Myocardial Blood Flow Quantification Using Positron-Emission Tomography
– Analysis and Practice in the Clinical Setting –

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Myocardial perfusion imaging (MPI) has played an important role in the diagnosis and risk assessment of coronary artery disease (CAD) since the early 1970s. Positron emission tomography (PET) MPI has high diagnostic accuracy and prognostic value. PET MPI can also be used to quantitatively evaluate regional myocardial blood flow (MBF) through a mathematical model. PET MBF measurements can be used in evaluating early-stage atherosclerosis with endothelial dysfunction right through to diagnosing CAD. PET/computed tomography scanners are now found in many facilities across North America, Europe, and Asia, and PET MBF quantification is expected to move from strictly research to more clinical applications. Nuclear cardiology has been a leader in quantification approaches that can be applied to other new imaging modalities. Therefore, it would be valuable to understand the basic aspects of quantification approaches. This review will address the basic aspects of MBF quantification and the additional value of quantification approaches in the clinical setting. (Circ J 2013; 77: 1662–1671)

Key Words: Blood flow; Endothelium; Positron-emission tomography; Quantification

Coronary artery disease (CAD) continues to be a leading cause of death in both developed and developing countries, so there is a need for accurate and widely available noninvasive diagnostic testing to detect the early stages of atherosclerosis in high-risk patients.

The role of any diagnostic imaging test is to support the clinical decision-making process so as to improve symptoms and outcomes in patients with CAD. Techniques for evaluating myocardial perfusion need to both identify patients with CAD and predict their future cardiovascular events.

Positron-emission tomography (PET) represents an advanced nuclear imaging technology that uses molecular probes to understand the physiological CAD process. PET myocardial perfusion imaging (MPI) has been shown to have more accurate diagnostic value than single-photon emission computed tomography (SPECT) MPI and high incremental prognostic value in patients with CAD. The US Food and Drug Administration (FDA) approved rubidium-82 (82Rb) for clinical use in 1989 and 13N-ammonia in 2000. US Medicare reimbursement began in 1995 for 82Rb and in 2003 for 13N-ammonia.

In Japan, the Japanese Ministry of Health, Labor and Welfare (JMHLW) granted funding approval for 13N-ammonia perfusion PET for the diagnosis of CAD in April 2012. According to the Japanese Circulation Society guidelines and the ACC/AHA/ASNC guidelines, PET MPI is considered to be a Class 1 indicator for the diagnosis of CAD. Therefore, it is expected that PET MPI will have wide clinical use in the near future.

PET is also uniquely suited to quantifying myocardial blood flow (MBF) using myocardial tracer kinetics. Measurement of regional MBF allows for the assessment of coronary flow reserve (CFR) and the evaluation of the physiological significance of coronary lesions. These quantitative measurements are considered to be part of a more comprehensive approach to detecting CAD. Endothelial dysfunction is the earliest abnormality in the development of coronary atherosclerosis. PET MBF measurements using a sympathetic stress protocol can also be used to non-invasively evaluate coronary endothelial dysfunction. Following recent technical developments, an increase in the clinical application of MBF quantification can be expected.

This review will describe the clinical utility of PET MPI for assessing the functional severity of coronary stenosis and for diagnosing CAD and microcirculatory abnormalities, including coronary endothelial dysfunction. Understanding the basic aspects of MBF quantification using PET MPI will help cardiologists appreciate the rationale for it. With that thinking in mind, we have included a review of the basic aspects of MBF quantification.
MBF Quantification With PET

Basic Theory and Imaging Techniques of PET and PET/CT

Basic Aspects of PET and PET/CT
Positrons (positively charged electrons) are emitted from the nuclei of unstable isotopes during radioactive decay. Positrons are annihilated after colliding with electrons, resulting in 2 coincident high-energy photons of 511 keV, which yield high sensitivity and temporal resolution. Photon attenuation in tissue can be accurately corrected with PET or computed tomographic transmission imaging, thus allowing for measurement of absolute radiopharmaceutical concentration (nmol/cc or Bq/cc) within the living body.\(^{10,11}\)

Characteristics of PET Myocardial Perfusion Tracers
Commonly used PET blood flow tracers can be divided into (a) inert, freely diffusible tracers such as \(^{15}O\)-labeled water and (b) physiologically retained tracers such as \(^{13}N\)-ammonia, \(^{18}F\)-labeled tracers, and \(^{82}Rb\) (Table 1).\(^{2-4,11,15}\) Physiologically retained tracers can be used in the identification of relative myocardial flow distributions (relative perfusion imaging), similar to SPECT MPI, but have more benefit in the clinical setting than does diffusible \(^{15}O\)-labeled water\(^{5,16}\) (Figure 1). \(^{13}N\)-ammonia produces high-quality images but sometimes shows a mild defect in the lateral wall even in normal subjects (Figure 1).\(^{17}\) Caution should therefore be exercised when evaluating the lateral wall region using this tracer. In contrast, acquiring relative perfusion imaging using \(^{15}O\)-labeled water is difficult because of its rapid clearance from myocardium. With both types of tracers, quantitative analysis of MBF can be performed using tracer kinetic models.

One of the characteristics of PET flow tracers is their short physical half-life.\(^{4}\) Repeated PET studies can usually be performed after a time duration of 5 times the isotope half-life. Therefore, \(^{15}O\)-labeled water and \(^{82}Rb\) are especially suitable for repeated data acquisition with various stress protocols (Figure 2).\(^{18,19}\)

The availability of a particular PET flow tracer needs to be considered before it is selected for clinical use. Production of \(^{13}N\)-ammonia and \(^{15}O\)-labeled water requires an on-site cyclotron and therefore they are not broadly available. \(^{82}Rb\) is produced from a strontium-82 (\(^{82}Sr\)/\(^{82}Rb\) generator and is widely used in centers without immediate access to a cyclotron.\(^{20,21}\) Recently introduced \(^{18}F\)-labeled perfusion tracers have a relatively longer half-life (110 min), which means they could possibly be delivered from pharmaceutical companies to hospitals.

Figure 1. Imaging protocol of adenosine or adenosine triphosphate with \(^{13}N\)-ammonia PET/CT, \(^{15}O\)-labeled water PET/CT or \(^{82}Rb\) PET myocardial perfusion imaging. ATP, adenosine triphosphate; CT, computed tomography; PET, positron-emission tomography.
Figure 2. Normal stress/rest PET myocardial perfusion images. The attenuation correction contributes to good image quality with $^{13}$N-ammonia and $^{82}$Rubidium. In contrast, the diffusible tracer, $^{15}$O-labeled water, has limited image quality. PET, positron-emission tomography.

Figure 3. Net extraction by the myocardium as a function of myocardial blood flow with (A) PET flow tracers and (B) SPECT tracers or other imaging. PET, positron-emission tomography; SPECT, single-photon emission computed tomography; Tl, thallium.
**Table 1. Common PET MBF Tracers**

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Tracer production</th>
<th>Half-life</th>
<th>Extraction fraction (stress flow) (%)</th>
<th>Radiation dosage (£Sv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rb-82</td>
<td>Generator</td>
<td>76 s</td>
<td>40 at stress</td>
<td>1.92 (80 mCi)</td>
</tr>
<tr>
<td>O-15 water</td>
<td>On-site cyclotron</td>
<td>110 s</td>
<td>100</td>
<td>2.5 (60 mCi)</td>
</tr>
<tr>
<td>N-13 ammonia</td>
<td>On-site cyclotron</td>
<td>9.97 min</td>
<td>&gt;90</td>
<td>2.4 (30 mCi)</td>
</tr>
<tr>
<td>C-11 acetate</td>
<td>On-site cyclotron</td>
<td>20 min</td>
<td>57 at stress</td>
<td>2.59 (20 mCi)</td>
</tr>
<tr>
<td>F-18 labeled</td>
<td>Regional cyclotron (can be delivered)</td>
<td>109.8 min</td>
<td>&gt;90</td>
<td>7.4 (10 mCi)</td>
</tr>
</tbody>
</table>

*Radiation dose is based on the total dose of standard rest/stress perfusion studies. MBF, myocardial blood flow; PET, positron-emission tomography.

**Figure 4.** One-tissue compartment model. The fractional rate constants, K1 and K2 (L/min), describe the flux of radiotracer between arterial blood (Ca), and myocardial tissue (Cm).

\[
\frac{dCm(t)}{dt} = K1Ca(t) - K2Cm(t)
\]

15O-labeled water passes freely across cell membranes, so the tracer is distributed over the vascular and extravascular spaces. This partition coefficient for 15O-labeled water is stable over a wide range of flow rates (Figure 3). Therefore, 15O-labeled water flow rate is considered to be one of the standard measurements of MBF.

On the other hand, the extraction fraction of physiologically retained radiotracers is decreased in high blood flow, thereby producing an underestimation of MBF based on the measurement of tissue uptake. However, the extraction fraction of these tracers is still higher than that of other contrast-enhancement agents for CT or magnetic resonance imaging (MRI) (Figure 3). Additionally, these physiological properties are incorporated into the kinetic models for calculation of MBF. In addition, patients with CAD usually have hyperemic MBF of less than 3.0 ml·min⁻¹·g⁻¹, and retained tracers still preserve relatively good extraction within this range. Interestingly, 18F-labeled perfusion tracers have a high extraction fraction and are expected to produce accurate MBF measurements. Originally, 11C-acetate was used to estimate myocardial oxidative metabolism. The initial distribution of 11C-acetate reflects MBF and so this tracer could also be used to measure MBF quantification.

**Recent Approaches to Reducing Radiation Exposure Using PET/CT**

A patient’s level of exposure to radiation depends on the dose and the physical half-life of the radionuclide. As mentioned before, a short physical half-life is a characteristic of PET perfusion tracers and is also associated with lower radiation exposure compared with SPECT MPI radiotracers. As shown in Table 1, the total radiation dose with stress and rest PET perfusion images is usually less than 5 mSv.

The new generation of PET/CT scanners have a 3-dimensional (D) data acquisition mode. With 3D data acquisition, there is increased scanner sensitivity and potentially improved image quality. The dosage of injected radiotracers is also reduced. The radiotracer dose is usually half of that for 2D PET acquisition. State-of-the-art PET/CT scanners have highly sensitive detectors in the PET component, which use lutetium-yttrium oxyorthosilicate crystals. These technological developments also result in a lower dosage of radiotracer injections and reduced radiation exposure.

**PET Perfusion Image Acquisition for MBF Quantification**

Vasodilator pharmacological stress is usually employed because of the short half-life of the tracers (Figure 1). List-mode data acquisition and ECG gating can produce static uptake images for MPI, dynamic image sequences for MBF quantification, and gated images for left ventricular (LV) function.

**MBF Quantification Using Tracer Kinetics**

Quantitative measurement of MBF using tracer kinetics is a great advance in PET MPI, and other cardiac imaging modalities such as CT and cardiovascular MRI (CMR) have also now focused on MBF quantification. PET has played a leading role in the development of MBF quantification since the 1980s. Thus, an understanding of tracer kinetics would be of value in the development of MBF quantification measurements using other imaging modalities.

Absolute measurement of physiological or biochemical function is obtained using tracer kinetics. A parametric physical model is fit to the time-activity curves of the arterial blood input function, Ca(t) and myocardial response function Cm(t). Ca(t) is usually measured using a region of interest in the LV cavity, and Cm(t) is sampled in various regions of the myocardium (Figure 4). These parameters are used to estimate quantitative rate constants (Figure 4).

**Net Retention Model**

The net retention model is a very simple approach and can be used to calculate absolute MBF directly from short, dynamic sequential images. The net retention equals the measured radio tracer concentration at time ‘t’ divided by the integral of the blood input function curve to that time or an earlier time point. This approach was initially applied to 82Rb, but many groups have shifted from this approach to compartment models.

**Compartment Models**

Compartments represent tissue volumes, which include physical factors (arterial blood and intracellular fluid) or biochemical factors (tracer compound and labeled metabolite). A mathematical model is constructed with parameters such as flux of...
Confounding factors should be taken into account in clinical settings. This includes patients with anemia, diabetes mellitus, and severe obstructive pulmonary disease.

**Commercially Available MBF Quantification Software**

In the early stage of PET MBF quantification, each center used its own in-house program. Some of this software has been well validated. Of these programs, FlowQuant, MuncHeart, and PMOD are commercially available. Through a project called RUBY, the international community is currently aiming to standardize the software.

**Validation of MBF Quantification and Assessment of Repeatability**

When applying MBF quantification in the clinical setting, validation is important, and new tests must have good repeatability.

Bergmann et al reported that 15O-water MBF measurements using PET were highly correlated with direct measurements of MBF in an open-chest dog model and postmortem microsphere. In human studies, hyperemic MBF has been inversely associated with coronary luminal stenosis using either 15O-water, 15N-ammonia, or 82Rb. Therefore, PET MBF quantification is a well-validated approach based on these data.

15O-water, 15N-ammonia, and 82Rb have shown reliable reproducibility for both rest MBF and hyperemic MBF in normal control individuals. These data indicate that PET is a reliable technique for MBF measurements in clinical research.

**Clinical Protocols**

**Hyperemic MBF and CFR**

Hyperemic MBF represents microcirculatory vascular function involving both vascular smooth muscle and endothelial function. Vasodilator agents can induce maximal microvascular vasodilatation. CFR is the ratio of near-maximal MBF during pharmacologically induced hyperemia to MBF at rest. Thus, CFR represents functional coronary vascular function. PET-measured CFR accurately reflects regional MBF as measured by intracoronary Doppler flow guide wire. Normal CFR measured by PET using 15N-ammonia, 15O-water, or 82Rb is 3.0–5.0.

**Participant Preparation**

As previously mentioned, most PET MPI is performed under a vasodilator stress protocol. Preparation of subjects is the same as for vasodilator stress with standard SPECT MPI. Participants should be instructed to fast for at least 6 h and to abstain from caffeine-containing products for 24 h prior to pharmacological stress tests.

**Vasodilator Pharmacological Stress**

Adenosine, ATP, diprydamole, and regadenoson (selective A2A agonist) are the established methods for PET MPI. These vasodilator agents block transport of adenosine into the cells and/or increase extracellular levels of adenosine, which causes coronary vasodilation by interacting with the adenosine A2 receptors in the cell membrane.

This approach is simple and widely used in various clinical settings. However, reduced CFR is associated with both endothelial and smooth muscle cell dysfunction. Thus, strictly speaking, vasodilator stress alone cannot be used to detect endothelial dysfunction. As we will discuss later, additional sympathetic stress tests are required to detect coronary endothelial dysfunction.

**Clinical Utility of PET and PET/CT**

**Additional Clinical Value of PET MBF Measurements in CAD**

Although myocardial PET relative MPI has shown better diagnostic accuracy than SPECT MPI, PET MBF quantification is expected to have additional diagnostic value in the clinical setting. Uren et al reported that patients with myocardial infarction (MI) showed reduced CFR in remote segments in comparison with a control group. Parkash et al reported that in 3-vessel CAD, in comparison with quantification analysis, visual analysis underestimated the perfusion defect areas (Table 2). Yoshinaga et al applied a more sophisticated MBF quantification approach to regional analysis with 82Rb and also reported a reduction of hyperemic MBF in regions with coronary stenosis that appeared visually normal (Figure 5). The measurement of a relative perfusion defect...
MBF Quantification With PET

combined with CFR reduction (<2.0) greatly improves the diagnostic accuracy of significant coronary stenosis from 79% to 92%. Globally reduced CFR is also an independent predictor for 3-vessel CAD. Yoshinaga et al further compared the clinical value of MBF quantification using $^{15}$O-water PET with that for $^{99m}$Tc SPECT MPI. Segments with coronary stenosis without a perfusion abnormality observed with $^{99m}$Tc SPECT MPI had reduced CFR compared with that in remote segments (Figure 6). Those studies showed the additional diagnostic value of PET MBF quantification in indicating the functional significance of a coronary stenosis or CAD diagnosis.

MBF quantification has recently been applied to the risk assessment of CAD. Herzog et al first revealed the additional prognostic value of MBF quantification using $^{15}$N-ammonia PET. Importantly, even visually normal PET stress MPI and CFR <2.0 significantly correlated with increased major cardiac events. Similarly, $^{82}$Rb PET/CT with MBF quantification has shown incremental prognostic value over that of relative perfusion imaging.

Cardiac CT is very reliable in ruling out CAD. However, its positive predictive values are moderate. Hybrid PET/CT scanners can simultaneously evaluate coronary anatomy and quantitative MBF. Although PET MBF estimation can not distinguish between microvascular disease and epicardial stenosis, a combined PET and CT approach shows improved accuracy in detecting significant stenosis. Globally reduced CFR can be an indicator of high-risk anatomic disease.

Coronary Endothelial Function Measurements Using PET

Endothelial dysfunction is the earliest abnormality in the development of atherosclerosis and is also independently associated with future cardiac events. Coronary endothelial cells protect the coronary artery by providing a mechanical barrier and releasing bioactive factors.

Coronary angiography, ultrasound (flow mediated vasodilation (FMD)), biomarkers, and PET are established diagnostic tests. PET MBF measurements using a cold pressor test (CPT) have been applied in patients with coronary risk factors. PET can noninvasively evaluate coronary endothelial function, a significant advantage of PET among the available diagnostic tests. There are 2 possible significant indications for this test in the clinical or prevention setting. First, FMD has a relatively narrow range of vasodilator response, usually 5–10% in normal individuals. In contrast, PET endo-

Figure 5. Representative images from a 58-year-old man with 3-vessel coronary artery disease. The ATP stress and rest $^{82}$Rb images show moderate reversible ischemia in the lateral region and mild reversible ischemia in the mid- to distal anterior region in relative perfusion imaging. In quantitative analysis, hyperemic MBF was 1.91 ml · min$^{-1}$ · g$^{-1}$ in the LAD territory, 1.78 ml · min$^{-1}$ · g$^{-1}$ in RCA territory, and 1.26 ml · min$^{-1}$ · g$^{-1}$ in LCX territory. ATP, adenosine triphosphate; CFR, coronary flow reserve; LAD, left anterior descending; LCX, left circumflex; MBF, myocardial blood flow; RCA, right coronary artery (partly modified with permission from Yoshinaga et al).
A CPT aims to increase sympathetic outflow and consequently to increase myocardial oxygen consumption. These factors can increase CBF and induce shear stress to the vascular lumen. In healthy blood cells, endothelium releases EDRF such as nitric oxide in response to shear stress. An adrenergically mediated vasoconstrictor also has effects on vascular smooth muscle. In normal blood vessels, endothelium-dependent vasodilation is dominant. Thus, abnormal responses to the CPT are thought to reflect altered endothelial function.

The PET MBF response to CPT closely correlates that observed in quantitative coronary angiography. Thus, the CPT is suitable for PET study settings.

### PET CPT Protocol

PET data acquisition during CPT is performed following standard vasodilator stress. The protocol for CPT involves immersing the patient’s hand in 4°C ice water. The nociceptive sensation during CPT is time-dependent and reaches a maximal level after approximately 1 min of stimulation. This response usually reaches a plateau, and the heart rate response decreases after 2 min. Therefore, PET dynamic data acquisition should start at 60 s after immersion in ice water and continue for at least 2–4 min while the tracer is simultaneously administered.

### Parameters of MBF Response During CPT

Under the CPT, MBF increases by 30–65% of baseline in normal individuals. This difference makes distinguishing between populations with early-stage coronary atherosclerosis risk and normal populations easier with PET. Second, recent data suggest that therapeutic interventions for coronary endothelial function in the asymptomatic cardiovascular disease risk population prevent the progression of epicardial structural disease. Changes in coronary arterial function may be closely related to structural changes. PET/CT is a more complex test to perform than FMD, but the advantage of the former is that it can be used to detect early-stage structural changes in the coronary artery, which may be tied to coronary endothelial function.
endothelial dysfunction (ie, vasoconstriction).\textsuperscript{3,4,61,62}

The MBF response during CPT, measured as the percent increase in MBF during CPT (called CPT response\textsuperscript{59,63}), has been widely used.\textsuperscript{13}

One group suggested an abnormal cut-off value of MBF increase as $<$40%.\textsuperscript{57} Although the numbers of studies and subjects are limited, \textsuperscript{13}N-ammonia, \textsuperscript{82}Rb and \textsuperscript{15}O-water showed a similar percent increase of MBF during CPT.\textsuperscript{13,21,64}

**Clinical Applications of PET Endothelial Function Measurements**

**CAD**

A reduced MBF response to CPT using PET has been associated with the risk of developing cardiovascular events.\textsuperscript{63} However, this endothelial function measurement applies mainly to subjects with risk factors.

**Coronary Endothelial Dysfunction in Relation to Coronary Risk Factors and Evaluation of Therapies**

Several coronary risk factors associated with atherosclerosis may cause a reduction in the MBF response during sympathetic stress in normal coronary arteries during coronary artery angiography or CT. As mentioned earlier, in the clinical research setting PET has been used to investigate the relationship between coronary endothelial dysfunction and such risk factors for CAD as hypercholesterolemia, diabetes, smoking, and hypertension.\textsuperscript{11,17,18}

**Diabetes Mellitus**

Alteration of coronary endothelial dysfunction has been demonstrated in patients with either type 1 or type 2 diabetes.\textsuperscript{65} The severity of endothelial dysfunction depends on glycemic control. Prior et al reported that the magnitude of endothelial dysfunction is associated with the severity of insulin resistance.\textsuperscript{66}

Quinones et al reported that 3 months of insulin-sensitizer treatment increased the percent change in MBF during CPT in insulin-resistant subjects.\textsuperscript{67} A 1-year glucose-lowering therapy improved coronary endothelial function in patients with type 2 diabetes. Importantly, this improvement was associated with slowed progression of coronary artery calcification.\textsuperscript{56}

**Hypertension and Antihypertensive Therapy**

Arterial hypertension often causes reduced CFR and coronary endothelial dysfunction.\textsuperscript{4,11} Angiotensin II receptor blockers (ARB) reduce vascular inflammation and oxidative stress by blocking the action of angiotensin II. Three months of olmesartan treatment significantly increased the MBF response during CPT compared with the response when calcium-channel blockers were used. This effect might be associated with an antioxidant property of ARB.\textsuperscript{68}

**Cigarette Smoking**

Cigarette smoke may alter vascular endothelium via oxidative stress. Campisi et al demonstrated an altered response of MBF during a CPT despite normal CFR in long-term smokers.\textsuperscript{58} Furthermore, even in young smokers, coronary endothelial function may already be blunted.\textsuperscript{69}

Relatively short-term smoking cessation restores coronary endothelial function in young smokers. In contrast, these favorable effects do not appear in middle-aged smokers.\textsuperscript{70} These findings suggest that endothelial damage is associated with the duration of smoking and that a longer time is required to recover from the effects of long-term smoking.

**New PET Endothelial Function Measurements Approach**

In most previous studies, PET MBF measurements during CPT have been performed using either \textsuperscript{15}O-labeled water or \textsuperscript{13}N-ammonia, which require immediate access to an on-site cyclotron. \textsuperscript{82}Rb is a PET perfusion tracer produced from an \textsuperscript{82}Sr/\textsuperscript{82}Rb generator and is widely used in PET centers without immediate access to a cyclotron.\textsuperscript{8,10,12} Therefore, \textsuperscript{82}Rb perfusion studies could be performed in larger populations.

Yoshinaga et al first evaluated the diagnostic value of \textsuperscript{82}Rb for coronary endothelial function measurements. Smokers showed reduced MBF response during the CPT using \textsuperscript{82}Rb, which was similar to the MBF response observed using \textsuperscript{15}O-labeled water as a standard measurement.\textsuperscript{21} That study suggests that \textsuperscript{82}Rb PET is applicable for risk assessments or evaluation of risk factor modification in subjects with coronary risk factors. This approach was confirmed by another group.\textsuperscript{84} Given the easy access to \textsuperscript{82}Rb, this approach is now expected to be widely applied in the clinical setting.

**On the Way to Widespread Clinical Use of PET/CT MPI**

The next step for PET MPI should be widespread clinical use. There are over 1,000 PET (PET/CT) scanners in North America and as of 2007 there were 212 PET institutions in Japan.\textsuperscript{16,73} In recent years, MBF quantification programs have become available commercially,\textsuperscript{86} increasing access to PET/CT MBF quantification around the world. Following the example of the USA, in 2012 the Japanese MHLW approved funding for \textsuperscript{13}N-ammonia perfusion PET. This approval might be the key to establishing wide clinical usage of PET MPI. To facilitate broad clinical application, there should be a standardized data acquisition protocol and easily accessible MBF quantification programs. There is great potential for the wide clinical use of generator-produced \textsuperscript{82}Rb, but in order to obtain MHLW approval for such use, clinical trials would have to be performed in Japan.

**Summary and Conclusions**

The noninvasive aspects and coronary specificity of MBF measurements using PET/CT can provide information on physiological coronary vasomotor function beyond that available through a standard visual or anatomical assessment alone. This quantitative approach provides diagnostic information beyond anatomical data. Recent hardware and software developments have made it possible to apply PET MBF quantification to the clinical setting. There are still some technical challenges for PET MBF quantification. Efforts to overcome these challenges and continued development of this approach are ongoing.

**Acknowledgments**

Y.T. is supported by the National Institute of Radiological Sciences Human Resource Development Program (Chiba, Japan). We thank Kumi Aijiki, MLT for her administrative support.

**Disclosures**

The authors’ work presented in this article was supported in part by grants from the Ministry of Education, Science and Culture of Japan (Category B, No. 23390294, Category Development, No. 24659550). K.Y. is supported by the Imura Clinical Research Award (Adult Vascular Disease Research Foundation).

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