CARDIAC PET SCAN: CLINICAL APPLICATIONS

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I INTRODUCTION AND TECHNICAL SUPERIORITY OVER SPECT

- **The Core Physical Principle:** Positron Emission Tomography (PET) detects pairs of collinear **511 keV gamma annihilation photons** emitted in opposite directions (180 degrees apart) when a positron emitted by a radionuclide collides with an electron in myocardial tissue (**electronic coincidence detection**).
- **Technical Advantages Over Single-Photon Emission Computed Tomography (SPECT):**
  - **Absolute Dynamic Quantification:** Unlike SPECT (which shows only *relative* regional perfusion normalized to the hottest myocardial segment and can completely miss **"balanced three-vessel or Left Main ischemia"**), dynamic first-pass PET quantifies **absolute Myocardial Blood Flow (MBF) in mL/min/g** at rest and peak hyperemia.
  - **Superior Spatial and Temporal Resolution:** Spatial resolution of **4 to 5 mm** (vs. 10 to 12 mm for conventional SPECT) with **routine CT-based Attenuation Correction** built into hybrid PET/CT scanners (eliminating diaphragmatic and breast soft-tissue attenuation artifacts).
  - **Lower Patient Radiation Dose and Rapid Protocol:** Short-lived perfusion radiotracers deliver low effective radiation doses (**1 to 3 mSv** vs. 6 to 10 mSv for Tc-99m SPECT) and allow complete rest-stress imaging in **30 to 45 minutes**.

II MYOCARDIAL PERFUSION IMAGING AND CORONARY MICROVASCULAR DYSFUNCTION (ANOCA / INOCA)

- **Cardiac Perfusion Radiotracers:**
  - **Rubidium-82 (82Rb):** Potassium analog produced on-site from a commercial **Strontium-82 / Rubidium-82 generator** (replaced every 4 to 6 weeks; **physical half-life = 75 to 76 seconds**); requires pharmacological vasodilator stress (adenosine, regadenoson, or dipyridamole).
  - **Nitrogen-13 Ammonia (13NH3): On-site cyclotron-produced** tracer (**half-life = 9.96 minutes**) with higher first-pass myocardial extraction (~80%) and superior image resolution (due to short positron range).
  - **Oxygen-15 Water (H215O):** On-site cyclotron tracer (**half-life = 2.0 minutes**); 100% freely diffusible and metabolically inert (the gold standard for research MBF quantification).
  - **Fluorine-18 Flurpiridaz (18F-Flurpiridaz — AURORA Phase III Trial / FDA Approved Sept 2024):** Novel mitochondrial complex-I binding tracer with a **110-minute half-life** (allowing regional cyclotron unit-dose distribution without an on-site cyclotron or generator), **very high first-pass extraction (~94%)** across all flow rates, shortest positron range (sharpest spatial resolution), and ability to perform **treadmill exercise PET** as well as pharmacological stress.
  - **Quantitative Myocardial Flow Reserve (MFR / CFR):**
  - **Calculation: MFR = Peak Hyperemic Stress MBF (normal >2.0 to 3.0 mL/min/g) / Resting MBF (normal ~0.7 to 1.0 mL/min/g).**
  - **Diagnostic Cut-off:** An **MFR (CFR) less than 2.0** (and especially **less than 1.5**) is definitively abnormal—unmasking either **balanced multivessel epicardial CAD** or diffuse **Coronary Microvascular Dysfunction (CMD / INOCA)** when epicardial arteries are non-obstructive (**ACC/AHA 2021 Chest Pain Guideline Class IIa**). Conversely, a normal global MFR (>2.0) carries a very high negative predictive value for excluding high-risk Left Main/3-vessel CAD and predicts a <1% annual cardiac mortality ("warranty period").
  - **Landmark Evidence — The PACIFIC Trial (Danad et al., *JAMA Cardiol* 2017):** Prospective head-to-head comparison of Coronary CTA, SPECT, and Quantitative 15O-Water PET against invasive **Fractional Flow Reserve (FFR <=0.80)** in 208 patients with suspected CAD; **PET achieved the highest overall diagnostic accuracy (85 percent; AUC 0.90), significantly outperforming both SPECT (77 percent) and Coronary CTA (74 percent)** on a per-patient and per-vessel basis.

Clinical Application	PET Radiotracer(s) & Patient Preparation	Pathognomonic Diagnostic Pattern	Guideline Class & Key Evidence
Epicardial CAD & Microvascular Angina (INOCA)	**82Rb, 13NH3, H215O, or 18F-Flurpiridaz** (Rest + Vasodilator Stress)	Regional stress perfusion defect (epicardial CAD) or **globally reduced MFR / CFR < 2.0** (balanced 3VD or **CMD**)	**Class I / IIa** (2021 ACC/AHA Chest Pain & 2024 ESC CCS); **PACIFIC Trial**
Myocardial Viability (Ischemic Cardiomyopathy)	**Perfusion (13NH3/82Rb) + Metabolic 18F-FDG** after **Oral Glucose Load + Insulin Clamp**	**Perfusion-Metabolism Mismatch** (low perfusion + preserved/high FDG) = **Viable Hibernating Myocardium**; **Concordant Match** = **Non-Viable Scar**	**Class IIa / IIb** pre-revascularization; **PARR-2 Trial**
Cardiac Sarcoidosis (Active Inflammation)	**Resting Perfusion + 18F-FDG** after **24-h High-Fat, Zero-Carb Diet + >12–18 h Fast (+ IV UFH)**	**Focal or Focal-on-Diffuse 18F-FDG uptake** with resting perfusion defect (active macrophage granulomas on dark background)	**Recommended** (HRS 2014 / AHA 2024 / ESC 2023) for diagnosis & steroid titration
Prosthetic Valve Endocarditis (PVE) & CIED Infection	**18F-FDG PET/CT** (with low-carb/fasting myocardial suppression)	Intense focal heterogeneous perivalvular, conduit, pocket, or lead **18F-FDG uptake**	**Class I Major Criterion** in **2023 ESC Endocarditis Guidelines**

III MYOCARDIAL VIABILITY ASSESSMENT IN ISCHEMIC CARDIOMYOPATHY

- **Metabolic Principle (The "Glucose Switch" of Hibernating Myocardium):** Under normal aerobic fasting conditions, healthy cardiomyocytes preferentially oxidize **Free Fatty Acids (FFAs)** (~70 to 80 percent of ATP production). Chronically hypoperfused, **hibernating cardiomyocytes** downregulate oxidative fatty acid metabolism, translocate **GLUT-1 and GLUT-4** transporters to the sarcolemma, and switch obligately to **anaerobic/aerobic glucose utilization (glycolysis)** to survive.
- **Dietary Protocol for Viability PET (Opposite of Sarcoidosis Protocol):** To stimulate maximal glucose uptake by all living myocytes, the patient is given an **oral glucose load (25 to 50 g) with supplemental IV insulin (or hyperinsulinemic-euglycemic clamp)** prior to injecting **18F-Fluorodeoxyglucose (18F-FDG)**.

- **Three Diagnostic Patterns (Combined Perfusion + 18F-FDG Viability Scan):**
  - **Normal:** Normal resting perfusion and normal 18F-FDG uptake.
  - **Perfusion-Metabolism Mismatch (Viable Hibernating Myocardium): Reduced resting perfusion** paired with **preserved or enhanced 18F-FDG uptake** (the highest-sensitivity non-invasive marker for predicting regional functional recovery after CABG). (Note: Normal resting perfusion with reduced FDG can occur in stunned/reperfused myocardium or LBBB septal remodeling.)
  - **Concordant Perfusion-Metabolism Match (Transmural Non-Viable Scar): Reduced resting perfusion** paired with **concordantly reduced/absent 18F-FDG uptake**.
  - **Landmark Trial — PARR-2 Trial (Beanlands et al., *JACC* 2007):** Randomized patients with severe ischemic LV dysfunction (LVEF <=35%) to FDG-PET-assisted management versus standard care; while the overall primary intention-to-treat composite narrowly missed significance (p = 0.16 due to 25% clinician non-adherence to PET recommendations), in the prespecified **subgroup where clinicians adhered to the PET viability recommendations** and in high-experience centers (**Ottawa-FIVE** substudy), FDG-PET guidance **significantly reduced composite cardiac death, MI, and hospital readmission (HR 0.62)**.

IV CARDIAC SARCOIDOSIS AND MYOCARDIAL INFLAMMATION

- **Strict Physiological Myocardial Suppression Protocol (Mandatory Exam Distinction from Viability PET):** Because normal cardiomyocytes avidly take up glucose after a meal (which would turn the entire LV bright and obscure inflammatory lesions), **Cardiac Sarcoidosis PET requires switching normal cardiomyocytes completely to Free Fatty Acid metabolism** so normal myocardium appears **"black/dark"** while **activated macrophages and CD4+ T-cells inside sarcoid granulomas** (which rely exclusively on insulin-independent **GLUT-1/GLUT-3** glycolysis) light up brightly:
- **Preparation:** At least **2 meals (24 hours) of a high-fat (>35 g fat), high-protein, strictly zero-carbohydrate (<3 g carb) ketogenic diet**, followed by a **12-to-18-hour fast**, plus **Intravenous Unfractionated Heparin (50 IU/kg IV bolus 15 minutes before 18F-FDG injection)** (heparin activates lipoprotein lipase to flood plasma with free fatty acids).
- **Diagnostic Patterns (Paired Resting Perfusion + 18F-FDG Scan):**
  - **Normal:** Normal perfusion and complete absence of myocardial 18F-FDG uptake.
  - **Early Active Inflammation:** Normal perfusion with **focal 18F-FDG uptake**.
  - **Advanced Active Inflammation + Scar ("Mismatch"): Resting perfusion defect** paired with **intense focal or focal-on-diffuse 18F-FDG uptake** (classically in the basal interventricular septum, lateral LV wall, and RV free wall, often accompanied by FDG-avid mediastinal/hilar lymph nodes).
  - **Burnt-Out Fibrotic Scar:** Resting perfusion defect with **absent 18F-FDG uptake** (indicates inactive scar; requires ICD evaluation rather than steroid escalation).

V INFECTIVE ENDOCARDITIS AND CIED INFECTION (ESC 2023 ENDOCARDITIS GUIDELINES)

- **Class I Major Diagnostic Criterion for Prosthetic Valve Endocarditis (PVE):** In the **2023 ESC Guidelines for the Management of Endocarditis**, abnormal intense focal or heterogeneous perivalvular **18F-FDG PET/CT** uptake (or **99mTc-HMPAO-labeled WBC SPECT/CT**) is a **Class I (Level B) Major Imaging Criterion** in the ESC Modified Duke Criteria for suspected **Prosthetic Valve Endocarditis (PVE)** when echocardiography is inconclusive (upgrading sensitivity from ~60% to >85–90%), and detects silent **extracardiac septic emboli / mycotic aneurysms** in 30 to 40 percent of patients. (Caution: Mild, homogeneous diffuse perivalvular uptake within 3 months of valve surgery or around BioGlue surgical adhesive can represent sterile postoperative inflammation and must be distinguished using qualitative pattern and quantitative SUV/spleen ratios.)
- **Cardiac Implantable Electronic Device (CIED) and LVAD Infections:** High diagnostic accuracy (most useful for pocket infection, less sensitive for lead endocarditis) and for localizing **vascular graft / aortic endograft** and **LVAD driveline/cannula** infections.

VI PRACTICAL CONSIDERATIONS IN THE INDIAN CLINICAL CONTEXT

- **The "Tuberculosis vs. Cardiac Sarcoidosis" FDG-PET Trap:** Both **Mycobacterium tuberculosis** (caseating granulomas) and **Cardiac Sarcoidosis** (non-caseating granulomas) produce **identical intense focal myocardial and mediastinal lymph node 18F-FDG uptake** on PET/CT. Starting empirical high-dose corticosteroids or infliximab based solely on a positive FDG-PET in an Indian patient without microbiological/histological exclusion of tuberculosis (**EBUS-TBNA of FDG-avid mediastinal nodes for Xpert MTB/RIF Ultra, AFB, and MGIT culture**, plus IGRA/Mantoux) can precipitate **fatal disseminated tuberculosis**.
- **Strict Carbohydrate Restriction Counseling in Vegetarian Indian Patients:** Because traditional Indian vegetarian diets are heavily carbohydrate-based (rice, roti, dal, milk, fruits), many Indian patients inadvertently consume carbohydrates before a sarcoidosis PET scan, causing **diffuse non-diagnostic LV FDG uptake**; providing an explicit written Indian ketogenic menu (paneer, eggs/meat, butter/ghee, non-starchy green vegetables, and plain water) is mandatory.

KEY REFERENCES

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