Clinical PET Myocardial Perfusion Imaging and Flow Quantification

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KEYWORDS

• PET • Myocardial perfusion imaging • Rubidium-82 • N-13-ammonia • Myocardial blood flow • Myocardial flow reserve • Flow quantification

KEY POINTS

- Cardiac PET has inherent advantages over single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI), including better imaging characteristics and the ability to quantify blood flow routinely.
- PET MPI has better sensitivity, specificity and accuracy than SPECT MPI in the detection of obstructive coronary artery disease.
- Myocardial flow reserve assessment can overcome the pitfall of balanced ischemia otherwise observed using conventional MPI in some patients with multivessel disease.
- PET MPI and flow quantification provide independent and incremental prognostic information for risk stratification.

INTRODUCTION

PET has evolved tremendously over the last 40 years. From humble beginnings in brain imaging, limited at first to a few research centers in the 1960s and 1970s,[1,2] PET has now grown to be a widely used modality in many disease areas. The development of numerous tracers imaging a wide range of biological pathways has lead to an ever-increasing reliance on PET in multiple clinical and research fields. The technology itself has seen many advances in recent years, including a 3-dimensional (3D)-mode acquisition, iterative reconstruction, hybrid systems (PET–computed tomography [CT] and PET–MR), and the (re)introduction of time-of-flight capabilities.

Although cardiac applications were first described in the 1970s, it was only once PET gained widespread use in oncologic imaging, with fluorodeoxyglucose (18-FDG), that the

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availability of PET systems really increased. This has lead to increased availability of PET in other fields, including cardiology. Furthermore, the approval of rubidium-82 generators for clinical use has opened the way for centers without an on-site cyclotron to consider routine PET myocardial perfusion imaging (MPI). Nitrogen-13-ammonia ($^{13}NH_3$) and O-15-water are also used for perfusion and flow measurements in some jurisdictions. A longer lived F-18–labeled radiopharmaceutical is presently undergoing phase III trials to obtain approval in North America and Europe.

This article focuses on the role of PET imaging in patients with known or suspected coronary artery disease (CAD). We start with an overview of the available radiotracers and imaging protocols, discuss their accuracy compared with single photon emission computed tomography (SPECT) MPI, and review the prognostic value and impact on clinical decision making. We will also discuss myocardial blood flow (MBF) quantification, including its role in the diagnosis of CAD and its prognostic value.

PET TRACERS FOR MYOCARDIAL PERFUSION IMAGING AND FLOW QUANTIFICATION

Both PET and SPECT rely on the same general principle: a radiolabeled perfusion tracer with known characteristics is administered to the patient, and external detectors are then used to count photons being emitted from the patient. In SPECT, the tracers emit gamma rays with or without characteristic x-rays, whereas in PET, the tracers emit positrons that, after traveling a short distance in the surrounding tissue, interact with an electron, leading to an annihilation event. This results in two 511-keV annihilation photons being emitted simultaneously at approximately 180° apart, which are then detected in coincidence by several rings of detectors positioned around the patient. PET has several advantages over SPECT, including greater sensitivity and count rate (because it uses electronic coincidence collimation instead of geometric physical collimation), better spatial resolution, and robust attenuation correction, which enables the quantification of regional tracer activity accurately and in absolute units (Bq/cc).[3] PET also allows the dynamic acquisition of activity versus time data, permitting MBF quantification in mL/min/g among other quantifiable biologic parameters. Most current commercial PET cameras are hybrid PET-CT machines, thus allowing fast, reliable, and accurate attenuation correction, with optional coronary artery calcium and/or angiography assessment.

The 4 main tracers used for PET MPI are rubidium-82-chloride (^{82}Rb), $^{13}NH_3$, oxygen-15-water, and fluorine-18-flurpiridaz; their main advantages, disadvantages, and characteristics are listed in **Table 1**. Only ^{82}Rb and $^{13}NH_3$ are currently in routine clinical use in North America; oxygen-15-water is also used in Europe and Japan. An ideal tracer for PET MPI should have a short positron range (better spatial resolution), high uptake within the myocardium and low washout (better myocardium/blood pool contrast), and a linear relationship between tracer uptake and MBF (increased ability to detect milder stenosis and ability to perform accurate MBF measurement).[4] Short and long half-life tracers both have advantages: shorter half-life results in less radiation exposure for the patient and the ability to perform rapid repeat testing, but longer half-life obviates the need for an on-site cyclotron, and also enables exercise stress imaging protocols.

Rubidium-82-Chloride

^{82}Rb is a short-lived radionuclide, with a half-life of only 76 seconds, and is a potassium analog. It enters the myocardium by passive diffusion and active transport, via the adenosine triphosphate–dependent sodium–potassium cotransporter. Because of this active transport, the uptake in the myocardium has a nonlinear relationship with MBF, which may decrease the sensitivity of conventional MPI for mild stenosis. ^{82}Rb also has the drawback of having the longest positron range among the commonly used PET tracers (root mean square of positron range of 2.6 mm for ^{82}Rb vs 0.23 mm for ^{18}F and 0.57 mm for ^{13}N). This can lead to decreased spatial resolution when compared with other tracers; the effects are nonlinear and apparent mainly in high-resolution images. Compared with conventional $^{13}NH_3$ images with ~10 mm reconstructed resolution, the higher ^{82}Rb positron range degrades the resolution by ~15%.

The short half-life has the advantage of enabling very fast imaging protocols while maintaining high count rates and a low effective radiation dose for the patient. A complete rest plus stress examination using weight-based dosing for 3D PET, including a low-dose CT for attenuation correction, can be less than 1.5 to 2 mSv.[5,6] The short half-life also permits repeat imaging within a few minutes should it be required for clinical research studies. On the downside, exercise stress testing is not generally performed. Although exercise PET MPI has been done with ^{82}Rb, the challenges of the short half-life generally preclude this application.[7]