READY for PET

Clinical Value of Cardiac PET

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OVERVIEW

There is growing excitement in the nuclear cardiology community regarding the emerging role of cardiac positron emission tomography (PET) myocardial perfusion imaging (MPI) for assessment of coronary artery disease (CAD) and other cardiovascular conditions. The purpose of this monograph is to highlight the clinical value of cardiac PET by outlining the many advantages it offers in managing patients with known or suspected CAD (***Table 1***).

Advantages of Cardiac PET
• Excellent diagnostic accuracy
• Consistently high image quality
• Protocol efficiency
• Low radiation exposure
• Peak-stress imaging and left ventricular ejection fraction (LVEF) reserve
• Myocardial blood flow (MBF) and myocardial blood flow reserve (MBFR)
• Coronary artery calcification assessment with PET/CT systems
• Robust prognostic data
• Applications beyond myocardial perfusion imaging

Table 1. Advantages of cardiac PET

EXCELLENT DIAGNOSTIC ACCURACY

PET MPI with myocardial blood flow reserve (MBFR) has been shown to have a higher diagnostic accuracy than other imaging modalities in a head-to-head study using invasive fractional flow reserve as the reference standard.[1] (***Figure 1***)

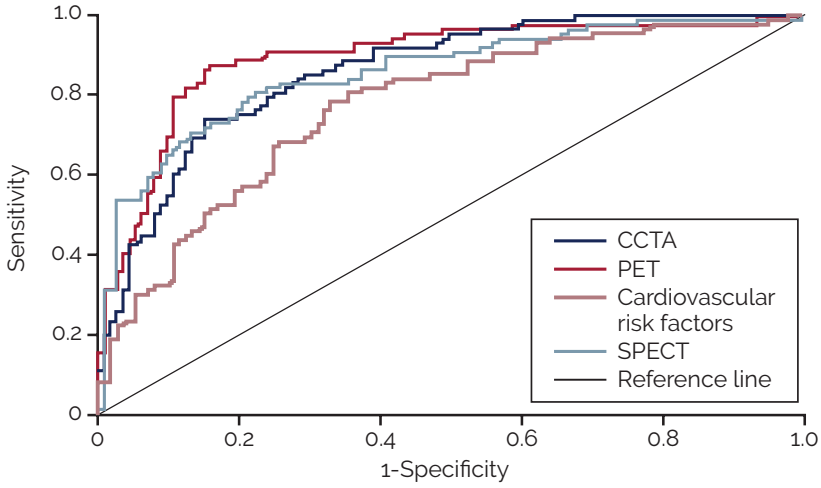

Figure 1. Diagnostic performance of cardiac imaging methods and traditional cardiovascular risk factors for the detection of coronary artery disease on a patient-based level.[1]

In this study, diagnostic accuracy was highest for PET (85%) compared with SPECT (77%) and CCTA (74%). The reasons for the high clinical performance of PET are multifactorial, including superior PET tracer properties and instrumentation, robust attenuation and scatter correction, and the ability to quantify absolute MBF and MBFR. Fundamental characteristics of PET imaging are summarized in ***Table 2***.

Characteristics of PET	
Attenuation correction	Routine and robust
Scatter correction	Routine and robust
Spatial resolution	Good (^{82}Rb) to excellent (^{13}N-NH_3, ^{18}F-flurpiridaz)
Myocardial tracer uptake	Moderate (^{82}Rb) to high (^{13}N-NH_3, ^{18}F-flurpiridaz)
Timing of stress imaging	Peak-stress (^{82}Rb) or early post-stress (^{13}N-NH_3)

Table 2. Characteristics PET

Figure 2 illustrates the excellent image quality obtained with both ^{82}Rb and ^{13}N-NH_3 MPI. Note the good separation of tracer uptake in the liver from the myocardium.

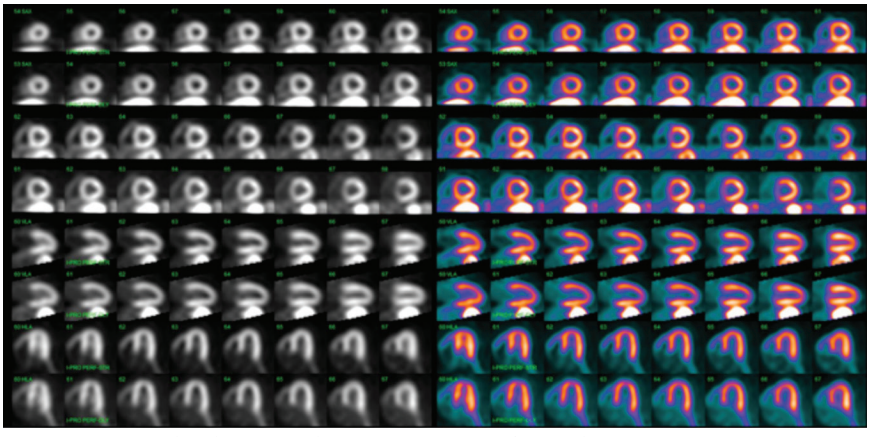

Figure 2a. Normal ^{82}Rb MPI study (Image courtesy of Timothy Bateman, MD)

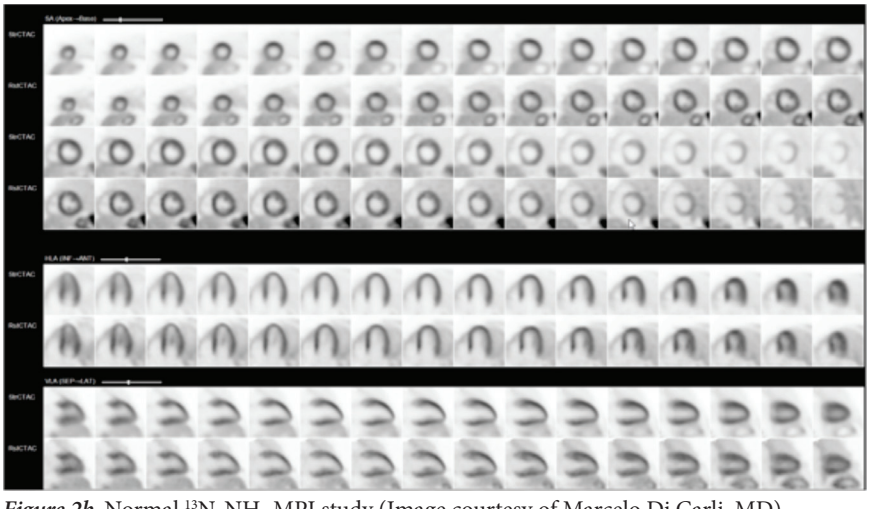

Figure 2b. Normal ^{13}N-NH_3 MPI study (Image courtesy of Marcelo Di Carli, MD)

Attenuation correction (AC) is used routinely for PET MPI. Routine and robust attenuation and scatter correction results in an accurate reflection of the myocardial tracer activity, with images less impacted by the patient's body size or shape.

PET systems also have high spatial resolution, 2.5 to 6.0 mm. The high spatial resolution allows for the detection of small areas of hypoperfusion and is one of the reasons for the high sensitivity of PET MPI. In addition, this high spatial resolution helps to mitigate any contamination of the left ventricle from adjacent splanchnic activity. PET spatial resolution is higher for ^{13}N-NH_3 and ^{18}F-flurpiridaz compared to ^{82}Rb due to differences in positron energy and resulting positron range, though high-quality diagnostic images are consistently obtained with all 3 radionuclides.

PET perfusion tracers demonstrate superior myocardial uptake leading to an accurate assessment of the true extent and severity of ischemia (***Figure 3***).[2] This in turn allows detection of flow heterogeneity and perfusion defects in the distribution of less-severe (but flow-limiting) coronary artery stenoses, improving the ability to identify the presence of multivessel CAD accurately.[3]

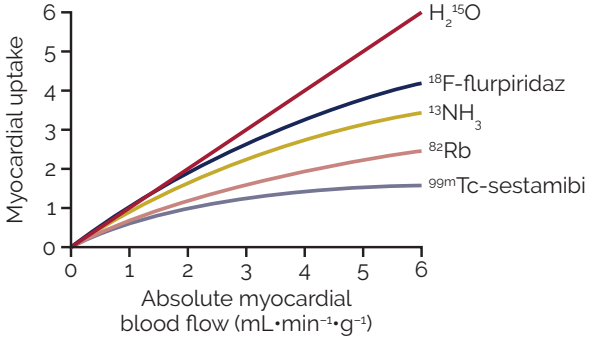

Figure 3. Kinetics of MPI perfusion tracers. Graphical representation of the relationship between absolute MBF and actual tracer uptake. Note that the PET MPI tracers demonstrate favorable myocardial uptake versus flow leading to high sensitivity for detection of multivessel coronary artery disease.[2]

Typically, there are trade-offs required in selecting an imaging modality for assessment of CAD, as selecting a test with high sensitivity usually requires sacrificing specificity; however, selecting PET MPI for assessment of CAD results in both high sensitivity and high specificity, and no clinical trade-off is required.

PROTOCOL EFFICIENCY

A complete rest-stress ^{82}Rb PET MPI study can be performed in as little as 20 to 35 minutes, greatly enhancing patient convenience and comfort as well as laboratory efficiency. ^{13}N-NH_3 rest-and-stress studies typically can be completed in 25 to 60 minutes, depending on the protocol utilized. The rapid-imaging protocols for PET MPI allow for late afternoon scheduling resulting in reduced hospital length of stay. The excellent efficiency of PET MPI was particularly beneficial during the height of the COVID-19 pandemic when minimizing the time of close contact between patients and staff was critically important.

LOW RADIATION DOSIMETRY

Radiation exposure for PET MPI is very low, with effective doses in the range of 1 to 3 mSv for ^{82}Rb and 2 to 4 mSv for ^{13}N-NH_3.[4-8] Furthermore, because of the short half-lives of ^{82}Rb (76 seconds) and ^{13}N-NH_3 (10-minutes), there is low radiation exposure to hospital personnel and family members, as the PET tracer decay is nearly complete before the patient leaves the PET imaging suite. The low radiation dosimetry of PET MPI is especially advantageous for serial imaging of patients with complex chronic CAD to limit the cumulative lifetime radiation exposure and for imaging younger patients. PET MPI allows nuclear cardiology laboratories to achieve easily the desired less than 9 mSv average

radiation dose recommended by the American Society of Nuclear Cardiology (ASNC). For purposes of reducing radiation dose, ASNC recommends using PET MPI as the first-line test when it is available.[9]

PEAK-STRESS IMAGING AND LEFT VENTRICULAR EJECTION FRACTION (LVEF) RESERVE

The timing of stress image acquisition is another important feature of PET MPI. Stress images with PET MPI are acquired at peak-stress (with ^{82}Rb) or early post-stress (with ^{13}N-NH_3). Therefore, the change in the left ventricular ejection fraction (LVEF) between rest and stress provides powerful diagnostic and prognostic information. When using ^{13}N-NH_3, gated PET images are acquired over 10 to 15 minutes, beginning 1.5 to 3 minutes after completion of the infusion of the pharmacologic stressor and therefore represents a blend of "peak-stress" and "early post-stress" images.[10] Gated PET images, using ^{82}Rb, are acquired over 5 to 7 minutes, beginning within 1 to 2 minutes after pharmacologic stress agent infusion and therefore represent true "peak-stress" images. LVEF and left ventricular volumes can be compared on resting and peak-stress gated ^{82}Rb PET images. In normal subjects, LVEF increases and left ventricular end-systolic volume (LVESV) declines on peak-stress gated ^{82}Rb PET images compared to resting images. A normal "LVEF reserve" (defined as peak-stress LVEF minus resting LVEF) of greater than or equal to 5% has a 97% negative predictive value for excluding left main or 3-vessel CAD.[11] In patients with severe and extensive obstructive CAD, the LVEF declines at peak-stress (LVEF reserve is negative) and LVESV increases at peak-stress, providing additional markers of high-risk CAD beyond perfusion findings.

MYOCARDIAL BLOOD FLOW QUANTIFICATION

Perhaps the single greatest advantage of PET MPI is its ability to quantify MBF in absolute units at rest and during peak hyperemic stress. This allows calculation of the MBFR, defined as the ratio of stress to resting MBF. Global MBFR has been demonstrated to have diagnostic value,[11] prognostic value,[12] and can be used to guide decisions regarding likelihood of benefit from early myocardial revascularization.[12] Quantification of MBFR can also be used to identify coronary microvascular disease and to verify appropriate response to the pharmacologic stress agent.[13] The tremendous clinical value of MBF quantification with PET MPI will be covered in detail in a separate monograph in this series.

CORONARY ARTERY CALCIFICATION ASSESSMENT WITH PET/CT SYSTEMS

The low-dose non-contrast CT images acquired for attenuation correction of PET/CT MPI studies can be used to assess for the presence of coronary artery calcification (CAC) as a marker of the presence of coronary artery atherosclerosis.[14] Alternatively, a formal coronary artery calcium score can be acquired to quantify CAC as part of the routine PET/CT protocol for patients without a prior history of documented CAD. In a patient with a normal PET MPI study, the absence of detectable CAC implies an excellent long-term prognosis. Conversely, the finding of CAC in a patient with an otherwise normal PET MPI study indicates the presence of subclinical nonobstructive coronary atherosclerosis and is associated with a higher rate of cardiac events and death in proportion to the amount of CAC. These patients will benefit from more aggressive risk-factor modification and closer clinical follow-up.

Assessment of CAC can also be helpful in guiding management for patients with normal "relative" PET perfusion images but with reduced global MBFR. In this scenario, absence of CAC makes balanced myocardial ischemia due to multivessel CAD very unlikely and suggests the presence of coronary microvascular disease or a failure to respond to vasodilator stress. Conversely, the presence of severe CAC indicates extensive coronary atherosclerosis and therefore increases the likelihood of balanced myocardial ischemia. Depending on the severity of the reduction in the MBFR and the LVEF reserve, further testing (possibly including invasive coronary angiography) may be indicated. ***Table 3*** summarizes the clinical information provided by PET/CT.

Clinical information available from PET/CT	
Perfusion relative to the most normal region	Yes
Resting and peak-stress (or early post-stress) LVEF and wall motion	Yes
Resting and peak-stress MBF and MBFR	Yes
LVEF reserve	Yes
Verification of response to vasodilator stress	Yes
Coronary artery calcification	Yes

LVEF, left ventricular ejection fraction; MBF, myocardial blood flow; MBFR, myocardial blood flow reserve

Table 3. Clinical information available from PET/CT

APPLICATIONS BEYOND MYOCARDIAL PERFUSION IMAGING

The combination of perfusion and myocardial metabolism using ^{18}F-fluorodeoxyglucose (^{18}F-FDG) remains the gold standard for clinical assessment of myocardial viability and is the only imaging modality capable of directly identifying the presence and extent of hibernating myocardium.[15] ^{18}F-FDG is also clinically useful for the assessment of cardiac sarcoidosis with several advantages compared to cardiac MRI (CMR) for sarcoidosis assessment (***Table 4***).[16]

^{18}F-FDG PET versus CMR for cardiac sarcoidosis		
	^{18}F-FDG PET	CMR
Detection of fibrosis / scar	++	+++
Measurement of LVEF and wall motion	+++	+++
Able to distinguish scar from active inflammation	+++	+
Assess response to therapy	+++	+
Feasible with severe renal failure	+++	+
Feasible with all CIEDs	+++	–

CIED, cardiac implantable electronic device; CMR, cardiac MRI; LVEF, left ventricular ejection fraction.

Table 4. ^{18}F-FDG PET versus CMR for cardiac sarcoidosis

^{18}F-FDG is also useful for the assessment of infective endocarditis and cardiac implantable electronic device (CIED) infection.[17-20] It can be used not only to assess for the presence and extent of the cardiac infection but can also be useful in the assessment of extra-cardiac complications, such as septic emboli. ^{18}F-FDG also plays an important role in the evaluation of vasculitis and vascular graft infections. Lastly, several PET agents are being investigated for cardiac amyloid imaging, including ^{18}F-florbetapir, ^{18}F-florbetaben, ^{18}F-flutemetamol,[21] and ^{18}F-sodium fluoride.[22]

THE CLINICAL VALUE OF CARDIAC PET

The clinical value of a cardiac imaging test can be defined both by its quality and cost-effectiveness. Quality can be thought of as directly proportional to the clinical information provided by the imaging test and inversely proportional to the radiation exposure. Using this definition, PET MPI clearly demonstrates superior quality as there is abundant clinical information provided (***Table 3***) at a low radiation dose. Similarly, the cost effectiveness of a cardiac imaging study can be defined as being directly proportional to the quality of the study and inversely proportional to its cost, both direct and indirect. PET MPI has the potential to reduce overall healthcare costs by facilitating earlier hospital discharge and reducing the need for layered testing and unnecessary invasive coronary angiography.[23]

CONCLUSION

Cardiac PET has emerged as a powerful tool for evaluation of patients with coronary artery disease and other cardiac conditions. The use of cardiac PET is expected to grow with increased availability of PET cameras, enhanced software programs, and new PET perfusion tracers (e.g., ^{18}F-flurpiridaz). The ability of cardiac PET to measure MBF and MBFR provides a powerful tool for the clinical evaluation of patients with CAD and other cardiac conditions.

Writing Committee
Dennis A. Calnon, MD, MASNC – Lead Author
Daniel Juneau, MD
Linda Giering, PhD
A. Iain McGhie, MD

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NOTES

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