

¹⁸F-FDG PET/CT in Inflammation and Infection Detection

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Preamble:

This guideline complements the guideline for the use of ¹⁸F-FDG in oncology. To avoid duplication, this guideline will not reproduce any statements that overlap. These include information concerning camera performance and quality control, general acquisition parameters, radiopharmaceutical control and acceptance and general and clinical aspects that may apply to both tumour and infection/inflammation imaging.

1. Introduction

¹⁸F-FDG is a glucose analogue which is taken up by living cells via cell membrane glucose transporters and subsequently phosphorylated with hexokinase inside most cells. ¹⁸F-FDG has been proposed for imaging infection/inflammation because it has been seen at sites of infection/inflammation during routine ¹⁸F-FDG imaging of cancer patients. Further studies showed that cells involved in infection and inflammation, especially neutrophils and the monocyte/macrophage family, are able to express high levels of glucose transporters, especially GLUT1 and GLUT3, and increased hexokinase activity.

The use of ¹⁸F-FDG imaging in inflammation and infection is rapidly evolving. Therefore, the indications mentioned within this guideline should be regarded as current advice and areas for clinical research rather than as fully approved clinical indications. Despite the limited literature available on the use of ¹⁸F-FDG for this indication, it can be expected that after further validation, this tracer will become a first-line tool for non-oncological indications.

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

Major indications:

- a. Sarcoidosis
- b. Peripheral bone osteomyelitis (non-postoperative, non-diabetic foot)
- c. Suspected spinal infection (spondylodiscitis or vertebral osteomyelitis, non-postoperative)
- d. Evaluation of fever of unknown origin (FUO), including true FUO (defined according to the criteria of Durack and Street), postoperative fever and recurrent sepsis, immunodeficiency (both induced and acquired) related FUO, neutropenic fever, and isolated acute-phase inflammatory markers
- e. Evaluation of metastatic infection and of high-risk patients with bacteraemia
- f. Suspicion of endocarditis
- g. Primary evaluation of vasculitides (e.g. giant cell arteritis)
- h. Therapy follow-up in all above mentioned indications

Other well-described applications, but without sufficient evidence-base for formal indication:

- a. Evaluation of potentially infected liver and kidney cysts in polycystic disease
- b. Evaluation of vascular prosthesis infections
- c. Suspected infection of intravascular devices, pacemakers, and catheters
- d. AIDS-associated opportunistic infections, associated tumours, and Castleman's disease
- e. Assessment of metabolic activity in tuberculosis lesions
- f. Assessment of organ involvement in fungal infections
- g. Therapy follow-up in above mentioned indications

To date, it is unclear if ¹⁸F-FDG imaging offers any significant advantage over radiolabeled white blood cell imaging in the following indications:

- a. Diabetic foot infections
- b. Joint prosthesis infections
- c. Inflammatory bowel diseases

4. Relation to other diagnostic procedures

Depending on the above mentioned indications, radiological techniques, such as ultrasound, CT and MRI play an important role, complemented by radionuclide imaging procedures.

5. Medical information necessary for planning

- a. Probability of an infection (low or high) and expected location
- b. Symptoms and signs
- c. Fever and inflammatory parameters: ESR, CRP
- d. Results of other relevant recently performed diagnostic imaging methods
- e. Recent trauma, surgery or recent invasive diagnostic procedures (within the last 4 weeks)
- f. Past medical history, including malignancy, recent chemotherapy or radiation therapy
- g. Immunosuppressive status of the patient
- h. Presence of joint prosthesis and date of insertion
- i. Presence of vascular graft, date of insertion and type of graft
- j. Presence of other foreign material
- k. Use of antibiotics, steroids and NSAIDs

6. Radiopharmaceutical

Tracer: ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG)

Nuclide: fluorine-18

Activity: depends on scanner used, patient age and body weight

Administration: intravenous injection

7. Radiation safety

See guideline for use of ¹⁸F-FDG in oncology. According to ICRP 106 there is no need to interrupt breastfeeding.

8. Patient preparation/essentials for procedure

- a. See guideline for use of ¹⁸F-FDG in oncology.
- b. It has been advocated that high serum glucose levels may interfere with the targeting of inflammatory and infectious sites due to competitive inhibition of ¹⁸F-FDG uptake by D-glucose. However, recent studies demonstrated that neither diabetes nor hyperglycemia at the time of the study have a significant impact on the false-negative rate in infection and inflammation imaging. This in contrast to tumour imaging, for which reduced uptake has been observed. Although efforts should be made to decrease blood glucose to a normal level if the study is indicated in those with usually unstable or poorly controlled diabetes, hyperglycaemia should not represent an absolute contraindication for performing the study.
- c. Delaying the commencement of steroid treatment till after the scan is strongly recommended. If this is not possible or if the patient is already under steroid treatment then scan under the lowest amount possible. The use of steroid treatment can result in a false-negative scan, especially in giant cell arteritis and other systemic vasculitides.
- d. Because the effect of antibiotics on ¹⁸F-FDG uptake is unknown, it is important to be aware of ongoing antibiotic treatment, but no general recommendation on withdrawal can be stated.

9. Acquisition and processing

See guideline for use of ¹⁸F-FDG in oncology.

10. Interpretation

Visual analysis:

- a. PET images are visually analysed by looking for increased ¹⁸F-FDG uptake, taking into consideration the pattern (focal, linear, diffuse), intensity, and relationship to areas of physiologic distribution. PET information is of course compared with morphological information obtained by CT.
- b. Carefully look at the presence of potential causes of false-negative results (lesion size, low metabolic rate, hyperglycaemia, lesions masked by adjacent high physiological uptake, concomitant drug use interfering with uptake, such as ongoing steroid therapy) and potential causes of false-positive results (injection artefacts, contamination, reconstruction artefacts from attenuation correction, pathological uptake not related to infection or inflammation).
- c. Care should also be taken in the interpretation of PET data corrected for attenuation using a low-dose CT scan (particularly when metallic material or implants are present). Assessment of both attenuation-corrected and non-attenuation-corrected images is recommended.

Semi-quantitative analysis

In contrast to the use in oncology, the SUV has not been validated in inflammation and infection. Therefore, the SUV should be used with caution in clinical practice.

There are no general criteria published for inflammatory and infectious disorders. Most research articles have defined interpretation criteria for the purposes of the study. Some authors have reported specific interpretation criteria that can be used, although no definitive consensus has been agreed upon.

11. Report

Significant findings should be addressed in a logical manner, grouped by significance or described by body regions. For important ¹⁸F-FDG findings, the location, extent, and intensity of abnormal uptake should be described, as well as the relevant morphological CT findings. Limitations should be addressed. Where appropriate, factors that can limit the sensitivity and specificity of the examination should be identified. In patients with known cancer, being evaluated for an episode of fever, try to separate uptake within a site of cancer from uptake in a site of inflammation or infection.

Possible sources of error include small lesions, low-grade infections, physiological uptake along exogenous material (i.e. an aseptic reaction to a foreign body, such as that associated with a vascular graft), artefacts (in particular, those related to overcorrection of attenuation after contrast injection or due to metallic implants, devices, and prosthesis), physiological uptake of ¹⁸F-FDG, treatment-related uptake and aseptic inflammatory reactive uptake (lymph node uptake in sterile arthritis, reactive lymph nodes in HIV-positive patients, atherosclerotic plaques, bone fractures, granulation tissue etc.).

Issues requiring further clarification:

Controversy still remains with regards to the role of ¹⁸F-FDG in infection and inflammation in the presence of artefacts caused by metallic implants and prostheses and the added value of SUV in improving the diagnostic accuracy of reporting. Strategies to differentiate infection from sterile inflammation (e.g. in vascular graft infections) need to be developed. The utility of ¹⁸F-FDG in monitoring response to anti-inflammatory, antibacterial and antifungal therapy should be further investigated.

12. Literature

- Jamar F, Buscombe J, Chiti A, Christian PE, Delbeke D, Donohoe KJ, Israel O, Martin-Comin J, Signore A. EANM/SNMMI guideline for ¹⁸F-FDG use in inflammation and infection. *J Nucl Med* 2013;54:647-58.
- Rabkin Z, Israel O, Keidar Z. Do hyperglycemia and diabetes affect the incidence of false-negative ¹⁸F-FDG PET/CT studies in patients evaluated for infection or inflammation and cancer? A comparative analysis. *J Nucl Med* 2010;51:1015-20.
- Gotthardt M, Bleeker-Rovers CP, Boerman OC, Oyen WJ. Imaging of inflammation by PET, conventional scintigraphy, and other imaging techniques. *J Nucl Med* 2010;51:1937-49.
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