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Positron Emission Tomography Assessment of Cardiovascular Inflammation

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OVERVIEW

^{18}F-FDG myocardial PET is becoming an accepted tool for diagnosing active cardiovascular inflammation. Increased glucose metabolism is a hallmark of activation of cells involved in both innate and adaptive immunity. The purpose of this document is to highlight the key elements of appropriately performed, high quality myocardial positron emission tomography (PET) to detect active cardiovascular inflammation. Topics covered include: indications, contraindications, optimal testing protocols, and reporting templates.

INDICATIONS

The 2016 American Society of Nuclear Cardiology (ASNC) imaging guidelines/Society of Nuclear Medicine and Molecular Imaging procedure standard for positron emission tomography (PET) nuclear cardiology procedures identifies appropriate indications for PET MPI, including identification of:

- Cardiac sarcoidosis activity.
- Prosthetic valve endocarditis.
- Cardiovascular device-related infections.

CONTRAINDICATIONS

Contraindications to PET imaging include:

- Inability to lie flat or still during image acquisition;
- Pregnancy;
- Weight exceeding the PET machine table limit or inability to fit inside the gantry;
- Claustrophobia (rarely).

PRECAUTIONS

- The presence of active congestive heart failure and/or recent ICD firing can cause myocardial glucose uptake unrelated to sarcoidosis.
- Morning dose of regular insulin should be held as patients are fasting overnight.
- Ensure no dextrose containing IV fluids (heparin, amiodarone, magnesium, etc) are used for 24 hours in inpatients.

TEST PREPARATION

- Assess patient's height, weight, chest circumference, ability to lie flat, pregnancy status, history of claustrophobia, history of diabetes, and any current peritoneal dialysis.
- Record precise dose and time of administration of ^{18}F-FDG and uptake period.
- If planning to use heparin protocol (see below), assess for bleeding tendencies, allergies, and history of heparin-induced thrombocytopenia with thrombosis.
- If hospitalized, limit glucose-containing intravenous medication administration.
- Any combination of the protocols in **Table 1** typically produces a substrate and hormonal environment favoring myocardial metabolism of fatty acids over glucose.

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Table 1. Methods to suppress glucose utilization by normal myocardium

Methods	Technique	Comments
Prolonged fast	Fast of 12-18 hours	Preferred for patients on tube feeds or patients scheduled for procedures requiring NPO
High fat/low carbohydrate diet	Two meals 24 hours prior to the study, followed by an overnight fast	High fat, protein permitted, low-to-no carbohydrate diet
IV unfractionated heparin	15-50 units of regular IV heparin 15 min prior to IV ^{18}FFDG administration or 500 IU of IV heparin 45 minutes and 15 minutes (total 1000 IU) prior to IV ^{18}F-FDG	Ensure patient has no contraindications to administration of IV heparin.* IV regular heparin drip is frequently prepared in D5W and should be discontinued whenever possible prior to the sarcoid protocol ^{18}F-FDG study.
Combined methods	High fat/low-carbohydrate diet for 2 meals, one day prior, followed by overnight fast, and IV regular heparin prior to administration of ^{18}F-FDG	

** including bleeding tendencies, allergy or history heparin-induced thrombocytopenia with thrombosis (HIT);*
IV = intravenous; NPO = Nil per os, nothing by mouth

^{18}F-FDG

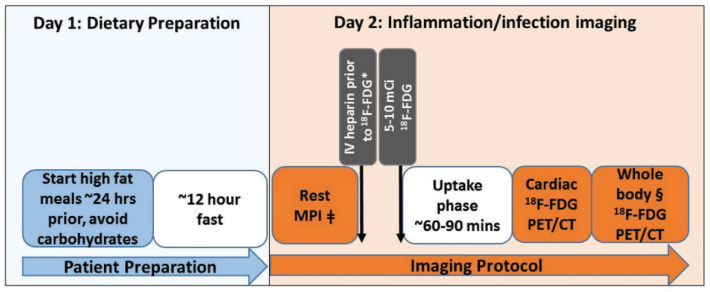
Table 2. Key characteristics of ^{18}F-FDG

Physical half-life	110-min
Supply source	Cyclotron
Positron range	Short (excellent spatial resolution)
Critical organ	Bladder (frequent voiding 3-4 hrs post-administration)

IMAGING PROCEDURE

- The typical imaging procedure comprises of rest MPI combined with ^{18}F-FDG imaging, except for infection imaging when MPI is not necessary.
- The typical clinical flow for assessment of cardiovascular inflammation/infection is shown in **Figure 1**.
- The preferred imaging protocol for ^{18}F-FDG PET is listed in **Table 3**.

Figure 1. Typical clinical flow for assessment of cardiovascular infection and infection with ^{18}F-FDG PET/CT



Rest MPI‡: Not needed for infection imaging. Use standard SPECT or PET protocols.
*: Suppression of physiological myocyte glucose uptake may be enhanced by giving IV unfractionated heparin (5-15 IU/kg) prior to administration of ^{18}F-FDG
§: Partial whole body to include at a minimum chest, liver and spleen for inflammation imaging.

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Table 3. Preferred ^{18}F-FDG PET myocardial inflammation protocol.

Exclude obstructive coronary artery disease/prior myocardial infarction and assess resting myocardial perfusion*	
Patient positioning	
Supine, arms raised above shoulders and supported	
CT topogram/scout scan for heart localization	
CT transmission scan for attenuation correction	
80-140 kVp, 10-20 mA, 4-5 mm slice thickness, ungated to ECG, field of view from carina to 2 cm below inferior heart border, obtain at end-expiration or during shallow breathing	
PET emission scan	
Acquisition mode	2D or 3D, static or list mode (simultaneous dynamic and ECG-gated)
^{18}F-FDG dose	5-15 mCi intravenously
Imaging delay after ^{18}F-FDG injection	90 min (minimum 60-90 min)
Imaging duration	10-30 min
Reconstruction	Filtered backprojection or iterative (e.g., ordered-subsets expectation maximization), reconstructed pixel size 2-3 mm, matched to perfusion images and between consecutive studies

**Needed only for detection of cardiac sarcoidosis and not for other indications. Exclusion of obstructive coronary artery disease and prior myocardial infarction can be done with a coronary angiogram (invasive or CT) or with rest/stress MPI (PET or SPECT). Rest MPI should typically be performed in the same imaging session with identical parameters for patient positioning, attenuation correction, and image reconstruction; see separate PET Myocardial Perfusion Imaging Practice Points document.*

INTERPRETATION

- ^{18}F-FDG images should be interpreted along with myocardial perfusion data.
- ^{18}F-FDG uptake limited to cardiac blood pool suggests proper dietary preparation; while this finding excludes active myocardial inflammation, it does not exclude myocardial fibrosis.
- Diagnosis of active cardiac sarcoidosis may be difficult, if not impossible, in patients who have coronary disease with ongoing ischemia.

Table 4. Interpretation of resting myocardial perfusion and ^{18}F-FDG uptake patterns.

^{18}F-FDG uptake	Interpretation ('Consistent With')
Absent	Normal or scar (in regions with perfusion defects)
Diffuse	Poor dietary preparation
Focal	Active inflammation
Focal-On-Diffuse*	Poor dietary preparation + active inflammation

**The specific case of focal uptake in the lateral wall with a diffuse basal pattern has been observed in healthy individuals. Other interpretation methods incorporating perfusion can be used.1*

REPORTING

- ^{18}F-FDG PET images should be reviewed for any evidence of abnormal uptake in other regions (i.e., hilar lymph nodes, lung lesions for sarcoidosis) for diagnosis of sarcoidosis and guiding biopsy sites.
- When using ^{18}F-FDG myocardial PET to assess for cardiovascular device infection, fused PET/CT images can help localize tracer uptake to specific device components (i.e., generator, leads, pump, cannula, driveline) and to distinguish device vs. superficial skin infection. Distribution and pattern of tracer uptake may be more important than intensity of uptake. Both CT attenuation correction and non-attenuation correction images should be reviewed to help recognize artifact of increased tracer uptake related to the high-density metal in the device.
- When using ^{18}F-FDG myocardial PET to assess for suspected prosthetic valve endocarditis, false-positive results are more likely early after prosthesis implantation and at surgical adhesive sites. False-negative results are more likely with small vegetations.
- The study report should include:
  - Whether the study is normal or abnormal, the clinical question being addressed, and potential quality issues (artifacts or other issues impacting interpretation)
  - Image quality and adequacy of suppression of physiological glucose utilization
  - Description of whole-body images
  - Statement about perfusion defects and relationship to ^{18}F-FDG findings

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SUGGESTED READING

Dilsizian V, Bacharach SL, Beanlands RS, et al. ASNC imaging guidelines/SNMMI procedure standard for positron emission tomography (PET) nuclear cardiology procedures. J Nucl Cardiol. 2016;23(5):1187-1226.

Chareonthaitawee P, Beanlands RS, Chen W, et al. Joint SNMMI–ASNC expert consensus document on the role of ^{18}F-FDG PET/CT in cardiac sarcoid detection and therapy monitoring. J Nucl Cardiol. 2017;24(5):1741-1158.

Tilkemeier PL, Bourque J, Doukky R et al. ASNC imaging guidelines for nuclear cardiology procedures : Standardized reporting of nuclear cardiology procedures. J Nucl Cardiol. 2017 Sep 15.