and pitfalls to be considered:

- An exploratory further optimization is presently being evaluated by EARL. This procedure would allow lowering the administered FDG activity for PET/CT systems with higher sensitivity or improved performance using new enhanced technology (e.g. better time-offlight performance, continuous bed motion or extended axial FOV, i.e. length of bed position). A prerequisite is that imaging sites first obtain EARL accreditation for that system and subsequently follow the instructions provided by the standard operating procedure (SOP) "EARL procedure for assessing PET/CTsystem specific patient FDG activity preparations for quantitative FDG PET/CT studies".
- A short emission acquisition duration per bed position could also be balanced by a higher administered FDG activity.
- For patients weighing more than 90 kg, increasing the emission acquisition time per bed position rather than increasing the administered FDG activity is recommended to improve image quality. Literature suggests that FDG activities higher than 530 MBq for patients above 90 kg should not be applied for L(Y)SO systems.
- A maximum administered FDG activity may be imposed by national law. If this is the case, increasing the emission acquisition time should be pursued to keep administered FDG activity within legal limits.
- If the PET acquisition duration for each bed position can be set separately, then the acquisition duration per bed position may be further reduced by up to 50% for bed positions outside the thorax and abdomen (i.e. at the level of the head, neck and legs) because overall attenuation in these body regions is lower. The FDG activity must still be calculated assuming the acquisition duration per bed position as used for bed positions at the level of the thorax and abdomen. Systems with continuous motion functionality may increase motion speed twofold outside the thoracic and abdominal regions.

- In all cases the administered FDG activity should not result in activities within the FOV that exceed the peak count rate capability of the PET/CT system in use. The Patient preparation and precautions emission acquisition duration should then be increased to keep image quality within acceptable limits.

For children and adolescents, administered FDG activity should adhere to the EANM or SNMMI recommendations on paediatric radiopharmaceutical administration or national activity limits, if national limits are lower. Furthermore, there are specific guidelines for FDG PET/CT in paediatric oncology.

*Patient preparation and precautions*

The main purpose of patient preparation is to reduce tracer uptake in normal tissue (kidneys, bladder, skeletal muscle, myocardium, brown fat) while maintaining and optimizing tracer uptake in the target structures (tumour tissue) and keeping patient radiation exposure levels as low as reasonably possible (ALARA). A generally applicable protocol is outlined below.

*Instructions to patients*

Non-diabetic patients should not consume any food or liquids other than plain (unflavoured) water for at least 4 h prior to the start of the FDG PET/CT study (i.e. with respect to the time of injection of FDG). In practice, this means that patients scheduled to undergo the FDG PET/CT study in the morning should not eat after midnight and preferably should have only a light meal (no alcohol and only a small amount of carbohydrates) during the evening prior to the FDG PET/CT study. Those scheduled for an afternoon FDG PET/CT study may have a light breakfast at least 4 h prior to the time of their PET/CT appointment.

Medication

*Medication can be taken as prescribed.*

1. Adequate pre-hydration is important to ensure a sufficiently low concentration of FDG in the urine (fewer artefacts) and for radiation safety reasons. For example, consumption of 1 l of water during the 2 h prior to injection is suggested. Where necessary, account for the volume of water in oral contrast agent if it is to be given for a diagnostic CT scan.
2. Coffee or caffeinated beverages are not recommended because even if "sugarless" they may contain traces of simple carbohydrates and have the potential to induce excitant effects; this may also be the case for "sugar-free" beverages.
3. Parenteral nutrition and intravenous fluids containing glucose should be discontinued at least 4 h before the time of FDG injection. In addition, the infusion used to administer intravenous pre-hydration must not contain glucose.
4. During the injection of FDG and the subsequent uptake phase, the patient should remain seated or recumbent and silent (this is particularly true for head and neck cancer patients) to minimize FDG uptake in muscles.
5. The patient should be kept warm starting 30-60 min before the injection of FDG and continuing throughout the subsequent uptake period and examination to minimize FDG accumulation in brown fat (especially relevant in winter or if the room is air-conditioned).
6. Patients must avoid strenuous exercise for at least 6 h before the FDG PET/CT study, and preferably for 24 h.

7. Patients should void their bladder immediately prior to the PET/CT to reduce urinary bladder activity.
8. The patient should be able to lie still in the PET/CT system for the duration of the examination (20-45 min). A specific inquiry about claustrophobia at the time the patient is scheduled for the study may decrease the number of non-diagnostic studies and cancellations, and allow premedication planning.
9. If possible, the patient should put his/her arms above the head; proper supporting devices (e.g. foam pallets) provided by the manufacturers should be employed whenever feasible.
10. When a diagnostic contrast-enhanced CT examination with intravenous contrast agent is to be performed, specific indications must be followed (see below).

*Serum glucose level before FDG administration:*

1. The main objectives of patient preparation with at least 4 h of fasting are to ensure low blood glucose and low insulinaemia, as insulin is directly responsible for glucose uptake by non-tumour cells. Although efforts should be made to decrease blood glucose to normal levels (typically 4-7 mmol/l) and insulinaemia to low levels, if the study is indicated in a patient with unstable ("brittle") or poorly controlled diabetes (often associated with infection), hyperglycaemia should not represent an absolute contraindication to the study, as fasting hyperglycaemia does not hamper the clinical value of FDG PET. Therefore we recommend the same advice and suggest recording the blood glucose level and any other information that could be relevant for interpretation of the investigation.
2. Blood glucose level must be measured prior to administering FDG. A glucose meter (or glucometer) or a similar bedside device capable of performing overall blood glucose measurements can be used for this purpose, but a blood glucose test must be performed with a calibrated and validated method if plasma glucose level is to be used for correction of SUV measurements.
3. It is good practice to check the blood glucose of the patient on arrival at the imaging centre to ensure the level is not too low (not below 4 mmol/l, about 70 mg/dl) or too high, since this may avoid an unnecessary wait.
4. For diabetic patients, it is suggested that the blood glucose level is checked upon arrival in order to initiate, if necessary, manoeuvres to lower the blood glucose level as soon as possible. Certain patients can be asked to arrive at the imaging centre earlier than usual to allow more time to correct possible hyperglycaemic situations.

*For clinical studies:*

1. If the plasma glucose level is lower than 11 mmol/l (about 200 mg/dl), the FDG PET/CT study can be performed.
2. If the plasma glucose level is higher than or equal to 11 mmol/l (about 200 mg/dl), the FDG PET/CT study should be rescheduled or the patient excluded depending on the patient's circumstances and the trial being conducted.

*For research studies:*

1. The recommended upper plasma glucose levels may range between 7 and 8,3 mmol/l (126 mg/dl and 150 mg/dl); the upper threshold should be specified in the

study protocol. Patients who fall outside the specified range of serum glucose levels are often excluded from the study, but reference should be made to the specific study protocol in reaching this decision. It should be stated whether the SUV reported is corrected for glucose and, if so, values should be given with and without glucose correction.

2. Glucose levels should be recorded and reported, to allow the calculation of glucose-corrected SUV post hoc. SUV may be reported with glucose correction although this is not common practice in many clinical centres. Note that specifically in response assessment studies, blood glucose levels may change with therapy, and it is strongly recommended that blood glucose levels be measured using validated and calibrated methods (no bedside devices) during sequential FDG PET/CT studies. There are few studies in the literature using glucose-normalized SUVs and there is no clear evidence that glucose normalization improves response monitoring or prediction of outcome as compared to uncorrected SUVs. It is also unclear whether the concept of glucose normalization is valid for malignant tumours. Glucose normalization implies that glucose metabolic rates are tightly regulated. In some malignancies with unregulated glucose metabolic rates, uncorrected SUVs can be more stable than glucose-corrected SUVs.
3. Reduction of the blood glucose level by administration of insulin can be considered, but the FDG PET/CT study should also be postponed depending on the type and route of the administration of insulin. Insulin should not be given to reduce glucose levels (this leads to greater muscle uptake of FDG) unless the interval between administration of insulin and administration of FDG is more than 4 h. The preferred route of administration is a subcutaneous injection. If insulin is administered it should be rapid-acting insulin (which reaches the bloodstream 15 min after injection, peaks at 60 min and is effective for 2-4 h). Other insulin types that are not recommended for immediate or delayed FDG PET/CT imaging are: regular or short-acting insulin (which reaches the bloodstream 30 min after injection, peaks at 2-3 h and is effective for 3-6 h), intermediate-acting insulin (effective for 12-18 h) or long-acting insulin (effective for 24 h). It is also possible to lower blood glucose in patients just above the cut off threshold by asking them to hydrate while ambulating and recheck the blood glucose periodically until an acceptable level has been achieved. Recently, intravenous administration of insulin before FDG administration has been discussed, but it has not yet been validated.

*Diabetes*

The following recommendations apply to patients with diabetes mellitus:

1. Type II diabetes mellitus (controlled by oral medication)

- The FDG PET/CT study should be performed in the late morning.
- Patients must comply with the fasting rules indicated above.
- Patients continue to take oral medication to control their blood sugar. If intravenous contrast agent is going to be administered, metformin should be discontinued at the time of the procedure and withheld for 48 h after the procedure (see below).

2. Type I diabetes mellitus and insulin-dependent type II diabetes mellitus

- Ideally, an attempt should be made to achieve normal glycaemic values prior to the FDG PET/CT study, in consultation with the patient and his/her attending medical doctor.

- There are three options for scheduling the FDG PET/CT study:

a. It can be scheduled for the late morning or midday. The patient should eat a normal breakfast by early morning (around 7:00 a.m.) and inject the normal amount of insulin. Thereafter the patient should not consume any more food or fluids, apart from the prescribed amount of water. FDG should be injected no sooner than 4 h after subcutaneous injection of rapid-acting insulin or 6 h after subcutaneous injection of short-acting insulin. FDG administration is not recommended on the same day as the injection of intermediate-acting and/or long-acting insulin.
b. It can be scheduled for the early morning. The presence of intermediate-acting insulin administered the evening before should not interfere with the PET/CT study and glycaemia will probably still be under control. If long-acting insulin was used the evening before, there could be a slight interference with the PET/CT study. Thus, if this is the preferred schedule, intermediate-acting (instead of long-acting) insulin is recommended. The patient should eat a normal breakfast after the PET/CT study and inject the normal amount of insulin.
c. In patients on continuous insulin infusion, if possible the FDG PET/CT study should be scheduled for the early morning. The insulin pump should be switched off for at least 4 h prior to FDG administration. The patient can have breakfast after the FDG PET/CT study and switch on continuous insulin infusion.

*Kidney failure*

FDG imaging can be performed in patients with kidney failure, although the image quality may be suboptimal and prone to interpretation pitfalls.

Recommendations for image optimization in specific circumstances, and extra notes

1. There is no reason for routine administration of sedatives (e.g. short-acting benzodiazepines) in adult patients. Sedatives may be considered in the case of tumours in the head and neck region to reduce muscle uptake or in claustrophobic patients. A number of agents have been tried and are being tested to reduce brown fat uptake (e.g. 5 mg of intravenous diazepam, administered 10 min prior to FDG, or 80 mg of propranolol given orally 2 h before FDG administration), but conflicting results have been reported. Patients should be instructed not to drive a car and to travel home accompanied after sedation.
2. When the patient is referred for the evaluation of a lesion in the heart or very close to the myocardium, additional dietary recommendations can be helpful. While there are many options for decreasing normal glucose uptake by the myocardium, common recommendations may include Eur J Nucl Med Mol Imaging instructions for the patient to follow a low carbohydrate diet for 24 h prior to the PET/CT study, or at least a low carbohydrate meal before starting the 6 h period of fasting before the study. The low carbohydrate diet helps switch the myocardium from using glucose as an energy source to using fatty acids, reducing the uptake of glucose by the myocardium.
3. Clinical value may be added to a whole-body or torso FDG PET/CT scan by adding a dedicated brain FDG PET/CT scan, which may be done on the same injected dose and in a single session before the whole-body or torso scan. This can be achieved in a short 5 min single field of view (FOV) head acquisition following the guidelines for acquisition and reconstruction of brain FDG PET/CT images. The technical qualities

of the brain scan as part of a whole-body FDG PET/CT scan are not sufficiently high for detailed diagnostic purposes. This pertains to resolution, voxel dimensions, signal to noise ratio, head fixation issues and possibly reconstruction algorithms. Thus, a dedicated brain FDG PET/CT scan may be added. The indications include primarily neurological or psychiatric clinical presentations, and suspected para-neoplastic disease (including limbic encephalitis). Many of these patients have a negative whole-body or torso FDG PET/CT scan, and the brain FDG PET/CT scan adds value by documenting the existence and extent of functional damage or abnormalities (regional inflammatory or epileptiform activity, defects following inflammation or from other conditions). The brain FDG PET/CT scan may help the differential diagnosis in patients in whom a tumour cannot be identified (neurodegeneration, toxic encephalopathy, primary neuro-infection). Furthermore, this strategy allows simultaneous treatment monitoring of activity in the tumour and para-neoplastic effects in the brain in tumour-positive patients.

4. Clinical experience suggests that proper hydration prevents urinary activity from causing problems in image interpretation of abdominal/pelvic tumours. If patients are properly hydrated before imaging, delayed imaging or furosemide intervention is very rarely necessary. It is noted that some centres use transurethral catheterization in this circumstance but the possible risk of urinary tract infection needs to be carefully weighed against the potential benefits of better image quality. In addition, if the pelvis is a site of particular concern, the CT may be performed first from the head to the pelvis followed by the emission acquisition in the opposite direction. This protocol minimizes the time delay between the CT and FDG imaging of the pelvis, and thus there is only minimal change in bladder volume between the two scans.
5. When a diagnostic CT scan with intravenous contrast agent enhancement is to be performed as part of the FDG PET/CT study, indications, contraindications and restrictions have to be assessed by a qualified physician. Medication that interacts with intravenous contrast agent (e.g. metformin for the treatment of diabetes) and relevant medical history (e.g. compromised renal function) should be taken into consideration:

- Renal function should be checked prior to contrast agent administration in all patients considered at risk of contrast agent nephrotoxicity. Routine creatinine testing prior to contrast agent administration is not necessary in all patients; the major indications are age over 60 years, pre-existing renal disease or impairment (including dialysis, kidney transplant, single kidney, renal cancer and renal surgery), history of diabetes mellitus, history of hypertension requiring medical therapy or use of metformin/metformin-containing drug combinations. Patients who do not have one of the above risk factors do not require a baseline serum creatinine determination before intravenous iodinated contrast agent administration. Estimated glomerular filtration rate is a better predictor of renal dysfunction than creatinine level alone. Patients with a high risk of nephrotoxicity are those with creatinine >13 mmol/l (1,5 mg/dl) and/or glomerular filtration <60 ml/min. If renal function assessment is required, a creatinine level and estimated glomerular filtration rate within the preceding 4 weeks is sufficient in most clinical settings, although it seems prudent to shorten this interval for inpatients and those with a new or heightened risk factor of renal dysfunction.

- Metformin is an oral hypoglycaemic agent. If intravenous contrast agent is going to be administered, metformin should be discontinued at the time of the procedure and withheld for 48 h after the procedure. If the risk of nephrotoxicity is high, metformin can be reinstituted only after renal function has been re-evaluated and found to be normal. If the risk of nephrotoxicity is low, metformin can be reinstituted without the need for renal function assessment. An alternative glucose-controlling drug should be considered during this time.
- The risk factors for contrast agent-induced nephropathy must be considered. The more important ones include: pre-existing renal insufficiency, diabetes mellitus, dehydration or volume depletion, concurrent nephrotoxic drugs, high dose of contrast agent, age greater than 70 years and cardiovascular disease. Patients with normal renal function are at very low risk of contrast agent-induced nephropathy. Recommendations for preventing contrast agent-induced nephropathy in patients at risk include: adequate hydration, administration of N-acetylcysteine, waiting at least 72 h between studies with contrast agent and use of iso-osmolar contrast agent. Discontinuing diuretics, non-steroidal anti-inflammatory agents and aminoglycosides may also decrease the risk of contrast agent-induced renal failure.
- Risk factors for adverse reactions to contrast agent must be assessed. A previous reaction to contrast agent is the most important of all the risk factors. Adverse reactions are classified as either idiosyncratic (anaphylactoid) or non-idiosyncratic. Life-threatening reactions are rare. Premedication reduces the risk of recurrent anaphylaxis, but in patients with a history of a severe reaction, an unenhanced CT is preferred.
- For CT imaging of the abdomen or pelvis, an intraluminal gastrointestinal contrast agent may be administered to improve visualization of the gastrointestinal tract on CT (unless it is not necessary for the clinical indication or it is medically contraindicated). Contrast agents must only be used in accordance with the recommendations given in section 7. Nowadays, water or water-based contrast agents are often used as an intraluminal contrast agent that provides improved image quality with reduced artefact. Water can be an effective contrast agent allowing better or equal distention in the bowel and better or equal diagnostic clarity compared with routine barium contrast agent.
- Some patients have difficulties such as claustrophobia, dyspnoea or inability to lie still for the duration of the scan. These patients should be carefully evaluated and an effort made to solve the problem with minimum consequences for the patient and the quality of the scan; sometimes, however, a solution cannot be found even if the study is repeated or rescheduled for another day. Occasionally sedatives can be of help in patients suffering claustrophobia. These issues should be noted in order to avoid potential pitfalls and to facilitate interpretation of suboptimal scans.

**9. Acquisition and processing**

*PET acquisition protocol*

1. Axial anatomical scan coverage: For most oncology indications, covering the base of the skull to the mid-thigh is sufficient. A longer scanning trajectory of the whole body may be used if appropriate. Extended whole body investigations are performed in patients with tumours that show a high probability of metastases in the head, skull, brain and lower extremities. In patients with tumours with a high risk of head

and brain metastasis but not metastasis in the lower extremities (e.g. lung cancer), it may be appropriate to perform an extended torso FDG PET/CT scan including the brain in the same scan. Limited-view tumour imaging can be considered for follow-up examinations if the disease is restricted to a defined region (e.g. solitary pulmonary nodule, suspicion of lung cancer, examination of hilar lymph nodes, head and neck tumours, assessment of therapy response). If limited-view imaging is performed in the setting of a longitudinal study, the FDG uptake time of the lesion being studied should be the same (to within 5 min) across all longitudinal imaging studies in the same patient.

2. Generally, the patient should be positioned with the arms elevated and supported above the head to avoid beam hardening artefacts in the abdominal and pelvic regions as well as artefacts caused by truncation of the measured FOV. If the patient is not able to keep the arms elevated above the head, one arm can be kept above the head with the other positioned alongside the body, or both arms can be positioned alongside and close to the body. Either way, every attempt should be made to avoid CT truncation. When using systems with extended CT FOVs, the arms may be positioned alongside the body to enhance patient comfort provided CT truncation is avoided. For examination of head and neck tumours a two-step protocol may be helpful:
    1. Head and neck portion with the arms down, then
    2. Apex of the lung through the mid-thigh with the arms up.
3. If the FDG PET/CT data are used for radiation planning, the investigation should be performed in the position used for radiotherapy treatment, employing the same dedicated positioning devices as are used in the radiotherapy department (e.g. the same radiotherapy table top, laser alignment, Eur J Nucl Med Mol Imaging immobilization devices and measures). These guidelines consider static acquisitions only. Radiotherapy planning may increasingly require respiratory gating, too, but this is not covered in the present guidelines.
4. When dedicated brain imaging is indicated:
    - Patient preparation should be as for brain scan
    - Arms down, head fixed in a head holder
    - CT topogram of head, followed by
    - Low-dose CT scan, followed by
    - Single FOV PET acquisition, 5 min acquisition 45-50 min after injection with injected doses of 300-400 MBq. If the suspected underlying indication for the brain scan is probably not cancer-related (dementia, etc.), the emission scan can be acquired earlier, up to 30 min after injection. However, identical time frames must be used for the same indications to render the results comparable. Arms down followed by one of the protocols described in the next section (CT protocols for the FDG PET/CT study). Brain image reconstruction performed independently for body scan following guidelines.
5. In general, FDG PET/CT is performed using a protocol comprising a scanogram/ scout scan/topogram and a low dose CT scan for attenuation correction (CT-AC) and anatomical correlation.
6. The CT-AC scan should be performed while the patient continues tidal or shallow breathing. In the case of CT systems with six or fewer rings, a protocol using breath

hold in normal expiration should be considered for the duration of scanning the thorax and upper abdomen.

7. A standard diagnostic CT scan with intravenous contrast agent may, if appropriate, be performed. Several strategies for performing PET/CT studies that include diagnostic CT imaging are provided in detail below.
8. Images should be reviewed before the patient leaves the department to ensure that the investigation is technically satisfactory (i.e. that the clinical question can be addressed properly) and to assess any need for additional imaging or urgent contact with the referring physician.
9. Online random correction should be based on the 'delayed coincidence time window' technique or random correction using a model based on (block) singles count rates.
10. During patient registration with the PET/CT system, users should carefully enter all information into the PET/CT console correctly. This includes, but may not be limited to, patient height and body weight, radiopharmaceutical and the net activity administered. Also the assay activity (i.e. FDG activity) and assay time (i.e. activity calibration time) should be noted and reported. In addition, the time of injection (usually not equal to the assay time or activity calibration time) should be noted and reported. If this information cannot be entered into the PET/CT system, it should be reported in the patient or scan report file.
11. Decay correction must be 'on' (see also section PET image reconstruction). CT protocols for the FDG PET/CT study
12. CT imaging within the framework of FDG PET/CT studies typically consists of a topogram and a single or multiple helical CT scans.
13. CT acquisition parameters (e.g. tube current, voltage, slice thickness, rotation time and pitch) should be chosen with regard to the objective of the CT investigation (e.g. attenuation and scatter correction, co-localization of radiologically equivalent interpretation). Specific local or national dose limits may apply for these types of CTsand should always be adhered to. Overall, CT scan parameters should be chosen such that patient exposure is minimized yet dose is adequate to obtain the necessary diagnostic information.
14. Ultra low-dose CT scans are now being introduced on some PET/CT systems, often in combination with iterative reconstruction methods (as discussed below), which may be applied to further reduce CT radiation dose.
15. For a diagnostic, contrast-enhanced CT scan, standard CT settings as suggested by related guidelines and the supervising radiologist or responsible physician should be employed. Modulation of the tube current is encouraged in the absence of metallic implants (e.g. orthopaedic braces) in the co-axial imaging range to lower patient exposure. Depending on the clinical question, intravenous and/or oral contrast agents may be employed. It might be appropriate to perform a diagnostic CT scan for particular regions of the body, followed by a low-dose CT scan of the rest of the body for CT attenuation correction and co-localization. In some instances, it might be preferable to begin with a low-dose CT scan of the body and then decide to add a diagnostic CT scan of a particular region, as the findings on the low-dose CT scan may influence the need for a contrast-enhanced or higher resolution regional view.
16. High intravenous or intestinal concentrations of contrast agent may cause artefacts in the reconstructed PET images following CT attenuation correction and thus

affect quantification. The impact of intravenous contrast agents on the accuracy of attenuation correction is considered acceptable when CT data are collected in the equilibrium or venous phase (i.e. delayed acquisition) and in some centres a contrast-enhanced CT scan only is performed, although uptake in reference regions such as the mediastinum and liver may be affected.

17. Arterial phase CT acquisitions should be avoided. In FDG PET/CT studies without the need for advanced quantification, intravenous contrast agents may be used directly (i.e. the CT scan can also be used for attenuation correction) during the FDG PET/CT study because the impact on visual image quality and interpretation is modest. However, deep inspiration for chest CT acquisition will cause a large degree of misregistration and may introduce unacceptable artefacts if the low-dose CT scan (with normal breathing) is replaced by such a diagnostic deep inspiration CT scan.
18. Deep inspiration chest CT scans should not be used for attenuation correction when PET quantification is required or intended. Therefore, for attenuation correction, the PET study ideally should be combined with a low-dose CT scan obtained during tidal or shallow breathing or with a contrast-enhanced CT scan obtained during tidal or shallow breathing (as described below).
19. The presence of a positive contrast agent (intravenous or oral) may minimally affect the CT attenuation map and, therefore, may affect SUV quantification. If this were the only aspect to be taken into consideration, the ideal would be to prohibit CT contrast agent administration. However, in some clinical situations (depending upon tumour type, tumour behaviour or level of anatomical interest), the benefit of CT contrast agents may outweigh the small errors induced in SUV measurement, which may include increased SUV variability. Each protocol should specify the desired approach for the given study. Most importantly, in the same subject, the same approach should be followed at all subsequent imaging time points. In the case of longitudinal studies in which a diagnostic contrast-enhanced CT scan may not be indicated in all PET/CT studies, strategies 1, 2a and 2b, as indicated below, should be followed.
20. If the FDG PET/CT study is performed with the purpose of quantitatively assessing FDG uptake and a diagnostic CT scan is required, the following PET and CT acquisition sequences or strategies should be followed, as indicated in the UPICT Oncology FDG PET/CT protocol and the FDG PET/CT QIBA profile:

    • *Strategy 1:*

    When CT is used for attenuation correction and localization only (not intended as a clinically diagnostic CT scan): CT topogram, followed by Low-dose CT scan, followed by PET acquisition

    • *Strategy 2:*

    When a contrast-enhanced diagnostic CT scan is also needed, one of the following options must be used:

    • *Strategy 2a:* (recommended as it avoids any, albeit possibly minimal, impact of intravenous contrast enhancement on attenuation correction and therefore SUV determination):

    Follow strategy 1

    Acquire an additional intravenous contrast-enhanced diagnostic CT scan with breathing instructions, if needed.

- *Strategy 2b:* Perform an intravenous contrast-enhanced diagnostic CT scan with breathing instruction, if needed.

  Follow strategy 1 with a delay of at least 60 sec to allow contrast agent to dilute over the body/blood pool.

21. In the case of protocols or scanning strategies that can be used in clinical practice, i.e. when there is no need for or intention to perform SUV-based quantification, the diagnostic CT scan with intravenous contrast agent may be used for attenuation correction. If contrast-enhanced CT is used for attenuation correction it may alter SUV quantification (<10% on average). Therefore, the strategies below are for image interpretation based on visual (uptake) assessment only. FDG PET/CT studies performed with the intention of assessing FDG uptake quantitatively should follow the recommendations given above (strategy 1, 2a or 2b). A deep-inspiration thoracic CT scan with a 20 sec delay from the beginning of contrast agent infusion can be included as it will provide additional information. However, this CT scan is used neither for attenuation correction nor for PET/CT image fusion, but rather to assess the lung parenchyma with thinner slices (2,5 mm), which is very useful for comparison with previous and/or future studies, and also allows evaluation of thoracic vessels.

    - *Strategy 3 (low-dose CT scan):*

    CT topogram, followed by a deep-inspiration thoracic CT scan with a 20 sec delay from the beginning of the contrast agent infusion (this CT scan is used neither for attenuation correction nor for PET/CT image fusion). Then followed by a whole-body low-dose CT scan (with shallow or tidal breathing) with a 45 sec delay after the thoracic CT scan (equilibrium or venous phase) if the thoracic CT scan was performed or with a 60 sec delay after the beginning of contrast agent infusion if the thoracic CT was not performed, followed by PET acquisition.

    - *Strategy 4 (diagnostic CT scan):*

    CT topogram, followed by a deep-inspiration thoracic CT scan with a 20 sec delay from the beginning of contrast agent infusion (this CT scan is used neither for attenuation correction nor for PET/CT image fusion), followed by A whole-body diagnostic CT scan (with shallow breathing) with a 45 sec delay after the thoracic CT scan (equilibrium or venous phase) if the thoracic CT scan was performed, or with a 60 sec delay after the beginning of contrast agent infusion if the thoracic CT scan was not performed, followed by PET acquisition.

22. Other specific protocols can be applied depending on the tumour type and the clinical indication.
23. Intravenous contrast agent is ideally administered with a programmable fluid injector at a speed of 2,5 ml/s for a catheter of 20 G×1,16″ if located in the antecubital fossa. If the catheter is placed elsewhere, the diameter of the catheter and/or the speed of infusion and delay may need to be adjusted.
24. Oral contrast agents allow better delineation of the gastrointestinal tract. A positive contrast agent (for example diluted barium) as well as a negative or water-based contrast agent (for example water or locust bean gum) can be used. High intraluminal concentrations of barium or iodinated contrast agents can cause an attenuation correction artefact in PET images, resulting in an overestimation of FDG accumulation at those sites. These artefacts can be avoided by using a negative contrast agent.

However, administration of water only as a negative intraluminal contrast agent itself is associated with fast reabsorption and can cause increased nonspecific FDG accumulation in the bowel. If quantification of the FDG PET/CT studies is required, the use of diluted positive contrast agents only, is recommended. The concentration of diluted positive contrast agents should be low enough to guarantee absence of attenuation correction artefacts, and this should be verified for each combination of PET/CT system, PET/CT image reconstruction software and contrast agent being used.

25. It should be ensured that the patient is lying within the CT-AC FOV and in the same position as during the PET acquisition. If the system is equipped with extended FOV capabilities this option should be used to avoid CT truncation.
26. Metal implants can cause severe artefacts on the CT image. Metal artefact reduction techniques may be used to minimize these artefacts. When the CT data are used for attenuation correction of the PET data, it should be considered that even when using metal artefact reduction techniques, metal implants will likely result in reduced PET image quality and will prevent proper quantification (at and near the metal implant). FDG uptake should be confirmed by inspecting the PET images without attenuation correction.

Pitfalls

1. In most PET/CT systems today, the measured FOV of the CT scanner is smaller than that of the PET scanner. Truncating the CT images causes reconstruction artefacts and thus inaccurate quantification of the PET study. When available, truncation correction algorithms may be applied during image reconstruction (and/or during processing of the CT data used for attenuation correction). As the amount of truncation may vary across studies and subjects, it will be difficult to ensure proper quantification across studies and subjects. It is, therefore, strongly recommended that any truncation of the CT images is avoided. If available, the use of extended CT and PET FOVs is recommended. It should be noted that truncation of the CT images may occasionally seriously affect scatter correction scaling as well, and may lead to inaccurate quantitative results.
2. Make sure that all clocks (including the dose calibrators - the one at the hospital and the one at the external laboratory dispensing the FDG - and the PET/CT system) are synchronized and that this is regularly checked. Consult the local service engineer when needed. Clocks should be synchronized with the official local time to within 1 min (in the case of studies using $^{18}$F).

Image reconstruction

*PET image reconstruction*

The PET emission data must be corrected for geometrical response and detector efficiency (normalization), system dead time, random coincidences, scatter and attenuation.

1. All the corrections necessary to obtain quantitative image data should be applied during the reconstruction process.
2. During image reconstruction, matrix sizes and zoom factors should be chosen such that reconstructed voxel sizes are within 3,0-4,0 mm in any direction.
3. When available, time-of-flight information should be used during reconstruction.

4. Resolution modelling during reconstruction or other new reconstruction or image processing methods may be applied. In the case of multicentre studies or when quantification is required, the use of these methods typically entails additional filtering during or after image reconstruction in order to meet the standardized/harmonized quantitative PET/CT system performance specifications, as detailed below. When these multicentre standards cannot be met, these reconstruction methods and settings should not be used for quantification of FDG uptake.
5. Spatial filters applied during or after reconstruction should not exceed a full-width at half-maximum of 7 mm, not even to mitigate Gibbs artefacts when using resolution modelling. In these cases the use of reconstructed images generated without resolution modelling should be considered.

It is good clinical practice to perform reconstructions with and without attenuation correction to identify potential reconstruction artefacts caused by the CT-AC. Both attenuation corrected (AC-PET) and non-attenuation-corrected PET (NAC-PET) images should be available for interpretation and lesions seen on the AC-PET images may need to be checked on the NAC-PET images, particularly when adjacent to highly attenuating materials, such as contrast agent or metal implants. Further standardization of reconstruction settings is necessary to obtain standardized and harmonized SUV recoveries. This requires reconstruction settings to be chosen so as to achieve matching convergence and spatial resolution across various systems and sites, especially within a multicentre setting. These reconstruction settings should thus be chosen to meet the multicentre QC harmonizing specifications for both calibration QC and image quality/SUV recovery QC, for example as described on the EARL website. Indicative reconstruction settings for each system type are provided on request through the EARL website.
It may be appropriate to perform multiple PET reconstructions with different reconstruction settings. For quantitative assessment of the FDG PET/CT study, the EARL-approved reconstruction settings, which meet the standardized performance standards, should be used. An additional reconstruction designed for optimal visual assessment may be performed for qualitative interpretation only. This reconstruction may be performed, for example, in order to maximize lesion detectability or to meet local preferences for visual interpretation of the FDG PET/CT study, as was suggested and demonstrated by Lasnon et al. Similar strategies may be applied for different PET/CT systems as well, provided quantitative interpretations/analyses are performed using the EARL approved reconstruction settings.

*CT image reconstruction*

For diagnostic CT scans, acquisition parameters should be determined according to specific or national radiology society guidelines. The CT data that are acquired during the PET/CT study are usually reconstructed using filtered back projection. Recently introduced iterative reconstruction methods for CT data may be applied, if available on the PET/CT system. Depending on the CT protocol and the clinical case, separate CT reconstructions may be performed for diagnostic purposes and CT-AC. The reconstructions will probably differ in their slice thickness, slice overlap, filter etc. In addition to the reconstruction kernel that modulates the image characteristics within the slices (i.e. spatial resolution, edge enhancement and noise texture), a longitudinal filter in the z-dimension is often used to optimize the resolution in the axial direction and to modify the slice sensitivity profiles. The

measured attenuation values (μ) are normalized to the density of water (μ water) in order to assign a device-independent numerical value in the framework of the reconstruction:
CT value = Hounsfield units = 1,000(μ – μ water)/μ water
In modern CT systems the spatial resolution in the z-direction is almost as high as the trans-axial resolution and nearly isotropic, allowing high-quality images in the coronal and sagittal views. Additionally, post-processing such as volume rendering or maximum intensity projections benefit from using the high-quality reconstructed CT data.

**10. Interpretation**

Image analysis and SUV calculations FDG PET images should be displayed with and without attenuation correction. On all slices (of the attenuation corrected data) quantitative information with respect to size and FDG uptake can be retrieved. Images must be evaluated using software that is able to display fused PET and CT data and use an SUV scale. Monitors used for image viewing should be approved for clinical use in radiology and nuclear medicine. Characteristics and settings of the monitor should be in line with published standards (e.g. the Medical Electrical Safety Standards, IEC 60601-1/EN 60601-1; the Medical ECM Standards, IEC 60601-1-2, EN 60601-1-2; or national guidelines). Moreover, viewing conditions (e.g. background light) must be appropriate to ensure adequate image inspection.
Image data should be stored on an approved PACS system and in DICOM format; further details and recommendations regarding image data format can be found in the QIBA FDG PET/CT profile.
The presence or absence of abnormal FDG accumulation on the PET images, especially focal accumulation, in combination with intensity of uptake and anatomical size should be evaluated. Absence of tracer accumulation in anatomical abnormalities seen on the CT scan or other imaging may be particularly significant. When appropriate, the report should correlate PET/CT findings with those of other diagnostic tests, interpret them in that context and consider them in relation to the clinical data. For response assessment, the images should be viewed over the same dynamic grey scale or colour scale range, i.e. a fixed colour scale; for example, from SUV=0 to SUV=10 using an inverse linear scale. Both uncorrected and attenuation-corrected images may need to be reviewed to identify artefacts caused by contrast agents, metal implants and/or patient motion. In clinical trials, criteria for visual analysis should be defined a priori within the study protocol.
SUV is increasingly used in clinical studies in addition to visual assessments. SUV is a measurement of the uptake in a tumour normalized on the basis of a distribution volume. Most of the published literature relates to SUV (normalized to body weight) measurements. SUV normalized to lean body mass (LBM) is referred to as SUL, and is a recommended quantitative measure of FDG uptake. SUL should preferably be calculated alongside SUV, as follows:
SUL = Act VOI (kBq/ml)/Act administered (MBq)/LBM (kg)
The following calculation is applied in the case of plasma glucose correction:
SUL glu = Act VOI (kBq/ml) × Gluc plasma (mmol/l)/Act administered (MBq)/LBM (kg) × 5,0 (mmol/l) where Act VOI is the activity concentration measured in the volume of interest (VOI) and Act administered is the net administered activity corrected for the physical decay of FDG to the start of acquisition and corrected for the residual activity in the syringe and/or administration lines and system. LBM is calculated according to the

formula of Janmahasatian et al.: LBMM = 9,270 × weight/(6,680 + 216×BMI) LBMF = 9,270 × weight/(8,780 + 244 × BMI) where LBMM and LBMF are the LBM for males and females, and BMI is body mass index (weight/height2), and weight and height are in kilograms and centimetres, respectively.
These formulas are clearly more realistic than the previously used James formulas, which fail at weights greater than about 120 kg. Patient height, weight and sex should be reported to allow other SUV normalizations, such as weight and body surface area. In these cases LBM is replaced by body weight and body surface area, respectively, in the SUL equations given above. The use of SUL is preferred for response assessment studies when large changes in body weight may occur during the course of the treatment. As stated above, plasma glucose levels should be measured using validated methodology and SUL should be calculated with and without plasma glucose correction in all response monitoring studies. Note that the measured glucose content (Gluc plasma) is normalized for an overall population average of 5,0 mmol/l so that the SULs with and without correction for glucose content (SUL glu and SUL, respectively) are numerically practically identical (on average).

*Physiological FDG distribution and interpretation criteria*
Accumulation of FDG can normally be seen in the brain, heart, kidneys and urinary tract at 60 min after injection. The brain has a high uptake of FDG (about 7 % of injected activity). The myocardium in a typical fasting state primarily uses free fatty acids, but after glucose load it uses glucose. In the fasting state, FDG uptake in the myocardium should be low, but this is variable. Unlike glucose, FDG is excreted by the kidneys into the urine and accumulates in the urinary tract. There is some degree of $^{18}$F-FDG accumulation in muscles that can be increased by serum insulin or following exercise. Uptake in the gastrointestinal tract varies from patient to patient and may be increased, for example, in patients taking metformin. Uptake is common in lymphoid tissue in Waldeyer's ring and in the lymphoid tissue of the terminal ileum and caecum. Physiological thymic uptake may be present, especially in children and young adults. Uptake in brown adipose tissue may be observed more commonly in young patients and when the ambient temperature is low. No physiological uptake is noted in bone itself (unless free $^{18}$F-fluoride is present as a contaminant), but bone marrow uptake can be present to a variable degree in patients receiving growth factors (granulocyte colony-stimulating factor, GCSF, and granulocyte macrophage CSF, GM-CSF) as well as in patients with marrow proliferation for other reasons such as infection, inflammation or anaemia, and following chemotherapy.

1. Due to the high physiological FDG uptake in the brain, FDG PET/CT is of limited value for detection of brain metastases. Consequently, FDG PET/CT is generally not used for the primary detection or exclusion of brain metastases.
2. Increased FDG uptake is observed in many neoplastic lesions, granulation tissue (e.g. wound healing), infections and other inflammatory processes. A detailed description of pitfalls and situations that can lead to false-positive (benign processes that can show FDG uptake) or false negative FDG PET/CT interpretation has been published.
3. Patterns of FDG uptake, established CT morphological criteria and correlation with patient history, physical examination and other imaging modalities may be helpful for differentiation between malignant and benign lesions.

4. SUVs and related quantitative measures, such as metabolic tumour volume (MTV) and total lesion glycolysis (TLG), have gained increasing importance for therapy response monitoring and for prognostic assessment.
5. There is no single lower limit of the intensity of FDG uptake for the detection of abnormal uptake within lesions as it depends on the degree of contrast between the tumour and its immediate surroundings. This contrast is related to several pathophysiological factors, the most significant of which are histology (FDG avidity of the type of tumour), volume of vital tumour cells, movement during static acquisition (e.g. blurred signals in the case of pulmonary foci) and physiologically high uptake in adjacent background. Furthermore, the sensitivity of FDG PET/CT may be reduced in diabetic patients with elevated glucose levels.
6. Although there are no conclusive data on the optimum interval between chemotherapy and FDG PET/CT, an interval of at least 10 days between the last treatment and the FDG PET/CT is generally considered adequate for measurement of response. This is because of the balance between any possible effects on tumour metabolism (such as macrophage impairment) and systemic effects (such as bone marrow activation following bone marrow depression, which may or may not be caused by growth factors). If an interval of 10 days is not possible, FDG PET/CT should be delayed as long as possible after the previous chemotherapy administration (i.e. until as close as possible to the next treatment cycle).
7. The effects of growth factors (G-CSF and GM-CSF) on FDG biodistribution (due to enhanced bone marrow uptake) generally last for more than 2 weeks after the final administration.
8. It is assumed that the (side) effects of radiotherapy are longer-lasting; investigation of patients with head and neck carcinoma treated with radiation has shown that radiation-induced inflammation can be seen on the FDG PET/CT images for 2-3 months after the end of treatment. Waiting 2 or 3 months following completion of radiation therapy before obtaining a PET/CT scan is clinically appropriate as patients rarely develop clinical problems in the first 3 months after treatment.
9. In patients who have undergone surgery, uptake depends on the extent of surgery, the presence of infection/inflammation in the wound, and how long after surgery images are acquired. For example, there are few visible signs of a mediastinoscopy after 10 days but sternotomy signs will remain visible for months. Following surgery, it is recommended that the FDG PET/CT be delayed for at least 6 weeks due to postsurgical inflammation, if the scan is primarily being done to assess the surgical field.
10. FDG PET/CT for diagnostic purposes is generally assessed using visual criteria, looking for focally increased uptake that may represent malignancy in the appropriate clinical context. It is unclear how SUV can contribute to patient assessment, partly because of the considerable variability in the methodology used. However, this document and several others propose harmonized quantitative FDG PET/CT imaging procedures in multicentre studies and harmonized quantitative interpretation criteria to assess treatment response

**11. Report**

The report is the main mode of communication between the physician interpreting the

imaging study and the referring physician, and it frequently leads to relevant changes in patient management. The SNMMI has recently published reporting recommendations for oncological FDG PET/CT imaging.

*Direct communication*
Abnormalities of immediate clinical importance should be directly or verbally communicated to the appropriate healthcare provider if a delay in treatment might result in significant morbidity. An example of such an abnormality would be a lesion with a high risk of pathological fracture. Other clinically significant unexpected findings should also be communicated verbally. Reporting of abnormalities requiring urgent attention should be consistent with the policy of the interpreting physician's local organization.

*Written communication*
Written documentation of verbal reporting should be made in the medical record, usually as part of the PET/CT report.

*Contents of the report*
1. Study identification
   The report should include the full name of the patient, medical record number and date of birth. The protocol name of the investigation should also be included, as well as the date and time of its performance. The electronic medical record usually provides these data, as well as a unique study number.
2. Clinical information
   At a minimum, the clinical history should include age, sex, weight, height, reason for referral and the specific question to be answered. If known, the diagnosis and a brief treatment history should be provided. The results of relevant diagnostic tests and prior imaging findings should be summarized. Information relevant for reimbursement should also be included.
3. Procedure description
   The type and date of comparison studies should be stated. If no comparison studies are available, a statement should be made to that effect.
   Blood glucose level before FDG administration should be documented.
   Study-specific information should include the radiopharmaceutical, the amount of injected activity in megabecquerels and/or millicuries, the route of administration (intravenous) and the date and time of administration. The anatomical site of administration is optional, but should be recorded. The name, dose and route of administration of regulated non-radioactive drugs and agents should also be stated. The type of PET/CT system should be specified, but specific equipment information is optional.
   A description of the procedure should include the time the patient was scanned or the time interval between administration of FDG and the start time of the acquisition. The part of the body that was covered should be described from the start to the end point. The position of the patient (supine or prone) and the position of the arms (elevated or to the sides) should be stated if non-standard.
   Description of the CT part of the investigation may be limited to a statement that a low-mAs CT was performed for attenuation correction and anatomical registration of

the emission images. However, findings should be reported. If the CT was optimized for diagnosis, then a more complete description of the CT protocol and anatomical findings should be provided. Dosimetric parameters should be included as required by regulations; here, DICOM structured reports may facilitate the extraction of the relevant dose information. The report should state whether CT with or without CT contrast agent was used for CT attenuation correction.

Routine processing parameters are usually not stated in the report, but any special circumstances requiring additional processing, such as motion correction, should be described.

4. Description of the findings

It is good practice to provide a structured report with concise concluding statements intended to answer the specific clinical question(s) posed, if possible. Nevertheless, there is great variation in the style of reporting. Recommendations with regard to biopsy, alternative radiological studies and follow up should also be included in the conclusion as appropriate. The interpretation provided by an imaging physician is the chief manifestation of the physician's expertise. Its content affects patient management and clinical outcomes, and it is also a legal document.

- The quality of the FDG PET/CT study, e.g. limited due to motion artefacts, abnormal biodistribution of tracer (FDG accumulation in muscles and/or brown adipose tissue), infiltration of tracer at the injection site or hyperglycaemia. CT-related artefacts should also be mentioned such as metallic artefacts and other information on large patient body habitus when the quality of the study is affected.
- A description of the location, the extent and the intensity (SUV and/or SUL) of pathological FDG accumulation related to normal tissue.
- A description of relevant findings on CT and their relationship to pathological FDG accumulation. FDG uptake may be reported as mild, moderate or intense and compared to the background uptake in, for example, the liver parenchyma (mean SUV 2,0-3,0; maximum SUV 3,0-4,0). However, criteria for visual interpretation need to be defined for each study protocol and may vary according to the type of cancer and for different tumour locations. Some criteria have already been proposed. Incidental FDG PET and CT findings should be included in the report, particularly if they are of clinical relevance.
- The CT part of the FDG PET/CT report must describe all relevant anatomical findings (some of which may be FDG PET-negative).
- Limitations: If necessary, confounding factors that might influence the sensitivity or specificity of the FDG PET/CT study may be mentioned such as small lesions (partial volume effect), inflammatory changes, muscle activity, high blood glucose levels at the time of injection, para-vascular infiltration of FDG or tissue injections.
- Clinical context: In the body of the report it can occasionally be helpful to address the findings of the study with respect to the clinical questions asked. However, this is more commonly done in the report Summary/Impression. Any interpretation or summary in the body of the report should also be repeated in the report Summary/ Impression.
- Complementary information: Comparison to previous investigations should be

part of the FDG PET/CT report. FDG PET/CT studies are more valuable if they are interpreted in the context of other imaging studies (CT, PET/CT, MRI etc.) and clinical data.

- Assessment of response to therapy: If an FDG PET/CT study is performed in the context of the assessment of response to therapy, the extent and the intensity of the FDG uptake should be documented and compared to prior measurements, if available. Examples of criteria for therapy response with FDG as a metabolic biomarker have been suggested by The European Organisation for Research and Treatment of Cancer. In 2009, Wahl et al. suggested the so-called PERCIST criteria for assessing solid tumour response. Furthermore, a five point scale has been proposed for assessment of lymphoma therapy response. Reporting of the change in intensity of the FDG uptake using semi-quantitative parameters – expressed as absolute or relative change – can be used for specific dedicated clinical questions. At present, relative changes in SUV during therapy represent the most robust parameters. The reliability of the results reported will depend on having comparable patient preparation, injection and scanning protocols, as well as comparable data analysis.

5. Summary and diagnosis/impression
   - Clearly identify the study as normal or abnormal.
   - The question asked in the study request should be directly addressed.
   - If possible, a definite diagnosis should be stated. Whenever possible this should provide a staging assessment (TNM or other) stating whether there are categories of uncertainty. Alternatively, a qualitative estimate of the likelihood of a diagnosis and the differential diagnoses should be given.
   - If appropriate, repeat investigations and/or additional investigations should be recommended to clarify or confirm findings.
   - For therapy evaluation, serial studies should be compared, using visual and/or semi-quantitative assessment as appropriate.
   - Document the communication of urgent or emergency findings to referring physicians or their deputy.
6. Additional notes

   The Royal College of Radiologists provides recommendations on reporting that include relevant aspects that should be taken into account:

- Limitations of staging: Every diagnostic test has a threshold. The threshold used may vary depending on the implications for treatment (to optimize diagnostic accuracy or according to treatment intent).

  Indeterminate lesions and management of uncertainty:

- Indeterminate lesions should be the point of clinical–radiological discussion and/or multidisciplinary review, if better characterization of the lesion will further affect patient management. The options for resolving uncertainties are discussion, further investigation, intervention and active monitoring (watch and wait).
- Multidisciplinary team meetings: Multidisciplinary team meetings allow a team approach to patient management to take into account and evaluate all aspects of the disease prior to individualized therapy planning. It should be possible to review all relevant investigations in a multidisciplinary meeting, especially when there is a discrepancy between clinical and imaging findings or other diagnostic uncertainty.

During the meetings, the results of the discussions should be recorded, and discrepancies noted and, if necessary, reported as an addendum to the imaging report. If additional tests are needed, these should be scheduled as soon as possible. The presence of a reporting radiologist or nuclear medicine specialist is essential.

- Imaging the treated patient or follow-up studies: The format of the report should mirror the one at baseline. Reports of follow-up studies must include clear statements regarding the detection of new disease as this implies metabolic progression of disease. Also, descriptions on the direction of change, indeterminate lesions and mixed responses and findings at variance with one another that may reflect different pathologies should be stated. For further reading see also the SNMMI's reporting guidance for oncological FDG PET/CT imaging, the Royal College of Radiologists' recommendations on reporting and the SNMMI's Procedure Standard for General Imaging.

**12. Literature**


- These guidelines have been adopted and adapted from the EHM procedure guidelines:
- Boellaard R, Delgado-Bolton R, Oyen WJG et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0, Eur J Nucl Med Mol Imaging 2015;42(2):328-54 DOI 10.1007/s00259-014-2961-x.
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