# Whole body [$^{18}$F]fluorodeoxyglucose positron emission tomography imaging for the diagnosis of pacemaker or implantable cardioverter defibrillator infection: a preliminary prospective study

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## Abstract

We studied the potential use of [$^{18}$F]fluorodeoxyglucose ($^{18}$F-FDG) whole body positron emission tomography (PET)–computed tomography for the diagnosis of device infection and extension of infection. Twenty-one patients with suspected device infection were prospectively included and compared with 14 controls free of infection. $^{18}$F-FDG uptake on the box and on the leads was visually and quantitatively interpreted (using the maximal standard uptake value). The final diagnosis was obtained either from bacteriological data after device culture ($n$ = 11) or by a 6-month follow-up according to modified Duke's criteria ($n$ = 10). Ten patients finally showed infection on bacteriological study ($n$ = 8) or during follow-up ($n$ = 2). Sensitivity, specificity, positive predictive value and negative predictive value were, respectively, 80%, 100%, 100% and 84.6% on patient-based analysis (presence or absence of infection). They were 100%, 100%, 100% and 100% for boxes, but only 60%, 100%, 100% and 73% for leads. Quantitative analysis could be useful for boxes but not for leads, for which the presence of a mild hot spot was the best criterion of infection. The four false negatives on leads received antibiotics for longer than the six true positives (20 ± 7.2 vs. 3.2 ± 2.3 days, p <0.01). Although the study was not designed for this purpose, management could have been modified by PET results in six of 21 patients. $^{18}$F-FDG PET imaging may be useful for the diagnosis of device infection, and could impact on clinical management. Interpretation of negative cases should be performed with caution if patients have received antibiotics.

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## Introduction

After pacemaker (PM) or implantable cardioverter-defibrillator (ICD) implantation, device infection of box and/or leads, although rare (0.5–5%, according to the most recent series, giving an average of 2%) [1,2], is a feared and serious complication, leading to combined double antibiotherapy with complete extraction of the material before discussion of secondary re-implantation.

A positive diagnosis of box infection (or, more precisely, infection of the pocket in which the box is implanted) may be clinically suspected in cases of external suppuration, but usually requires bacteriological samples to demonstrate septicaemia, associated with transthoracic echocardiography (TTE) and transoesophageal echocardiography (TEE) to confirm images suggestive of vegetation on leads.

However, even when vegetation is demonstrated, differential diagnosis between infection and thrombus may be difficult [3]. Furthermore, infection staging and identification of other septic locations may be very important in order to monitor treatment efficacy before any re-implantation.

Inflammatory cells have a high affinity for [$^{18}$F]fluorodeoxyglucose ($^{18}$F-FDG), which explains the use of $^{18}$F-FDG positron emission tomography (PET) imaging in pathological processes that involve lymphocytes, plasmocytes and or/macrophage infiltration [4–9]. Although neutrophils are the hallmark of prosthetic infection, $^{18}$F-FDG uptake of mononuclear cells has been used for the diagnosis of infection such

as prosthetic infection [4–6], tuberculosis [7] or vascular prothesis [9]. Therefore, whole body $^{18}$F-FDG PET imaging could be useful for the diagnosis of device infection. Nevertheless, $^{18}$F-FDG PET imaging is not free of potential pitfalls. First, the mechanical rubbing of the box against muscles and/or soft tissue may lead to mild inflammation, and falsely increase both $^{18}$F-FDG uptake and as electrical stimulation of surrounding muscles owing to electrical leakage from the box. Second, in the case of infection, the size of the leads (1.5–3 mm in diameter) and of the vegetation might be below the PET–computed tomography (CT) spatial resolution (7 mm), impairing interobserver reproducibility and diagnostic accuracy if $^{18}$F-FDG uptake is not very high.

The present study aimed: (i) to prospectively evaluate the use of $^{18}$F-FDG PET-CT whole body imaging in patients suspected of having sepsis after PM or ICD implantation for positive diagnosis of infection and identification of other septic locations; (ii) to define the best methodology for image analysis (i.e. visual or quantitative interpretation); and (iii) to assess interobserver reproducibility.

To quantify $^{18}$F-FDG update and determine abnormal threshold values, a control population was prospectively selected, consisting of asymptomatic patients referred to our institution for oncological indications and undergoing PM or ICD implantation at least 1 year before PET study, with stable disease and without any clinical or biological symptoms of infection.

## Materials and Methods

### Population: group 1

All patients suspected of having device infection were consecutively included from 8 August 2007 to 15 September 2009. Device sepsis was clinically suspected because of: (i) unexplained persistent or recurrent fever >38°C, and/or (ii) chronic inflammatory syndrome with increased C-reactive protein, and/or (iii) positive blood culture independently of the TTE and TEE results, and/or (iv) clinical suspicion of pocket infection on the basis of inflammation and/or liquid effusion. Consent was obtained from all patients before examination, although $^{18}$F-FDG-PET has approval in France for location of occult infection or in cases of fever of unknown origin. These patients constituted group 1. Analysis was independent of sex, age, reason for implantation, date of implantation and device type.

### Control group: group 2

In the same time period, 14 patients with asymptomatic implanted PM, referred for PET-CT imaging in our institution for oncological purposes, were prospectively included. Patients were selected independently of sex, age and reason for implantation. Clinical and biological infectious syndrome was an exclusion criterion, but did not, in fact, occur in this group.

### Final diagnosis

The decision on device extraction was made without taking account of PET results. However, in the case of other septic locations being discovered on PET, this information was transmitted to the clinician. The final diagnosis of presence or absence of infection was based either on bacteriology (blood culture or device analysis performed after device extraction) or, when no device was extracted, on a prolonged follow-up of 6 months with modified Duke's criteria [10]. Patients with clinical suspicion of device infection and presenting infectious endocarditis according to these criteria were considered to be positive for device infection. Diagnosis was ruled out if clinical symptoms and/or biological abnormalities returned to normal during this follow-up without fulfilling the modified Duke's criteria; if not, and if no other aetiology was found, device extraction was decided on.

### $^{18}$F-FDG PET acquisition

Whole body PET-CT imaging was performed on a dedicated Philips Gemini PET/CT system (Philips Medical Systems, Andover, MA, USA) after intravenous administration of 5 MBq/kg of $^{18}$F-FDG (maximum, 500 MBq) in patients at rest, after an 8-h fasting period. PET-CT imaging was performed 1 h after $^{18}$F-FDG injection, with scanning from the base of the skull to above knee level. The CT acquisition parameters were as follows: 4-mm-thick transaxial images; pitch, 1.5; 120 kV and 120–160 mAs; slice thickness, 5 mm with rebuilding in 2-mm slices every 2 mm; pitch, 1; collimation, 16 × 1.5; standard resolution; and field of view, 600 mm. No oral or intravenous contrast was used. PET data were acquired in three-dimensional mode, at 2 min per step. Non-attenuation-corrected slices, slices corrected for attenuation by an iterative method (three-dimensional high-resolution Row Action Maximum Likelihood Algorithm) and a CT attenuation map were reconstructed. The native PET slice thickness was 4 mm. Glycaemia was controlled at the time of the study, and was <9 mM in all consecutive patients, even though glycaemia was not a criterion for patient exclusion.

### Data management

*Visual analysis.* Data for both groups were first visually analysed by two independent observers, blind to the clinical and