Procedural recommendations of cardiac PET/CT imaging: standardization in inflammatory-, infective-, infiltrative-, and innervation- (4Is) related cardiovascular diseases: a joint collaboration of the EACVI and the EANM: summary

Riemer H.J.A. Slart 1,2*, Andor W.J.M. Glaudemans 1, Olivier Gheysens 3, Mark Lubberink 4, Tanja Kero 4,5, Marc R. Dweck 6, Gilbert Habib 7,8, Oliver Gaemperli 9, Antti Saraste 10,11, Alessia Gimelli 12, Panagiotis Georgoulis 13, Hein J. Verberne 14, Jan Bucerius 15, Christoph Rischpler 16, Fabien Hyafil 17,18, and Paola A. Erba 1,19,20; 4Is Cardiovascular Imaging: a joint initiative of the European Association of Cardiovascular Imaging (EACVI) and the European Association of Nuclear Medicine (EANM)

1Medical Imaging Centre, Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, Groningen, The Netherlands; 2Faculty of Science and Technology, Biomedical Photonic Imaging, University of Twente, Enschede, The Netherlands; 3Department of Nuclear Medicine, Cliniques Universitaires Saint-Luc, Brussels, Belgium; 4Department of Surgical Sciences/Radiology, Uppsala University, Uppsala, Sweden; 5Medical Imaging Centre, Uppsala University Hospital, Uppsala, Sweden; 6British Heart Foundation Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, UK; 7Cardiology Department, APHM, La Timone Hospital, Marseille, France; 8Aix Marseille Université, IRD, APHM, MIP, IHU Méditerranée Infection, Marseille, France; 9HeartClinic, Hirslanden Hospital Zurich, Zurich, Switzerland; 10Turku PET Centre, Turku University Hospital, University of Turku, Turku, Finland; 11Heart Center, Turku University Hospital, Turku, Finland; 12Fondazione Toscana G. Monasterio, Pisa, Italy; 13Department of Nuclear Medicine, Faculty of Medicine, University of Thessaly, University Hospital of Larissa, Larissa, Greece; 14Department of Radiology and Nuclear Medicine, Amsterdam UMC, location AMC, University of Amsterdam, Amsterdam, The Netherlands; 15Department of Nuclear Medicine, Georg-August University Göttingen, Göttingen, Germany; 16Department of Nuclear Medicine, University Hospital Essen, University of Duisburg-Essen, Essen, Germany; 17Department of Nuclear Medicine, DMU IMAGINA, Georges-Pompidou European Hospital, F75015, Paris, France; 18University of Paris, PARCC, INSERM, F75007, Paris, France; 19Department of Nuclear Medicine, University of Pisa, Pisa, Italy; and 20Department of Translational Research and New Technology in Medicine, University of Pisa, Pisa, Italy

Received 27 September 2020; editorial decision 12 October 2020; accepted 13 October 2020

With this summarized document we share the standard for positron emission tomography (PET)/(diagnostic)computed tomography (CT) imaging procedures in cardiovascular diseases that are inflammatory, infective, infiltrative, or associated with dysfunctional innervation (4Is) as recently published in the European Journal of Nuclear Medicine and Molecular Imaging. This standard should be applied in clinical practice and integrated in clinical (multicentre) trials for optimal standardization of the procedural and interpretations. A major focus is put on procedures using [18F]-2-fluoro-2-deoxyglucose ([18F]FDG), but 4Is PET radiopharmaceuticals beyond [18F]FDG are also described in this summarized document. Whilst these novel tracers are currently mainly applied in early clinical trials, some multicentre trials are

*Corresponding author. Tel: +31 50 3611835. E-mail: r.h.j.a.slart@umcg.nl
This article is adapted from Slart, RHJA, Glaudemans, AWJM, Gheysens, O, et al. Procedural recommendations of cardiac PET/CT imaging: standardization in inflammatory-, infective-, infiltrative-, and innervation (4Is)-related cardiovascular diseases: a joint collaboration of the EACVI and the EANM. Eur J Nucl Med Mol Imaging (2020). https://doi.org/10.1007/s00259-020-05066-5
© The Author(s) 2020. Published by Oxford University Press on behalf of the European Society of Cardiology.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
Introduction

Nuclear imaging plays a pivotal role in cardiac infectious, inflammatory, infiltrative, and inflammatory disorders. Cardiac amyloidosis, sarcoidosis, large vessel vasculitis (LVV), infective endocarditis (IE), infected cardiac implantable electronic devices (CIEDs), vascular graft infection (VGI), and myocardial innervation dysfunction are the main indications for the use of nuclear medicine procedures in both diagnosis and response assessment.

Positron emission tomography/computed tomography (PET/CT) and PET/magnetic resonance (MR) imaging (MRI) are non-invasive diagnostic tools that allows detection of radiopharmaceutical accumulation in tissues with high sensitivity and provides precise quantification of their local concentration. The most commonly used tracer at present is the fluorine-18 labelled glucose analogue $[^{18}F]2$-fluoro-2-deoxyglucose ($[^{18}F]$FDG). $[^{18}F]$FDG accumulation in tissues is proportional to their glucose utilization and reflects the glucose metabolism of cells. This glucose metabolism is increased in cancer, but also in infectious and inflammatory processes. Anatomical and morphological information derived from the combination with CT (PET/CT) can be used to improve the localization, extent and characterization of lesions detected by $[^{18}F]$FDG PET. Beyond $[^{18}F]$FDG, several other PET radiopharmaceuticals are available for imaging cardiovascular diseases as described further in this document. The recently established joint cardiovascular imaging group (4Is joint collaboration group) between the European Association of Nuclear Medicine (EANM) and the European Association of Cardiovascular Imaging (EACVI) focuses on Infiltrative, Inflammatory, Infectious, and Innervation dysfunctional (4Is) cardiovascular diseases. This 4Is joint collaboration group is working on recommendations for imaging procedures in the field of 4Is cardiovascular diseases.

The purpose of this review is to assist in performing PET/CT and PET/MR for cardiovascular imaging in the field of 4Is, starting from the selection of the proper radiopharmaceutical based on the specific patients’ clinical condition and extending to the correct use of imaging acquisition protocols, post-processing, interpretation and reporting, as recently published in the European Journal of Nuclear Medicine and Molecular Imaging. Proposing a standardized imaging procedure will promote the appropriate use of PET/CT and PET/MRI in clinical practice, increase the quality of investigator driven clinical trials and allow comparison between studies thereby contributing to evidence-based medicine.

Clinical indications in cardiovascular diseases

$[^{18}F]$FDG PET/CT and PET/MR have an increasingly relevant role in inflammation and infection imaging: they are a rapidly evolving imaging modalities. However, no appropriateness criteria have been developed to date for these indication in cardiovascular diseases. It must be emphasized that the level of evidence available at this time for using PET/CT and PET/MRI with either $[^{18}F]$FDG or novel PET radiopharmaceuticals varies for many of the indications described in this document but randomized controlled trial data (as with most forms of cardiovascular imaging) are consistently lacking.

General indications for 4Is cardiovascular PET/CT include: Non-invasive diagnosis, imaging-guided biopsy diagnosis, therapy response, monitoring, and prognosis.

Radiopharmaceuticals

Most PET radiopharmaceuticals are labelled with $^{18}F$, but some are labelled with the shorter living $^{11}C$ (T1/2 20 min), or are generator-produced $^{68}Ga$ (T1/2 68 min). The most promising radiopharmaceutical developments include the application of existing tracers such as $[^{18}F]$NaF in atherosclerosis, and the use of radiolabelled compounds for detection of cardiac amyloidosis ($[^{18}F]$Florbetaben, $[^{18}F]$Florbetapir, $[^{18}F]$Flutemetamol, and $[^{18}F]$PiB). $[^{68}Ga]$DOTA conjugated peptide ($[^{68}Ga]$DOTATOC, DOTATALE, DOTANOC) compounds with affinity to SSRs, and $[^{18}F]$FLT, hold promise in detecting cardiac sarcoidosis with the advantage of having no physiological myocardial uptake which is the main disadvantage of $[^{18}F]$FDG. The $[^{18}F]$-labelled sympathetic nerve PET radiopharmaceuticals ($[^{18}F]$LMI1195 (generic name $[^{18}F]$Flubrobenguane) are promising with potential to aid clinical decision-making e.g. for optimal selection of patients requiring an implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy (Supplementary data online, S1).

PET/CT technical procedures

This background information of cardiovascular imaging in the 4Is field can be found in the main technical manuscript and Supplementary data online, S1. The technical background exists of patients’ preparation, camera acquisition, data reconstruction, and data analysis for the $[^{18}F]$FDG- and non-$[^{18}F]$FDG PET/CT procedures. Additionally, an overview is given of contrast-enhanced CT and PET/MR procedures, and PET/CT pitfalls (Supplementary data online, S2) in 4Is cardiovascular imaging.
Suppression of [18F]FDG signal in the myocardium should be evaluated. In absence of adequate myocardial suppression of the [18F]FDG signal, the compliance of the patient to the preparative procedures should be checked and this information included in the report.

General visual analysis
Data can be evaluated with commercially available software systems. Both CT-attenuation corrected and non-corrected PET images have to be evaluated in the coronal, transaxial, and sagittal planes, as well as in tridimensional maximum intensity projection (MIP) cine mode. FDG-PET images are visually analysed by assessing increased myocardial [18F]FDG uptake, taking into consideration the pattern (focal, focal on diffuse, linear, diffuse), intensity, and relationship to areas of physiologic distribution in the near surroundings. PET information should always be compared with morphologic information available on CT, including CT scans where available. It must be kept in mind that the sensitivity of [18F]FDG for infection and inflammation is not absolute and that even in the case of negative PET results, a thorough interpretation of the CT scan is essential.

General quantitative analysis (SUV)
In contrast to its use in oncology, standardized uptake value (SUV) has only been partly validated in inflammation and infection. Therefore, SUV metrics should be used with caution in clinical practice, particularly regarding the use of specific SUV cut-off values. In a [18F]FDG PET study in IE, a SUV cut-off >3.3 was suggested to avoid false-positive findings. However, extrapolation of this cut-off value to other cardiovascular disease states is difficult, in part due to differences in the underlying pathophysiology and the intensity of inflammation. Moreover, care has to be taken when extrapolating absolute SUV cut-off values acquired between different hospitals and scanners because of the variation in these values related to differences in the scanner and reconstruction methods used.

General interpretation criteria
To evaluate clinical [18F]FDG PET-CT imaging, the following should be taken into consideration:

- Clinical question
- Clinical history: fever, infection, inflammatory/auto-immune symptoms
- Prior imaging findings
- Brief treatment history, with particular regards to the presence of cardiac/vascular devices, date of implantation/extraction, surgical/post-surgical complications
- Concomitant treatment including date of initiation/withdrawal of antimicrobial therapy, steroids, statins, beta-blockers, etc.
- Biomarkers: CRP/ESR value at the time of imaging, results of blood cultures (number of positive blood culture, germ type)
- Scanning protocol (±cardiac gating, CT angiography (CTA))
- Adequate patient preparation
- Physiologic distribution of [18F]FDG, and evaluation of its individual variations in the specific patient
- Localization of abnormal uptake according to anatomic imaging data
- The presence and aspect of the [18F]FDG signal (focal/diffuse and homogeneous/heterogeneous) and persistence of PET signal on non-attenuation corrected (NAC) images. The presence of a focal, heterogeneous [18F]FDG signal that persists on NAC PET images is an imaging aspect in favour of an infectious process.
- Intensity of [18F]FDG uptake (e.g., SUVmax)
- Correlation with data from previous clinical, biochemical, and morphologic examinations
- Presence of potential causes of false-negative results (lesion size, low metabolic rate, hyperglycaemia, lesions masked by adjacent high physiologic uptake, concomitant drug use interfering with uptake, such as ongoing steroid therapy in systemic disorders)
- Presence of potential causes of false-positive results (injection artefacts and external contamination, reconstruction artefacts from attenuation correction, use of surgical glue in previous operations, normal physiologic uptake, pathologic uptake not related to infection or inflammation)

Specific scoring, interpretation and reporting criteria for 4IS disorders
Prosthetic and native valve endocarditis and cardiac devices
IE comprises native valve endocarditis (NVE) and infection of intra-cardiac prosthetic material. The latter includes prosthetic valve endocarditis (PVE, covering all types of prosthetic valves, clips, annuloplasty rings, intracardiac patches, and shunts), and IE related to CIED, which include pacemakers, ICDs, and LVADs.
Prosthetic valve endocarditis

Study indication
Suspected PVE, and/or septic embolisms, spread of infection, portal of entry (POE).

Image analysis and interpretation
The location, pattern, and intensity of the [18F]FDG signal at the valve: intra-valvular (in the leaflets), valvular (following the supporting structure of the valve) or peri-valvular (next to the valve). A peri-valvular signal is in favour of infection, but infection cannot be excluded in the presence of intra-valvular or valvular [18F]FDG signal. Focal and heterogenous uptake is consistent with an infected valve. A typical location for abscesses in PVE is the aorto-mitral trigon, but abscesses can develop in any region in contact with prosthetic material. The probability of infection increases with the intensity of the [18F]FDG signal at the valves/prosthesis. The previous use of surgical adhesives can result in false positive scan findings soon after valve surgery. Post-operative inflammation can also lead to a false positive scan, but depending on the level of risk for infection and a non-complicated valve surgery, scans <3 weeks surgery can be considered.

Several metrics have been tested to quantify the [18F]FDG signal in PVE. The easiest semiquantitative parameter to measure is the highest SUV (SUVmax) in the valvular region. Another semiquantitative parameter that has been proposed is the prosthesis to background ratio that takes into account the variability of the signal related to residual blood pool activity and image noise, by correcting valve SUV values by background activity in remote non-affected myocardium.

Whole-body [18F]FDG PET imaging is particularly useful in patients with a suspicion or proven PVE to identify septic embolism, mycotic aneurysms, and the POE.

[18F]FDG PET is less suited to detect cerebral septic embolism and mycotic aneurysms of intra-cerebral arteries owing to the high physiological uptake of [18F]FDG in the brain. In these cases, CT or MRI is the exam of choice.

Septic emboli appear as focal areas of [18F]FDG uptake and are typically located in the spleen, the liver, the lungs, and the kidneys. Uptake at the inter-vertebral disks and/or the vertebral bone (spondylodiscitis) suggests metastatic infection, which can also be observed in muscles and joints (septic arthritis). Embolic events can be clinically silent in 20% of cases, especially those affecting the spleen or brain. Septic emboli appear typically on CTA as hypodense lesions. [18F]FDG PET is more sensitive and specific than CTA for the detection of septic emboli.4,17

[18F]FDG PET imaging in IE is also useful to identify the POE. Typical portals of entry that can be identified are dental abscesses, spondylodiscitis, infected central catheters, skin infection, and colonic cancers’ polyps.5,17

In order to facilitate the interpretation of [18F]FDG PET images, we suggest classification of the [18F]FDG findings as follows:3,18,19

Typical findings
• presence of focal, heterogeneous, valvular/peri-valvular [18F]FDG uptake persisting on NAC images and corresponding to an area of suspected infection on echocardiography or CTA (mobile mass, peri-vascular thickening, aneurysm, or new peri-valvular regurgitation).
• high [18F]FDG signal in the absence of prior use of surgical adhesives.
• presence of focal [18F]FDG uptake in organs with low-background uptake consistent with septic embolism, mycotic aneurysms or the POE.

Atypical findings
• diffuse, homogeneous, valvular [18F]FDG signal that is absent on NAC images
• low [18F]FDG signal

ECG-gated cardiac FDG PET acquisitions may improve detectability of IE.20,21 In all cases correlation with clinical features echocardiography and CT findings is mandatory. In doubtful cases, white blood cell single-postion emission tomography (WBC-SPECT) can further help define the presence/absence of infection at PVE.3

In patients who present with suspected NVE, the use of [18F]FDG-PET/CT is less well established. The relatively low sensitivities of FDG PET/CT reported in the literature for evaluation of NVE can be accounted for by both physiological and technical factors.22 The more frequent presence of isolated valve vegetations, rare paravalvar involvement, lower predominance of polymorphonuclear cells, and increased fibrosis in NVE compared with PVE results in reduced inflammatory response and subsequently lower FDG uptake.23 Notably, the lower sensitivity of FDG PET/CT is offset by a near perfect specificity for detection of NVE and its unrivalled ability to identify septic emboli.22 Thus, FDG PET/CT might provide clinically useful information and beneficially impact management in a subset of patients with suspicion of NVE, and the application of gated-PET may further improve it.21 The study indication, image analysis and interpretation are in general comparable with PVE.

Infection of cardiac implantable electronic devices

Study indication
Suspected infection of CIED.
Defining the extent of infection in a proven CIED infection.
Positive blood culture in a patient with CIED.

Image analysis and interpretation
Presence and aspect of the [18F]FDG signal (focal/linear) and persistence on NAC images. The presence of a focal or linear [18F]FDG signal that is located on or alongside a lead on CT and persists on NAC images are characteristics in favour of an infectious process. Late PET acquisitions might prove particularly useful in case of persistent high blood signal on PET images acquired at 1 h p.i.

CIED infection might be confined to the leads, the pocket or involve both sites. From a clinical perspective, it is important to differentiate superficial incisional infection which does not require CIED system extraction, from infection limited to the pocket, and those extending to the leads which are commonly associated with systemic infection and/or IE.24,25 In CIED infections, the presence of [18F]FDG uptake should be described as pertinent to generator pocket (superficial or deep) and/or to the leads (intravascular or intracardiac
portion of the leads). In addition, signs of cardiac (valvular or pericar-
dial) involvement as well as systemic signs of infections (septic embol-
ism), in particular in the lung parenchyma and POE should be
carefully assessed and reported.

The presence of [18F]FDG uptake along pacing leads, in particular
in the same location as mobile elements on echocardiography and in
association with septic pulmonary emboli appearing as multiple focal
[18F]FDG spots, is highly suggestive of pacing lead infection.26 The
contrast between [18F]FDG signal along the pacing lead and residual
blood signal is usually improved with delayed PET acquisitions (3 h
p.i.).27 In addition, every positive blood culture should be carefully
evaluated and prompt active exclusion of CIED infection with other
diagnostic techniques.28

The pattern and intensity of [18F]FDG uptake should be described
considering that:

- Moderate [18F]FDG uptake in relation to post-operative residual
  inflammation can be found up to 2 months after CIED implant-
  ation but is usually of lower intensity than in case of infection.
- A focal [18F]FDG signal is often present at the point of entry of
  the lead into the subclavian vein that resembles a focal inflam-
  mation. The semi-quantitative ratio of maximum activity con-
  centrated of the pocket device over mean count rate of lung
  parenchyma26 or normalization of SUVmax around the CIEDs
  to the mean hepatic or blood pool activity 29 might help in dif-
  ferentiating mild post-operative residual inflammation up to 2
  months after device implantation vs. infection.

Table 1 Interpretation of contrast-enhanced CT scans acquired alongside PET/CT imaging in 4Is

| Disease                          | Contrast application | Advantages and scoring methods                                                                 | Comments                                                                 |
|----------------------------------|----------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Infective endocarditis and cardiac device infection | ++                   | – Visualization of abscesses                                                                  | Some imaging centres do not deem the administration of contrast medium to be mandatory. |
|                                   |                      | – Visualization of thrombi/vegetations on valves/probes                                         |                                                                         |
|                                   |                      | – Visualization of septic embolism as infarcts in terminal vessels (e.g. spleen, kidney, brain) |                                                                         |
|                                   |                      | – Detailed examination of valves (potentially important in surgical procedures)               |                                                                         |
| Cardiac sarcoidosis               | +/-                  | Superior morphological allocation of the PET signal (e.g. myocardial vs. lung uptake; organ involvement) | Contrast agent generally not required if perfusion study (PET and SPECT) is available. |
| Large vessel vasculitis           | ++                   | Visualization of the vessels to exclude relevant stenosis and score wall thickness:          | In the presence of a recent angiographic scan (CT/MRT), a low-dose CT is sufficient. |
|                                   |                      | 0 = no mural thickening                                                                        |                                                                         |
|                                   |                      | 1 = slight mural thickening                                                                    |                                                                         |
|                                   |                      | 2 = mural thickening                                                                            |                                                                         |
|                                   |                      | 3 = long and strong circumferential mural thickening OR as measurement: 2–3 mm                  |                                                                         |
| Atherosclerosis                   | +++                  | Visualization and quantification of calcium, vascular stenosis and plaque composition          | CTA is clinically recommended and aids in the interpretation of the PET scans particularly in the coronary arteries. |
|                                   |                      | – Agatston score in mainly applied for calcium burden and risk assessment in coronary artery disease |                                                                         |
|                                   |                      | – Vascular stenosis is evaluated on CTA and categorized as non-obstructive or obstructive      |                                                                         |
| Vascular graft infection          | +++                  | – Visualization of peri-graft gas and fluid.                                                    | The sensitivity and specificity of CT is moderate and variable.         |
|                                   |                      | – Aneurysm expansion/pseudo-aneurysm formation                                                 |                                                                         |
|                                   |                      | – Detailed examination of vascular graft                                                       |                                                                         |
| Cardiac amyloidosis               | -                    | – Assessment of thickness of the left ventricular myocardium                                   | Only patients with a clinical suspicion receive this specific examination (septum thickness usually already available). |

+, no contribution; +/-, some contribution; ++, good contribution; ++++, excellent contribution.
The presence and location of the signal and its persistency on NAC PET images should be described according to the signal intensity and its location. For CTA analysis and interpretation, see Table 1.

The evaluation of remote septic emboli should be performed similar to cases of PVE, but with close attention also paid to the lung parenchyma. In doubtful cases, WBC-SPECT can further help define the presence/absence of infection at PVE.3,4,28

Left ventricular assist device infection

Study indication
- Suspected infection of LVAD.
- Evaluation of the extent of infection of LVAD.
- Positive blood culture in a patient with LVAD.

Image analysis and interpretation
LVADs are generally subdivided into five regions that have to be assessed separately: driveline exit site, driveline within the subcutaneous tissues, LVAD pump, LVAD inflow cannula, and LVAD outflow cannula.

- The presence, intensity and location of the \([^{18}F]\)FDG signal across the different components of the device and the persistency of the signal on NAC images should be described.30,31
- The analysis of the FDG signal in the pump and cannula is more complex because of the artefacts caused by the device. The persistency of \([^{18}F]\)FDG uptake on NAC and its association with infiltration around the pump on the non-enhanced CT is highly suggestive of infection. In doubtful cases, WBC-SPECT can help define the presence/absence of infection of the pump and cannula.32

Infection of the driveline can be treated by re-implantation of a new driveline in another site, whereas infection of the pump and cannula usually requires long-term antibiotic therapy.

Vascular graft infection
VGI is a rare but severe complication after vascular surgery, associated with high morbidity and mortality rates.33 Early diagnosis of VGI is important for correct and early surgical and/or antibiotic treatment, which improves the outcome. Aortic graft are frequently used at the time of valve surgery, with infection of valves and grafts often co-existing.

Recently, the European Society for Vascular Surgery (ESVS), in collaboration with the EANM, published clinical practice guidelines for the care of patients with vascular graft/endograft infection.5

Study indication
Diagnosis of suspected VGI.

Image analysis and interpretation
The following aspects need to be carefully considered:

- Vascular graft uptake pattern: focal \([^{18}F]\)FDG uptake is more consistent with infection than diffuse low level activity. The exact location of the focal uptake, its distribution and intensity should be recorded as well as \([^{18}F]\)FDG uptake in regional lymph nodes.

- The intensity of \([^{18}F]\)FDG accumulation can be assessed visually using a scoring system of 0-4: Grade 0, \([^{18}F]\)FDG uptake similar to the background; Grade I, low \([^{18}F]\)FDG uptake, comparable with that by inactive muscles and fat; Grade II moderate \([^{18}F]\)FDG uptake, clearly visible and higher than the uptake by inactive muscles and fat; Grade III, strong \([^{18}F]\)FDG uptake, but distinctly less than the physiologic urinary uptake by the bladder; and Grade IV, very strong \([^{18}F]\)FDG uptake, comparable with the physiologic urinary uptake by

| Table 2 | Interpretation of combined rest perfusion and \([^{18}F]\)FDG imaging in cardiac sarcoidosis |
|---|---|
| Rest perfusion | \([^{18}F]\)FDG | Interpretation |
| Normal perfusion and metabolism | Normal | No uptake | Negative for cardiac sarcoidosis |
| Normal perfusion and metabolism | Normal | Diffuse | Diffuse (usually homogeneous) \([^{18}F]\)FDG most likely due to suboptimal patient preparation |
| Normal perfusion and metabolism | Normal | Isolated lateral wall uptake | May be a normal variant |
| Abnormal perfusion or metabolism | Normal | Focal | Could represent early disease or false positive |
| Abnormal perfusion or metabolism | Defect | No uptake | Perfusion defect represents scar from sarcoidosis or other etiology |
| Abnormal perfusion and metabolism | Defect | Focal in area of perfusion defect | Active inflammation with scar in the same location |
| Abnormal perfusion and metabolism | Defect | Focal on diffuse with focal in area of perfusion defect | Active inflammation with scar in the same location with either diffuse inflammation or suboptimal preparation |
| Abnormal perfusion and metabolism | Defect | Focal in area of normal perfusion | Presence of both inactive scar and inflammation in different segments of the myocardium or inactive scar and false positive physiological \([^{18}F]\)FDG uptake |

Adapted from Slart et al.5
the bladder. Focal uptake, with an intensity grade >II is suspected of VGI.34 However, in addition to visual assessment, [18F]FDG uptake should also be quantified with SUVmax for all arterial graft territories and normalized for background activity in the liver or blood pool usually in the caval vein. Diffuse, homogeneous and low intensity [18F]FDG uptake can be observed in the majority of non-infected vascular graft prostheses particularly shortly after surgery. This is related to the body’s response to foreign material, and should be considered to avoid misinterpretation of PET/CT studies in patients referred for suspected prosthetic infection.35

Whole-body imaging: describe remote locations in the body with abnormal increases in [18F]FDG uptake. Mycotic aneurysm appears typically as a focal [18F]FDG signal in a region corresponding to the arterial wall of the aorta or a peripheral artery, and should be confirmed with CTA.

Comparison with prior [18F]FDG PET scans: if the scan is performed to determine response to therapy, then the distribution and intensity of the signal should be compared to prior scans: increase in uptake, no change in uptake, decrease in uptake.

Abnormalities on low dose CT should also be described. For CTA analysis and interpretation, see Tables 1 and 3. In doubtful cases, WBC-SPECT can further help define the presence/absence of infection at the vascular graft.36

Cardiac sarcoidosis
The role of [18F]FDG PET for the diagnosis of extra-cardiac sarcoidosis is well established. The assessment of cardiac sarcoidosis is more complex but is now recommended for clinical use by international guidelines.6,37 Serial assessment of the inflammatory status using [18F]FDG PET might be helpful for monitoring therapy efficacy and for deciding treatment continuation, tapering or change of treatment.

Study indication
Suspicion of cardiac sarcoidosis according to the Heart Rhythm Society (HRS) guidelines.37

Monitoring of treatment in patients with established cardiac sarcoidosis.

Image analysis and interpretation
Left ventricle: uptake pattern (i—no [18F]FDG uptake, ii—diffuse [18F]FDG uptake, iii—focal [18F]FDG uptake, iv—focal on diffuse [18F]FDG uptake; exact location of the focal uptake; extent of the uptake; intensity of the uptake).

Right ventricle: uptake pattern (grades 1–4), exact location of the focal uptake, extent of the uptake, intensity of the uptake.

Combination of [18F]FDG and perfusion imaging (MPI): Perfusion defects in patients with cardiac sarcoidosis can represent areas of scar or inflammation. However, perfusion defect in combination with abnormal [18F]FDG uptake represents focal inflammation (Table 2) and can help differentiate pathological from physiological [18F]FDG activity. [18F]FDG and MPI patterns have been described as ‘early’ (only [18F]FDG-positive), ‘progressive inflammatory’ ([18F]FDG positive without major perfusion defects), ‘peak active’ (high [18F]FDG uptake with small perfusion defects), ‘progressive myocardial impairment’ (high [18F]FDG uptake with large perfusion defects), or ‘fibrosis-predominant’ ([18F]FDG negative, but with perfusion defects).5 In patients with areas of increased [18F]FDG uptake but no clear perfusion defects, this may represent either early cardiac sarcoid beyond the resolution of perfusion imaging, or false positive physiological [18F]FDG uptake.

As an alternative to MPI, [18F]FDG PET can be compared with CMR late gadolinium enhancement images. Areas of increased [18F]FDG that correspond to non-infarct areas of late gadolinium enhancement are highly suggestive of active cardiac sarcoidosis. Areas of typical late gadolinium enhancement with no [18F]FDG uptake are consistent with scarred, non-active sarcoid regions. Regions of [18F]FDG uptake without late enhancement either representing early sarcoidosis beyond the sensitivity of CMR or false positive physiological [18F]FDG activity. Myocardium with neither increased [18F]FDG nor late enhancement is considered as normal.38

Whole-body imaging: describe extra-cardiac locations with increased [18F]FDG uptake.

Comparison with prior [18F]FDG PET scan: if scan is performed in the context of assessing therapy response, then both the distribution and intensity should be compared to prior scans (increase, equal or decreased uptake).

SUV quantification can be applied in cardiac sarcoidosis diagnosis, which may provide prognostic information.39

Abnormalities on low dose or on diagnostic CT scan should be described (Table 1).

Comparison with other (hybrid) imaging modalities: cardiac (PET)/MR40 and echocardiography. CMR has limited value to assess treatment response because the majority of these patients receive intra-cardiac devices that may preclude CMR or produce artefacts when MR compatible ICD is implanted.

[68Ga]DOTA conjugated peptides maybe promising as alternative cardiac sarcoidosis, with the benefit of no physiological myocardial uptake. [68Ga]DOTA conjugated peptides can either be scored visually for intensity and distribution, or semi-quantitatively using SUVs.41

Large vessel vasculitis
LVV is defined as a disease mainly affecting the large arteries, with two major variants, Takayasu arteritis (TA) and giant cell arteritis (GCA). Vasculitis can be distributed locally in the branches of the external carotid artery or the aorta and its main branches more centrally in the thorax. Recent recommendations and statements have been provided, based on the available evidence and consensus of experts in the field, describing patient preparation, as well as [18F]FDG PET/CT(A) acquisition and interpretation for the diagnosis and follow-up of patients with suspected or diagnosed LVV.7,8

In circumstances where there may be cardiac involvement, patients with LVV should be further investigated (additional myocardial perfusion imaging, CMR, CT coronary angiography). This includes the risk of cardiovascular toxicity related to drug therapy used in LVV.9,2

Study indication
Diagnosis of LVV.

Monitoring of LVV activity.
Image analysis and interpretation

Large vessels as well as the cranial and extra-cranial arterial structures.

Uptake pattern: diffuse circumferential $[^{18}F]$FDG uptake around the vessel, that is different from the more regional and focal uptake observed in atheroma. The exact location of the uptake, its distribution across the vascular system, and its intensity (vascular scoring 0–3 against the liver) should be documented (Table 3).

Whole-body imaging: describe extra-vascular locations with increased $[^{18}F]$FDG uptake.

Comparison with prior $[^{18}F]$FDG-PET scans: if scan is performed to assess response to therapy, then extent and intensity should be compared to prior scans: increase in uptake, equal uptake, decrease in uptake.

Abnormalities on low dose CT should be described.

Comparison with other imaging modalities: echocardiography, MRI, and with specific PET amyloid compounds that have been evaluated in patients with AL and ATTR cardiac amyloidosis.

For $[^{11}C]$-PIB, $[^{18}F]$-florbetapir, $[^{18}F]$-florbetaben, and $[^{18}F]$-flutemetamol, see Supplementary data online, S1.

So far, the evidence for using clinical PET/MRI in 4Is is very limited, but some overview papers have been published in the field of cardiovascular diseases.

The 4Is-team

A multidisciplinary team approach has been proposed as the model in oncology in many hospitals and medical centres. More recently, this approach has been extended to cardiology with the successful introduction of the heart valve team for the assessment of patients being considered for transcatheter aortic valve implantation. In the field of IE, a multidisciplinary approach for evaluating patients with IE has also been introduced in order to improve management and outcome. This example can be extended to all complex disease states including the 4ls. We would therefore advocate creation of a 4ls-team of experts to improve clinical assessment of decision-making for these complex patients.

To be effective, the structure of a 4ls-Team has to be modelled on the local health systems, including cultural and socio-economic aspects. Its success is contingent upon knowledge of one’s own area of expertise as well as that of the team members, flexibility of roles, and comfort and skills in supplying and receiving interdisciplinary education. To promote effective collaboration, the team must address issues of group dynamics, including clarification of individual roles, team unity, communication, and patterns of decision-making and leadership. The clinical imager plays an active role in the teamwork programme and in the local educational planning, developing ‘capabilties’ and ‘competences’, core skills, knowledge and attitudes to facilitate inter-specialist communications. The challenge of the clinical imager within the 4ls-team is to establish a new professional
perspective: a new vision of the imager, no longer thinking as an individual, but rather as an integral player and contributor to the team, translating the image content into clinical planning and a decision-making process that enhance the quality of patient care.

Conclusions

With this summarized document we provided a standard for PET/CT imaging in inflammatory, infective, infiltrative, and innervation dysfunctional (4Is) cardiovascular diseases. It can be applied in clinical practice and integrated in (multicentre) clinical trials for optimal procedural standardization. 4Is related cardiovascular diseases are generally complex and often require wide ranging expertise and a multidisciplinary approach for optimal diagnosis and management. New PET 4Is radiopharmaceuticals beyond [18F]FDG are available, but are currently mainly in the clinical research phase. Further clinical evaluation of the most promising PET tracers is warranted before their implementation in routine clinical practice.

Supplementary data

Supplementary data are available at European Heart Journal - Cardiovascular Imaging online.

Acknowledgements

We thank the EANM Committees, EANM National Societies, and the EACVI bodies for their review and contribution. We acknowledge the contribution of previous guidelines on which the present are based.1,3,9

Compliance with ethical standards

Ethics approval

These guidelines do not contain any studies with human participants or animals performed by any of the authors.

Liability statement

This guideline summarizes the views of the EANM Cardiovascular and Infection & Inflammation Committees and the EACVI. It reflects recommendations for which the EANM and the EACVI cannot be held responsible. The recommendations should be taken into consideration of good practice of nuclear medicine & cardiology imaging and do not substitute for national and international legal or regulatory provisions.

Conflict of interest: none declared.

References

1. Jamar F, Buscombe J, Chiti A, Christian PE, Delbeke D, Donohoe KJ et al. EANM/SNMMI guideline for 18F-FDG use in inflammation and infection. J Nucl Med 2013;54:647–58.
2. Slart RHJA, Glaudemans AWJM, Paus, J, Blankenstein R, Schwartz RG et al. Document Reading Group. A joint procedural position statement on imaging in cardiac sarcoidosis from the Cardiovascular and Inflammation & Infection Committees of the European Association of Nuclear Medicine, the European Association of Cardiovascular Imaging, and the American Society of Nuclear Cardiology. J Nucl Cardiol 2018;25:298–319.
3. Slart RHJA, Glaudemans AWJM, Paus, J, Blankenstein R, Schwartz RG et al. Document Reading Group. A joint procedural position statement on imaging in cardiac sarcoidosis from the Cardiovascular and Inflammation & Infection Committees of the European Association of Nuclear Medicine, the European Association of Cardiovascular Imaging, and the American Society of Nuclear Cardiology. J Nucl Cardiol 2018;25:298–319.
4. Erbs PA, Lancelotti P, Vilacosta I, Glaudemans AWJM, Lancelotti P, Hyafil F, Blankenstein R, Schwartz RG et al. Recommendations on nuclear and multimodality imaging in IE and CIED infections. Eur J Nucl Med Imaging 2018;45:1795–815.
5. Slart RHJA, Glaudemans AWJM, Paus, J, Blankenstein R, Schwartz RG et al. Document Reading Group. A joint procedural position statement on imaging in cardiac sarcoidosis from the Cardiovascular and Inflammation & Infection Committees of the European Association of Nuclear Medicine, the European Association of Cardiovascular Imaging, and the American Society of Nuclear Cardiology. J Nucl Cardiol 2018;25:298–319.
6. Slart RHJA, Glaudemans AWJM, Paus, J, Blankenstein R, Schwartz RG et al. Document Reading Group. A joint procedural position statement on imaging in cardiac sarcoidosis from the Cardiovascular and Inflammation & Infection Committees of the European Association of Nuclear Medicine, the European Association of Cardiovascular Imaging, and the American Society of Nuclear Cardiology. J Nucl Cardiol 2018;25:298–319.
7. Slart RHJA. Writing group, Reviewer group, Members of EANM Cardiovascular, Members of EANM Infection & Inflammation, Members of Committees, SNMMI Cardiovascular: FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (RIG), and endorsed by the SNM. Eur J Nucl Med Imaging 2018;45:1250–69.
8. Dejaco C, Rammo S, Duffner C, Besson FL, Bley TA, Blokman D et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheum Dis 2018;77:636–43.
9. Dorbala S, Ando Y, Bokhari S, Disperezieri A, Falk RH, Ferrari VA et al. ASNC/AHA/AES/EANM/HFSA/ASCM/RNS/ppmii consensus recommendations for multimodality imaging in cardiac amyloidosis: part 1 of 2-evidence base and standardized methods of imaging. J Nucl Cardiol 2019;26:2065–73.
10. Dorbala S, Ando Y, Bokhari S, Disperezieri A, Falk RH, Ferrari VA et al. ASNC/AHA/AES/EANM/HFSA/ASCM/RNS/ppmii consensus recommendations for multimodality imaging in cardiac amyloidosis: part 2 of 2-Diagnostic criteria and appropriate utilization. J Nucl Cardiol 2019;27:659–73.
11. Bucerus J, Hyafil F, Verbernie HJ, Slart RH, Lindner O, Schiara R et al. On behalf of the Cardiovascular Committee of the European Association of Nuclear Medicine (EANM). Position paper of the Cardiovascular Committee of the European Association of Nuclear Medicine (EANM) on PET imaging of atherosclerosis. Eur J Nucl Med Imaging 2016;43:780–92.
12. Slart RHJA, Tia RA, Ebongh PH, Schwager M. Autonomic Innuervation of the Heart. Role of Molecular Imaging. 1st ed. Heidelberg: Springer; 2015.
13. Dorbala S, Di Carli MF, Delbeke D, Abbas A, DePuey EG, Dilsizian V et al. SNMMI/EANM/SNMMI/SNMMI/ASNC/SCTC guideline for cardiac SPECT/CT and PET/CT 1.0. J Nucl Med 2013;54:1485–507.
14. Osborne MT, Hulten EA, Murtby VL, Skalí H, Taqueti VR, Dorbala S et al. Patient preparation for cardiac fluorine-18 fluorodeoxyglucose positron emission tomography imaging of inflammation. J Nucl Cardiol 2017;24:846–99.
15. Swart LE, Gomes A, Scholten AM, Sinha B, Tanis W, Lam MGEH et al. Improving the diagnostic performance of (18F)fluorodeoxyglucose positron emission tomography/computed tomography in prosthesis heart valve endocarditis. Circulation 2018;138:1412–27.
16. Swart LE, Scholten AM, Tanis W, Nieman K, Brogers AI, Verzijlbergen FJ et al. 18F-fluorodeoxyglucose positron emission/computed tomography and computed tomography angiography in prosthetic heart valve endocarditis: from guidelines to clinical practice. Eur Heart J 2018;39:3739–49.
17. Habb G, Erba PA, Jung B, Donal E, Cossyl B, Lamoche C et al. EURO-ENDO Investigators. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study. Eur Heart J 2019;40:3222–32.
18. Hyafil F, Rouzet F, Le Guludec D. Nuclear imaging for patients with a suspicion of infective endocarditis: be part of the team! J Nucl Cardiol 2017;24:207–11.
19. Gomes A, Glaudemans AWJM, Tourn DJ, van Melle JP, Willems TP, Maas AH et al. Diagnostic value of imaging in infective endocarditis: a systematic review. Lancet Infect Dis 2017;17:e1–14.
20. Cremer PC. Diagnostic uncertainty in prosthetic valve endocarditis: value of (18F)FDG PET/CT and the need for standardization. JACC Cardiovasc Imaging 2020;Aug 16;S1936-878X(20)30630-6.
22. Pelletier-Galameau M, Abikzer G, Harel F, Diluzio V. Detection of native and prosthetic valve endocarditis: incremental attributes of functional FDG PET/CT over morphologic imaging. Curr Cardiol Rep 2020;22:93–w.

23. de Camargo RA, Sommer Bitencourt M, Meneghetti JC, Soares J, Goncalves LFT. Procedural recommendations of cardiac PET/CT imaging. J Nucl Cardiol 2020;70:583–94.

24. King D, Wallot F, Lacroix D, Marque C, Kouakam C, Kacem S et al. Local symp- toms at the site of pacemaker implantation indicate latent systemic infection. Heart 2004;90:882–6.

25. Borgioni MG, Burri H, Deharo JC, Stark C, Kenngren C, Sagny L et al; ESC Scientific Document Group. 2018 EHRA expert consensus statement on lead extraction: recommendations on definitions, endpoints, research trial design, and data collection requirements for clinical scientific studies and registries: endorsed by APHRA/RSHS/LSRHS. Europace 2018;20:1217.

26. Sarrazin JF, Philippe F, Tessier M, Guimond J, Molin F, Champagne J et al. Usefulness of fluorine-18 positron emission tomography/computed tomography for identification of cardiovascular implantable electronic device infections. J Am Coll Cardiol 2012;59:1616–25.

27. Leccisotti L, Perna F, Lago M, Leo M, Stefanelli A, Cagnolini ML et al. Cardiac amyloidosis: device infection: delayed vs standard FDG PET/CT imaging. J Nucl Cardiol 2014;21:622–3.

28. Blomstrom-Lundqvist C, Traykov V, Erba PA, Burri H, Nielsen JC, Borgioni MG et al; ESC Scientific Document Group. European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiacl implantable electronic device infections-endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), International Society for Cardiovascular Imaging (ISCIVID) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Europace 2020;22:515–49.

29. Memmott MJ, James J, Armstrong IS, Tout D, Ahmed F. The performance of quantitation methods in the evaluation of cardiac implantable electronic device (CIED) infection: a technical review. J Nucl Cardiol 2016;23:1457–66.

30. Rack F, Rozen F, Benali K. FDG-PET for the detection of infection in left ventricule assist device: is there light at the end of the tunnel? J Nucl Cardiol 2019;26:1222–4.

31. Dell’Aquila AM, Avramovic N, Mastrobuoni S, Motekallemi A, Wisniewski K, Scherler M et al. Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography for improving diagnosis of infection in patients on CF-LVAD: longing for more ‘insights’. Eur Heart J Cardiovasc Imaging 2018;19:532–43.

32. De Vaugelade C, Mesguich C, Nubret K, Camou F, Greib C, Dournes G et al. Infections in patients using ventricular-assist devices: comparison of the diagnostic performance of (18)F-FDG-PET/CT scan and leucocyte-labelled scintigraphy. J Nucl Cardiol 2019;26:42–55.

33. Valentine RJ. Diagnosis and management of aortic graft infection. Semin Vasc Surg 2001;14:292–301.

34. Saleem BR, Berger P, Vaartjes I, de Keizer B, Vonken EJ, Slart RH et al. Modest utility of quantitative measures in (18)F-fluorodeoxyglucose positron emission tomography scanning for the diagnosis of aortic prosthetic graft infection. J Vasc Surg 2015;61:965–71.

35. Keidar Z, Pirmashali N, Leiderman M, Nitecki S, Israel O. 18F-FDG uptake in cardiac sarcoidosis. JACC Cardiovasc Imaging 2013;40:1457–66.

36. Abulzi M, Sifiou I, Wuylaya-Gariepy M, Khoubabi M, Israel JM, Emens B et al. 18F-sodium fluoride PET/CT/MRI myocardial imaging in patients with suspected cardiac amyloidosis. J Nucl Cardiol 2019;Sept 11.

37. Nensa F, Kloot J, Tezgha E, Poppel TD, Heusch P, Goebel J et al. Feasibility of FDG-PET/MRI in myocarditis: comparison to CMR using integrated PET/MRI. J Nucl Med 2018;59:95–8.

38. Nazir MS, Ismail TF, Reyes E, Chribini A, Kaufmann PA, Plein S. Hybrid positron emission tomography-magnetic resonance of the heart: current state of the art and future applications. Eur J Heart Cardiovasc Imaging 2018;19:962–74.

39. Habib G, Bucciacucci-Ducci C, Caffino ALP, Cardin N, Charron P, Cosyns B et al.; EACVI Scientific Documents Committee. Multimodality imaging in restrictive cardiamyopathies: an EACVI position paper in collaboration with the “Working Group on myocardial and pericardial diseases” of the European Society of Cardiology Endorsed by The Indian Academy of Echocardiography. Eur Heart J Cardiovasc Imaging 2017;18:1090–121.

40. Robson PM, Dey D, Newby DE, Berman D, Li D, Fayad ZA et al; MR/PET imag- ing of the cardiovascular system. JACC Cardiovasc Imaging 2017;10:1165–79.

41. Erba PA, Habib G, Glaudemans AVWM, Miro JM, Slart RHJA. The round table approach in infective endocarditis & cardiovascular implantable electronic devices infections: make your e-Team come true. Eur J Nucl Med Mol Imaging 2017;44:1107–8.

42. European Nuclear Medicine Guide [Internet]. 2018 https://www.eanm.org/public press/european-nuclear-medicine-guide/.

43. Emens B, Benali K, Mahida B, Lariviere D, Le Guludec D, Papo T et al. Comparison between visual and numerical metrics for the evaluation of patients with Takayasu arthritis with 18F-FDG-PET. Nucl Med Commun 2018;39:77–88.

44. Grayson PC, Aheashemi S, Bagheri AA, Civelek AC, Cupps TR, Kaplan MJ et al. (18)F-fluorodeoxyglucose-postinfection tomography as an imaging biomarker in a prospective, longitudinal cohort of patients with large vessel vasculitis. Arthritis Rheumatol 2018;70:439–49. An increased major vessel uptake by 18F-FDG-PET/CT in NIH criteria inactive patients with Takayasu’s arteritis. Clin Exp Rheumatol 2018;36:88–92.

45. Imfeld S, Rottburger C, Schegk E, Ashchwarden M, Juengling F, Staub D et al. [18F]FDG positron emission tomography in patients presenting with suspicion of giant cell arteritis-lessons from a vasculitis clinic. Eur J Cardiovasc Imaging 2018;19:933–40.

46. Nielsen RD, Hansen IT, Kramer S, Haraldsen A, Hjorthaug K, Bogsrud TV et al. Simple dichotomous assessment of cranial artery inflammation by conventional 18F-FDG-PET/CT shows high accuracy for the diagnosis of giant cell arteritis: a case-control study. Eur J Nucl Med Mol Imaging 2019;46:184–93.

47. Soniano A, Pazzolla G, Boardi L, Casali M, Muratore P, Pipitone N et al. Distribution patterns of 18F-fluorodeoxyglucose in large vessels of Takayasu’s and giant cell arteritis using positron emission tomography. Clin Exp Rheumatol 2018;36:99–106.

48. Vaidyanathan S, Chattopadhyay A, Mackle SL, Scarsbrook AF. Comparative ef- fectiveness of (18)F-FDG PET-CT and contrast-enhanced CT in the diagnosis of suspected large-vessel vasculitis. BJR 2018;91:200247.

49. Hohnhann C, Mchets G, Schmutz P, Rister R, Mader N, Ohler M et al. Diagnostic challenges in infective endocarditis: is PET/CT the solution? JCM Eur J Nucl Med Mol Imaging 2019;46:1617–23.

50. Diemberger I, Bonfiglioli R, Martignani C, Graziosi M, Biffi M, Lorenzetti S et al. Contribution of PET imaging to mortality risk stratification in candidates to lead extraction for pacemaker or defibrillator infection: a prospective single study. Eur J Nucl Med Mol Imaging 2019;46:194–205.

51. Granados U, Fuster D, Pericas JM, Lloips JL, Ninot S, Quintana E et al; Hospital Clinic Endocarditis Study Group. Diagnostic accuracy of 18F-FDG PET/CT in in- fective endocarditis and implantable cardiac device infection: a cross- sectional study. J Nucl Med 2019;60:326–32.

52. Kumita S, Yoshinaga K, Miyagawa M, Momose M, Kiso K, Kasa T et al. Committee for diagnosis of cardiac sarcoidosis using 18F-FDG PET, Japanese
Society of Nuclear Cardiology, Recommendations for (18)F-fluorodeoxyglucose positron emission tomography imaging for diagnosis of cardiac sarcoidosis-2018 update. Japanese Society of Nuclear Cardiology recommendations. J Nucl Cardiol 2019; 26:1414–33.

65. Tuominen H, Haarala A, Tikkanakari A, Korkola P, Kahonen M, Nikus K et al. (18)F-FDG PET in Finnish patients with clinical suspicion of cardiac sarcoidosis: female sex and history of atrioventricular block increase the prevalence of positive PET findings. J Nucl Cardiol 2019; 26:394–400.

66. Tuominen H, Haarala A, Tikkanakari A, Kahonen M, Nikus K, Sipila K. 18FDG-PET in a patient cohort suspected for cardiac sarcoidosis: right ventricular uptake is associated with pathological uptake in mediastinal lymph nodes. J Nucl Cardiol 2020; 27:109–17.

67. Lee JH, Lee GY, Kim SJ, Kim KH, Jeon ES, Lee KH et al. Imaging findings and literature review of (18)F-FDG PET/CT in primary systemic AL amyloidosis. Nucl Med Mol Imaging 2015; 49:182–90.

68. Oliveira-Santos M, Castelo-Branco M, Silva R, Gomes A, Chichorro N, Abrunhosa A et al. Atherosclerotic plaque metabolism in high cardiovascular risk subjects—a subclinical atherosclerosis imaging study with (18)F-NaF PET-CT. Atherosclerosis 2017; 260:41–6.

69. Dweck MR, Chow MW, Joshi NV, Williams MC, Jones C, Fletcher AM et al. Coronary arterial 18f-sodium fluoride uptake: a novel marker of plaque biology. J Am Coll Cardiol 2012; 59:1539–48.

70. Kim JH, Lee ES, Park KY, Seok JW, Kwon OS. Comparison of (18)F-FDG and (18)F-NaF positron emission tomography on culprit carotid atherosclerosis: a prospective study. JACC Cardiovasc Imaging 2019; 12:370–2.

71. Ishiwata Y, Kaneta T, Nawata S, Hino-Shishikura A, Yoshida K, Inoue T. Quantification of temporal changes in calcium score in active atherosclerotic plaque in major vessels by (18)F-sodium fluoride PET/CT. Eur J Nucl Med Mol Imaging 2017; 44:1529–37.

72. Quirce R, Martinez-Rodriguez I, Banza I, Jimenez-Bonilla J, Martinez-Amador N, Ibanez-Bravo S et al. New insight of functional molecular imaging into the atheroma biology: 18f-NaF and 18f-FDG in symptomatic and asymptomatic carotid plaques after recent CVA. Preliminary results. Clin Physiol Funct Imaging 2016; 36:499–503.

73. Blomberg BA, Thomassen A, de Jong PA, Simonsen JA, Lam MG, Nielsen AL et al. Impact of personal characteristics and technical factors on quantification of sodium 18F-fluoride uptake in human arteries: prospective evaluation of healthy subjects. J Nucl Med 2015; 56:1534–40.

74. Martineau P, Finnerty V, Giraudelle G, Authier S, Harel F, Pelletier-Galarneau M. Examining the sensitivity of 18F-NaF PET for the imaging of cardiac amyloidosis. J Nucl Cardiol 2019; Mar 4.

75. Voo S, Kwae MH, Sluimer JC, Schroder FH, Wiertz R, Bauwens M et al. Imaging intraplaque inflammation in carotid atherosclerosis with 18F-fluorocholine positron emission tomography-computed tomography: prospective study on vulnerable atheroma with immunohistochemical validation. Circ Cardiovasc Imaging 2016; 9:e004467.

76. Verweij N, Bruijnjen S, Gent Y, Huisman M, Jansen G, Molthoff C et al. (18)FLUORO-PEG-FOLATE pet: a novel imaging technique to visualize rheumatoid arthritis. Ann Rheum Dis 2017; 76:1047.

77. Norikane T, Yamamoto Y, Maeda Y, Noma T, Dobashi H, Nishiyama Y. Comparative evaluation of (18)F-FLT and (18)F-FDG for detecting cardiac and extra-cardiac thoracic involvement in patients with newly diagnosed sarcoidosis. EJNMMI Res 2017; 7:69–0.

78. Rayamajhi S, Mittal BR, Maturu VN, Aggarwal R, Bal A, Dey P et al. (18)F-FDG and (18)F-FLT PET/CT imaging in the characterization of mediastinal lymph nodes. Ann Nucl Med 2016; 30:207–16.

79. Elman EC, El-Sady MS, Kijewski MF, Khor YM, Jacob S, Ruberg FL et al. Early detection of multiorgan light-chain amyloidosis by whole-body (18)F-florbetapir PET/CT. J Nucl Med 2019; 60:1234–9.

80. Baratto L, Park SY, Hatami N, Gulaka P, Vasanawala S, Yohannan TK et al. (18)F-florbetaben whole-body PET/MRI for evaluation of systemic amyloid deposition. EJNMMI Res 2018; 8:66–1.

81. Law WP, Wang WY, Moore PT, Mollee PN, Ng AC. Cardiac amyloid imaging with 18F-florbetaben PET: a pilot study. J Nucl Med 2016; 57:1733–9.

82. Dietemann S, Nikouluo R. Amyloid PET imaging in cardiac amyloidosis: a pilot study using (18)F-flutemetamol positron emission tomography. Ann Nucl Med 2019; 33:624–8.

83. Zelt JG, Mileniczuk LM, Orlandi C, Robinson S, Hadzis T, Walter O et al. PET imaging of sympathetic innervation with [(18)F]Flurobenguan vs [(11)C]mHED in a patient with ischemic cardiomyopathy. J Nucl Cardiol 2019; 26:2151–3.

84. Sinusas AJ, Lazewatsky J, Brunetti J, Heller G, Srivastava A, Liu YH et al. Biodistribution and radiation dosimetry of LM1195: first-in-human study of a novel 18F-labeled tracer for imaging myocardial innervation. J Nucl Med 2014; 55:1445–51.

85. Pizzaro C, Kluenfer K, Dabir D, Thomas D, Gaertner FC, Essler M et al. Cardiovascular magnetic resonance imaging and clinical performance of somatostatin receptor positron emission tomography in cardiac sarcoidosis. ESC Heart Fail 2018; 5:249–61.

86. Rominger A, Saam T, Vogl E, Ubles C, la Fougere C, Forster S et al. In vivo imaging of macrophage activity in the coronary arteries using 68Ga-DOTATATE PET/CT: correlation with coronary calcium burden and risk factors. J Nucl Med 2010; 51:133–9.

87. Tarkin JM, Joshi FR, Evans NR, Chowdhury MM, Fig N, Shah AV et al. Detection of atherosclerotic inflammation by (68)Ga-DOTATATE PET compared to (18)F-FDG PET imaging. J Am Coll Cardiol 2017; 69:1774–91.

88. Noordzij W, Elvan A, Demirel F, Jager PL, Tio RA, Slart RH. Symptomatic denervation in patients with ischemic cardiomyopathy and risk on ventricular tachyarrhythmias: A pilot study. Q J Nucl Med Mol Imaging 2018; 62:349–35.

89. Rosengren S, Skibsted Clemmensen T, Tolbod L, Granstam SO, Eiskjaer H, Wikström G et al. Diagnostic accuracy of [(11)C]PIB positron emission tomography for detection of cardiac amyloidosis. JACC Cardiovasc Imaging 2020; 13:1337–47.

90. Kero T, Lindstro L, Sorensen J, Lubberink M. Accurate analysis and visualization of cardiac [(11)C]PIB uptake in amyloidosis with semiautomatic software. J Nucl Cardiol 2016; 23:741–50.

91. Kero T, Sorensen J, Antoni G, Wilking H, Carlson K, Vedin O et al. Accurate analysis and visualization of cardiac [(11)C]PIB uptake in amyloidosis with semiautomatic software. J Nucl Cardiol 2016; 23:429–35.

92. Antoni G, Lubberink M, Estrada S, Axelsson J, Carlson K, Lindsjo L et al. In vivo quantification of (11)C-PIB kinetics in cardiac amyloidosis with semiautomatic software. J Nucl Cardiol 2020; 27(3):774–84.

93. Antoni G, Lubberink M, Estrada S, Axelsson J, Carlson K, Lindstro L et al. In vivo visualization of amyloid deposits in the heart with 11C-PET and PET. J Nucl Med 2013; 54:213–20.

94. Boelgaard R, Delgado-Bolton R, Oyen WJ, Giannarini F, Tatsch K, Escher W et al. FDG PET/CT: EANM procedure guidelines for tumour imaging version 2.0. Eur J Nucl Med Mol Imaging 2015; 42:328–5.