Specific Preparations for ^{18}F-FDG-PET/CT in Critically Ill Patients on Intensive Care Units

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1. Introduction

Critically ill patients, e.g. those from the Intensive Care Unit (ICU), generally show a different ^{18}F-FDG-distribution pattern than other patients. Most ICU patients experience a metabolic crisis, in which hyperglycaemia is a major problem. This affects ^{18}F-FDG metabolism and leads to an altered physiological distribution of ^{18}F-FDG. Other variables, such as use of sedatives and blood lactate level, also influence the physiological distribution of ^{18}F-FDG in critically ill patients. Apart from this, it is often a logistical challenge to organize an ^{18}F-FDG-PET scan for these patients. Many problems can be addressed to attain an adequate investigation, due to co-operation between the intensivist and the nuclear medicine physician. In doing so, the nuclear medicine physician needs a clear protocol and must recognize the physiological changes that occur in a critically ill patient.

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

- Fever of unknown origin
- Continuing fever while on (adequate) antibiotic treatment
- Suspicion of a malignancy or auto-immune disease
- Suspicion of recurrence of known malignancy or staging of a malignancy
- Response assessment

4. Relation to other diagnostic procedures

- Supplementary to other diagnostic tests

5. Medical information necessary for planning

- Height and weight
- Mental state: awake/sedated / comatose / vegetative state
- When sedated; which sedative used
- Feeding: normal / enteral / parenteral
- Respiratory assistance
- Use of (intravenous) insulin
- Known gastric retention
- Acidotic state / Elevated lactate
- Known malignancies / infections / auto-immune disease / Known locations

6. Radiopharmaceutical

Tracer:	^{18}F-FDG
Nuclide:	Fluorine-18
Activity:	Centre dependent; as per out-patients/ non-admitted patients.
Administration:	Intravenously (i.v.)

7. Radiation safety

- Location of ^{18}F-FDG administration: If the administration takes place outside the nuclear medicine department, adequate preparation will decrease the chance of radioactivity contamination.
- Other radiation safety procedures or contra-indications are the same as for standard ^{18}F-FDG-PET-scans.
- There are no lead-shielded compartments on an ICU. Therefore special attention should be focused on keeping distance from the patient after administration and limiting exposure time. This can be an issue with unstable patients.
- Direct contact with a patient directly after administration of the ^{18}F-FDG should be limited to a maximum of 10 min. If necessary ICU-staff should take turns to achieve this.
- The above mentioned contact limit is based upon the assumption the injected dose is 400 MBq ^{18}F-FDG intravenously. Applied biologic clearance, physical half-life and biological half-life of ^{18}F-FDG are according to de ICRP publication 106.

8. Patient preparation/essentials for procedure

Fasting:

Normal preparation:

- Normal food intake: At least 4-6 h of fasting before ^{18}F-FDG injection.
- Enteral feeding: At least 4-6 h of fasting.
- Parenteral feeding: At least 4-6 h of fasting.

Please note that insulin administration should be stopped or minimised when patients are in a fasting state.

No glucose-infusion for patient support during fasting.

Carbohydrate free diet:

- For suspected myocardial involvement or thoracic pathology, in order to diminish the myocardial ^{18}F-FDG uptake. Advice can vary per centre. We advise 12 h of a carbohydrate free diet followed by 12 h of fasting.
- For enteral feeding and parenteral feeding consult treating intensivist or dietician.
- If your centre has carbohydrate free enteral or parenteral feed available, a carbohydrate free diet can be followed. We advise 12 h of a carbohydrate free diet followed by 12 h of fasting.
- If your centre has no carbohydrate free enteral or parenteral feed available, we advise at least 18-24 h of fasting.
- Additionally an intravenous bolus injection of heparin 50 units/kg can be administered 15 min prior to ^{18}F-FDG administration for better myocardial suppression.
- When gastric retention is present, consider a longer period of fasting in patients with a normal eating pattern or enteral feeding.

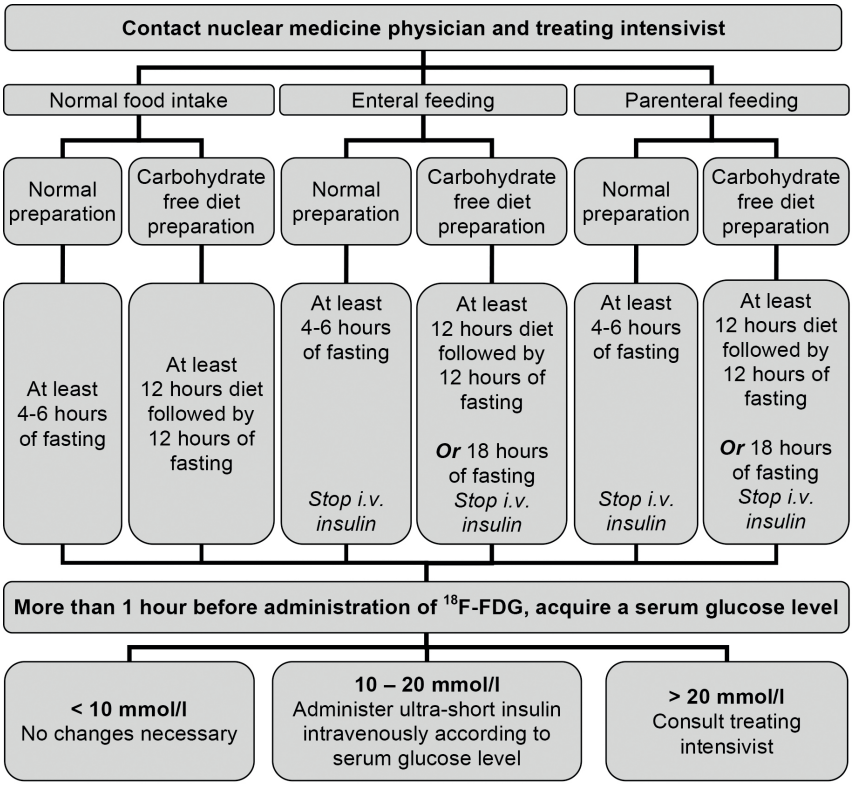
Hyperglycaemia:

* As commonly known, hyperglycaemia decreases ^{18}F-FDG-PET sensitivity. Regulating glucose levels in a critically ill patient is challenging and extra attention is needed for ensuring an adequate level before ^{18}F-FDG administration. Several studies show an adequate scan quality in 75-95% of hyperglycaemic patients after intravenous administration of short acting insulin, at least 60 min before ^{18}F-FDG administration. An interval of less than 60 min between i.v. insulin and ^{18}F-FDG administration results in increased muscle and liver uptake, leading to poor scan quality and decreased sensitivity.

- Most ICU's cease metformin and subcutaneous insulin injections upon admission, for better glucose regulation with intravenous insulin. Confirm this with your hospital ICU.
- 1 h before FDG-administration acquire a serum glucose level. If necessary, at this moment a bolus injection of intravenous ultra-short insulin (USI) can be administered. USI available in the Netherlands are insulin aspart (Novorapid®), insulin lispor (Humalog®) or insulin glulisine (Apidra®). According to the serum glucose level, a last bolus of USI can be given to patients without known insulin resistance:
    - <10 mmol/l; no change necessary
    - 10-12 mmol/l: 2 units of i.v. USI
    - 12-14 mmol/l: 3 units of i.v. USI
    - 14-16 mmol/l: 4 units of i.v. USI
    - 16-18 mmol/l: 5 units of i.v. USI
    - 18-20 mmol/l: 6 units of i.v. USI
    - >20 mmol/l: consult treating intensivist. Will a higher USI administration induce an adequate drop in serum glucose level? Is the treating intensivist willing and confident to administer a higher dose?
    - Patients with type 2 Diabetes Mellitus may require higher doses, this should be established on a patient to patient basis.

- Check serum glucose level right before ^{18}F-FDG administration. When the serum glucose level is >20 moll/l, consider cancelling the examination.
- ^{18}F-FDG-administration at least 60 min after additional bolus injection with USI.

9. Flowchart



Attention: flowchart does not include the additional heparin bolus of 50 units/kg 15 minutes prior to ^{18}FDG-administration in the carbohydrate free diet preparation.

10. Acquisition and processing

Acquisition:

- Acquisition from head to toes is advised.
- Acquisition 50-70 min after ^{18}F-FDG administration is advised.
- Preparation on ICU; confirm sufficient length of tubing and wires for acquisition.
- Preparation on ICU; empty urinary catheter or bladder before scan.
- Patient positioning should facilitate an acquisition without putting strain on tubing or wires.

Reconstruction parameters are the same as for to other ^{18}F-FDG-PET protocols. No additional reconstructions are needed.

11. Interpretation/pitfalls

Brain and myocardial metabolism:

*Sedatives: Use of sedatives may influence the physiological distribution of ^{18}F-FDG. Table 1 shows the results of different studies. Apart from brain and myocardial ^{18}F-FDG

uptake, the effect of sedatives on tumour uptake or physiological organ uptake has not been described.

Table 1. Effect of sedatives on ^{18}F-FDG distribution

Type	Sedative	Brain	Myocardium
GABA-A-receptor-antagonists	Propofol	+	+
	Propofol + isoflurane*	-	+
	Isoflurane	- 28%	+ 91%
Benzodiazepines	Diazepam	-	NA
NDMA-receptor-antagonists	Ketamine	+	NA
	Ketamine + xylazine	- 39%	- 64%
	Ketamine + diazepam	-	NA
	Tiletamine + zolazepam	-	-
Barbiturates	Pentobarbital	≈/-	NA
	Thiopental**	- 50%	NA

*Legend: Percentages are presented, when available. + = increased ^{18}F-FDG-uptake; - = decreased ^{18}F-FDG-uptake; NA = not available; *effect of isoflurane is greater than propofol, **Higher tumour-to-background ratio in 3 neuro-oncological patients.*

*Comatose patients and patients in vegetative state: Global brain activity is decreased due to decreased neuron stimulation, which in turn leads to decreased ^{18}F-FDG uptake. Literature describes a decrease of ± 45% in comatose patients, a decrease of 49% in patients in a vegetative state and a decrease of 65% in patients in a prolonged vegetative state, compared to patients who are awake.

Hyperlactataemia:
*Quantified by dynamic PET; the balance between glucose and lactate is 90%:10% in an euglycaemic state. In a patient with hyperlactataemia, brain metabolism prefers lactate over glucose, which leads to a decrease in ^{18}F-FDG-uptake in the brain. Several studies (mainly animal studies) have investigated this phenomenon. The contribution of lactate in brain metabolism can rise up to 40%, quantified by dynamic PET. In ^{18}F-FDG-PET scanning this could lead to decreased uptake in de brain.
*Hyper-Warburgism: This phenomenon is currently only described in patients with lymphoma. Tumour cells prefer anaerobic glucose metabolism which has lactic acid as end product. In extreme cases this phenomenon leads to excessive glucose consumption and excessive lactate production. Lactate is not further metabolised by the tumour cell

and is released into the blood pool. Due to the extreme competition, the brain "protects" itself by switching to lactate-metabolism (as described above). On ^{18}F-FDG-PET a decreased brain uptake and extensive increased tumour uptake is seen.

12. Report

- Applied preparation; period of fasting, carbohydrate free diet
- Tracer and administered activity
- Administration location
- Glucose level at time of administration
- Interval between USI and administration of FDG and number of units administered
- Interval between administration and scan
- Scanned area (head to toe, etc.)
- If appropriate: sedative used, comatose patient or patient in vegetative state.

13 Literature

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